**Communication from Public**

| | |
|---|---|
| **Name:** | |
| **Date Submitted:** | 05/30/2019 04:29 PM |
| **Council File No:** | 18-1104 |
| **Comments for Public Posting:** | You can find the following article at: https://calmatters.org/articles/commentary/teenage-protections/?fbclid=IwAR3-XLSWzpsH3vs6sKorgFkeqptnBYoHCtAElTPTDWJQzmkt-K_L0Ny-YVg |

# We now have results for key laws advocates promised would 'protect' teenagers. They don't.



Guest Commentary

Guest Commentary: Find out more about submitting a commentary.

**By Mike Males**, *Special to CALmatters*

In 2016, fewer than 6% of California adolescents reported trying cigarettes, down from 10% in 2015, 13% in 2009, 15% in 2007, and 19% in 2003.

Why on earth did legislators feel the need to intervene in such a hugely positive youth trend?

For no apparent reason, they did. In 2016, California raised its "smoking age" from 18 to 21, with severe penalties for tobacco retailers and others who provide tobacco or e-cigarettes to persons under 21.

"Now we can know that our youth are less likely to be addicted to this horrible drug of tobacco," said bill sponsor, then Sen. Ed Hernandez, a Democrat from West Covina. A poorly-designed Institute of Medicine report predicted that raising the tobacco age to 21 would reduce teens' trying cigarettes by 12%.

Did that happen? No.

UCLA's Center for Health Policy Research's annual survey of 1,600 adolescents found 2017, the first full year the 21 smoking age was in effect, was the first since the survey began 15 years ago that teenagers' cigarette use failed to decline.

The biggest effect of the age-21 law may be to jeopardize the employment of adult teenagers in hundreds of thousands of jobs across the state that handle tobacco products, penalizing a young age group already suffering 30% unemployment and huge student debts.

The failure of the law to reduce smoking and teens' actual increase in "vaping" in 2017 in its first year, when such laws typically have their biggest effect, is troubling – if anyone cares.

After all, legislative and safety officials show no interest in repealing their 1998 teen driving law, despite disastrous results.

As with teen smoking prior to the age-21 law, teen driving fatalities had been falling sharply—by 50% from 1987 to 1997 to record low levels—under California's previous driving law.

Then, legislators decided to mess things up.

In 1998, lawmakers enacted a new "graduated driver license" law imposing costly, cumbersome bans and requirements on new drivers ages 16 and 17. Experts predicted big declines in deaths.

Again, experts were wrong. The graduated-licensing law quickly proved a calamity. Teen driving deaths halted their previous decline in 1998 and began a five-year increase.

The California Department of Transportation reported the law had no effect on younger teenagers and accompanied increased traffic deaths among older teenagers.

My 2005 Journal of Safety Research and follow-up studies found California's teen-driving law was statistically associated with increased young-driver fatalities that persisted over time. A 2007 Journal of the American Medical Association paper, the best and largest national study, found teen driving laws associated with more deaths among older teens.

Long-term research associated California's graduated driver licensing law with around 60 more traffic deaths per year among young people than occurred under the old licensing system.

In 2008, I presented the law's bad results to the California Senate. None of the law's advocates, including the California Highway Patrol, the California Automobile Association, and legislators, challenged my findings. They just didn't seem to care.

Another pointless intervention was restricting persons age 18-20 from obtaining credit cards. Legislative hearings rang with claims of beer-happy kids going wild with plastic.

In fact, "credit cards are the least of millennials' debt burden," Credit Karma reports. The biggest young-age debt category by far: education loans, which have skyrocketed due to the failure of legislators themselves to fund higher education.

If lawmakers, agencies, and experts want to improve youthful safety, repeal the teen driving, smoking, and credit card measures, cut out worthless juvenile curfews, revisit the state's antiquated drinking age of 21, and start dismantling measures that arbitrarily segregate and punish youths.

Despite high levels of youth poverty, disadvantage, and debt (the real correlates of teenagers' ills), today's young people have improved behaviors dramatically on their own across a variety of fronts. They deserve more freedoms, not repressions.

---

*Mike Males is senior researcher for the Center on Juvenile and Criminal Justice, [email protected] He wrote this commentary for CALmatters. Read his past commentaries here, here, here, here, and here.*

## Communication from Public

**Name:**
**Date Submitted:** 05/30/2019 04:31 PM
**Council File No:** 18-1104
**Comments for Public Posting:** You can find the original article at : https://californiaglobe.com/fr/the-california-crusade-against-tobacco-flavors-from-foolish-to-dangerous/

CALIFORNIA GLOBE



# The California Crusade Against Tobacco Flavors: From Foolish to Dangerous

*Ban on harm reduction products leaves only the most toxic options*

By Dr. Brad Rodu, May 3, 2019 6:31 am

HIGHLIGHT OPINION

The FDA promotes a myth that teen 'vaping epidemic' is caused by unscrupulous manufacturers and retailers.

"Crusades typically start out by being admirable, proceed to being foolish, and end by being dangerous." Russell Baker used these words in a 1994 *New York Times* column describing the anti-tobacco crusade, noting that the holy war was entering the last stage. Now, 25 years later, California legislators are fighting their own crusade—against the so-called teen vaping "epidemic"—with a proposed ban on flavored tobacco products.

First, let's examine the "epidemic." Authorities generously define "current use" of any drug by children as at least once in the past month. The FDA, using this definition in a national survey, reported that vaping among American high school students increased substantially in 2018. The FDA was only telling part of the story; about half of those kids had vaped five or fewer days, the equivalent of trying products at a party. And most frequent e-cigarette users are not virgins with respect to cigarette smoking; most of them have smoked in the past.

Drug use by underage children is a serious matter. That makes it entirely baffling that California legislators ignore higher rates of alcohol and marijuana use among high schoolers, facts that have been known for decades. These behaviors have nothing to do with flavors, but instead demonstrate that kids are attracted to adult behaviors and products.

The FDA promotes the myth that a teen vaping epidemic is caused by unscrupulous manufacturers and retailers. This isn't true, especially in California, where the violation rate in FDA inspections was only 4% in 2018, one of the lowest in the country (here and here).

Since retailers aren't the problem in California, a ban on flavored tobacco products isn't the solution. This is harassment without reason. Even advocates of alcohol prohibition 100 years ago didn't try to ban flavors.

A flavor ban is supposed to stop kids from using nicotine, but is that a worthwhile objective? Nicotine, while addictive, is not the cause of any diseases associated with smoking. It is as safe to consume as caffeine, another addictive drug used daily by millions of adults and teens.

Because nicotine is so safe, prohibitionists fabricate hazards. One frequent claim is that nicotine can harm teenage brains. That may be a legitimate argument – for laboratory mice. If it was true for humans, then 40 million current smokers – and even more former smokers – who started as teens and smoked for decades would have demonstrable brain damage. There is no scientific evidence of such injury, nor to support the claim of youth brain risk. If California legislators want to protect children's brains, they should ban football, as there is unequivocal evidence linking concussion-producing sports activities to chronic traumatic encephalopathy (here, for example).

A flavor ban will not affect vapers who make their own vaping liquids. This segment of the market is already large and growing; a few examples can be found here, here and here. A ban might cause the current retail market to fracture in two: one segment selling concentrated, unflavored nicotine liquids, and another selling flavors. A high-tax jurisdiction like Chicago, where a prohibitively high per-milliliter tax is imposed on nicotine liquids, demonstrates what happens when the market is bifurcated.  Vape shops there sell 30 ml bottles of zero-nicotine e-liquids (no tax) and small concentrated bottles of high-strength nicotine that are taxed. Flavor bans will simply encourage consumers to purchase flavorless e-liquids, and then buy flavoring that is widely available in grocery stores and online, such as here and here.

## Unintended Consequences

A flavor ban would create unintended consequences. Flavors would no longer be supplied by legitimate companies. Instead, do-it-yourselfers would be adding flavors with unknown chemistry to concentrated nicotine solutions. It is worth noting that the only known death attributable to vapor products in the U.S. resulted from a young child accidentally ingesting pure nicotine.

Politicians routinely ignore another basic economic fact: bans drive black markets. Economists and legal scholars use the terms “bootleggers” (black market retailers) and “Baptists” (legislators and other misguided do-gooders), calling them “unlikely allies from the tobacco wars [who] try to fight off a game-changer [e-cigarettes].”

Two years ago, California was already the sixth biggest cigarette black-market state. Legislators should not create a bootlegger paradise for flavored tobacco, when they haven’t even solved the bootleg marijuana problem. The legislature legalized cannabis in 2016, but retained high taxes; the black market is now worth $3.7 billion, four times the legal market. The same rush to stigmatize vaping will doubtlessly create a black market in this category, as well.

The California crusade to ban flavors isn’t just foolish, it’s dangerous. With the exception of menthol, the ban will have the least impact on sales of cigarettes, the deadliest tobacco products. But it will remove from retail shelves many more smoke-free products – including e-cigarette liquids, dip, chew and snus. These products are vastly less hazardous than cigarettes. Imagine if alcohol opponents had only banned flavors during Prohibition. Beer, wine and other flavored spirits would have been eliminated, leaving only pure alcohol on retail shelves. That policy would have been an abject failure, as would any similar ban on flavored tobacco products.

About    Latest Posts

### Dr. Brad Rodu

For over twenty years, Dr. Brad Rodu has studied the science behind tobacco harm-reduction (THR) strategies. Dr. Rodu's research in comparative epidemiology established the scientific foundation for tobacco harm-reduction. Dr. Rodu earned his D.D.S. at Ohio State University and completed a residency in oral pathology at Emory University in Atlanta. He was the recipient of NCI and ACS fellowships during his tenure at the University of Alabama at Birmingham. In 2003, he served as an expert witness at a Congressional hearing on tobacco harm reduction, and has presented at numerous international forums, including one convened in London at the British Houses of Parliament. Learn more at his website Tobacco Truth .

**Spread the news:**

Tagged FDA, flavored tobacco products, Tobacco Flavors, vaping

## RELATED ARTICLES

# Communication from Public

| | |
|---|---|
| **Name:** | Annie Tegen, MPH, Tobacco-Free Kids |
| **Date Submitted:** | 07/11/2019 01:47 PM |
| **Council File No:** | 18-1104 |
| **Comments for Public Posting:** | The Campaign for Tobacco-Free Kids is pleased to submit these written materials in support of efforts to reduce tobacco use, particularly among youth. The Campaign for Tobacco-Free Kids is the nation’s largest non-profit, non-governmental advocacy organization solely devoted to reducing tobacco use and its deadly toll by advocating for public policies that prevent kids from using tobacco, help smokers quit and protect everyone from secondhand smoke. |

**Submission of Campaign for Tobacco-Free Kids**

**In Support of Banning the Sale of Flavored Tobacco Products, Including Menthol Cigarettes**

**Los Angeles, CA**

## Table of Contents

**Campaign for Tobacco-Free Kids (CTFK) Evidence Summary** ........ 1
**Key Excerpts from FDA Reports on Menthol Cigarettes** ........ 14
**Response to JUUL Cessation Studies** ........ 17
**CTFK Flavored Tobacco Products Fact Sheet** ........ 21
**CTFK Menthol Cigarettes Fact Sheet** ........ 31
**CTFK Menthol Cigarettes Marketing Fact Sheet** ........ 39

The Campaign for Tobacco-Free Kids is pleased to submit these written materials in support of your efforts to reduce tobacco use, particularly among youth. The Campaign for Tobacco-Free Kids is the nation's largest non-profit, non-governmental advocacy organization solely devoted to reducing tobacco use and its deadly toll by advocating for public policies that prevent kids from using tobacco, help smokers quit and protect everyone from secondhand smoke. While we are based in DC, we play an active role in flavor and menthol campaigns in California.

First, we would like to commend Los Angeles for being a national leader in its commitment to reducing the death and disease from tobacco use. It is encouraging to see that the city continues to take thoughtful, evidenced-based steps to reduce the number of kids who start using tobacco and help tobacco users quit. While your city has made great strides in reducing tobacco use, tobacco use remains the number one preventable cause of premature death and disease in Los Angeles and the nation.

Prohibiting the sale of flavored tobacco products, including menthol cigarettes, is a critical step that will help protect children from the unrelenting efforts of the tobacco industry to hook them to a deadly addiction. Flavored tobacco products are designed to alter the taste and reduce the harshness of tobacco products so they are more appealing and easy for beginners, who are almost always kids. These products are pervasive and are marketed and sold in a variety of kid-friendly flavors. With their colorful packaging and sweet flavors, flavored tobacco products are often hard to distinguish from the candy displays near which they are frequently placed in retail outlets.

Most insidious among these flavors is menthol, which delivers a pleasant minty taste and imparts a cooling and soothing sensation. These characteristics successfully mask the harshness of tobacco, making it easier for beginner smokers and kids to tolerate smoking.

In prohibiting the sale of flavored tobacco products, Los Angeles would join over 200 localities nationwide. In California alone, at least 40 localities have restricted the sale of flavored tobacco products, and more than half of these—including San Francisco and Sacramento—have enacted complete bans on flavored products, including menthol cigarettes.

**E-Cigarette Use by Youth is Skyrocketing**

We are at a critical juncture in our nation's public health history. After making tremendous progress in reducing youth tobacco use over the past several decades, e-cigarettes—JUUL in particular—are threatening to undermine declines in overall youth tobacco use.

Two recent national surveys show that youth use of electronic cigarettes has skyrocketed in the United States, reaching what the FDA Commissioner and the U.S. Surgeon General have called "epidemic" levels.

- The 2018 National Youth Tobacco Survey (NYTS) showed that between 2017 and 2018, current e-cigarette use increased by 78 percent among high school students and by 48 percent among middle school students. In 2018, more than 3.6 million middle and high school students were e-cigarette users – an alarming increase of 1.5 million students in just one year.[1] Similarly, the 2018 Monitoring the Future survey found that youth vaping of nicotine nearly doubled in 2018 among 12th and 10th graders – *the single largest increase in youth use of any substance in the survey's 43-year history.*[2]

- The increase in e-cigarette use has driven a 38 percent increase in use of any tobacco product among high school students (from 19.6 percent in 2017 to 27.1 percent in 2018).[3]

- While California has made tremendous progress in bringing the high school smoking rate to a historic low of 2%, five times more students—10.9%—are using e-cigarettes.[4] In Los Angeles, 36% of high school students have tried e-cigarettes.[5]

According to the CDC, “The rise in e-cigarette use during 2017-2018 is likely because of the recent popularity of e-cigarettes shaped like a USB flash drive, such as JUUL; these products can be used discreetly, have a high nicotine content, and come in flavors that appeal to youths.”[6] A study from Truth Initiative found that a quarter of youth and young adult JUUL users don’t refer to JUUL use as “e-cigarette use” or “vaping,” but rather as “JUULing.”[7] Therefore, it is likely that existing surveys still may not be capturing the full spectrum of youth e-cigarette use.

**Flavored E-Cigarettes Have Fueled the Popularity of These Products Among Kids**

E-cigarettes did not become popular with kids by accident. E-cigarette makers have introduced products with thousands of flavors that appeal to young people and engaged in the kind of marketing that mirrors what the cigarette industry did for decades. The 2016 Surgeon General Report on e-cigarettes concluded that, **“E-cigarettes are marketed by promoting flavors and using a wide variety of media channels and approaches that have been used in the past for marketing conventional tobacco products to youth and young adults.”**[8]


In recent years, there has been an explosion of sweet-flavored e-cigarettes. As of 2017, there were more than 15,500 unique e-cigarette flavors available online, including many kid-friendly flavors like gummy bear, cotton candy, and peanut butter cup.[9] Research shows that flavored products are not only popular among youth, but may play a role in initiation and uptake of tobacco products.

- According to the FDA’s Population Assessment of Tobacco and Health (PATH) study, 97% of current youth e-cigarette users have used a flavored e-cigarette in the past month and 70.3% say they use e-cigarettes “because they come in flavors I like.”[10]

- Another national study found that current use of menthol or mint flavored e-cigarettes among high school e-cigarette users also increased from 42.3 percent in 2017 to 51.2 percent in 2018.[11]

- In California, over 85% of youth e-cigarette users use flavored e-cigarettes.[12]

The use of flavors in e-cigarette products is of even greater concern because e-cigarettes are the subject of extensive advertising campaigns, and there is evidence that young people are exposed to significant amounts of e-cigarette advertising. By mimicking the tobacco industry's strategies, including celebrity endorsements, slick TV and magazine advertisements, and sports and music sponsorships, e-cigarette advertising has effectively reached youth and young adults. The 2016 NYTS found that 78.2 percent of middle and high school students—20.5 million youth—had been exposed to e-cigarette advertisements from at least one source, an increase from 68.9 percent in 2014.[13]

When JUUL was first launched in 2015, the company used colorful, eye-catching designs and youth-oriented imagery and themes, such as young people dancing and using JUUL. JUUL's original marketing campaign included billboards, YouTube videos, advertising in Vice Magazine, launch parties and a sampling tour. Posts on social media platforms like Twitter and Instagram also fueled JUUL's popularity among youth.[14]



**Youth E-Cigarette Users Struggle with Nicotine Addiction**

The number of youth now using e-cigarettes is alarming and raises serious concerns that e-cigarettes could be an entryway to nicotine addiction.  Though there is insufficient research on the long-term effects of using e-cigarettes in general, the use of such products raises concerns because they contain nicotine. Nicotine is a highly addictive drug and young people are especially vulnerable to nicotine addiction. There is mounting evidence that large numbers of youth are not just experimenting, they are becoming addicted. The NYTS found that nearly 28 percent of current high school e-cigarette users and 16 percent of middle school e-cigarette users – more than 900,000 middle and high school students – used the products on at least 20 days in the past month.[15]

Nicotine can have lasting damaging effects on adolescent brain development. The brain continues to develop through the early to mid-twenties. According to the Surgeon General, "because the adolescent brain is still developing, nicotine use during this critical period can disrupt the formation of brain circuits that control attention, learning, and susceptibility to addiction."[16] Because of these risks, the Surgeon General found that, "The use of products containing nicotine in any form among youth, including in e-cigarettes, is unsafe."[17]

In 2015, JUUL Labs, maker of the most popular e-cigarette, introduced JUULpods which all contained flavorings and 0.7mL e-liquid with 5% nicotine by weight, which they claim to be the equivalent amount of nicotine as a pack of cigarettes, or 200 puffs. The advertised 5% nicotine level by weight is the equivalent of 5.9% by volume, making JUUL three or more times as powerful as most e-cigarettes on the market at the time.[18] Since JUUL's introduction to the marketplace, JUUL's competitors, seeking to emulate the company's success, have flooded the U.S. market with similar pod-based e-cigarettes that have nicotine levels even higher than 5%, resulting in what some researchers have referred to as a "nicotine arms race."[19] JUUL and other high nicotine pod devices use nicotine salts rather than free-base nicotine and as a result, these products deliver extremely potent doses of nicotine and allow for rapid nicotine absorption.[20] According to a 2018 Surgeon General advisory on e-cigarette use among youth, nicotine salts allow users to inhale high levels of nicotine more easily and with less irritation than e-cigarettes that use free-base nicotine. As a result, it could be easier for young people to initiate the use of nicotine with these products.[21] Experimenting with a product that contains high concentrations of nicotine, like JUUL, can quickly result in dependence.[22] One study estimated that youth could meet the threshold for nicotine addiction by consuming just one quarter of a JUULpod per day.[23]

These statistics are confirmed by parents, teachers, and pediatricians across the country. E-cigarette use, especially JUUL, has permeated schools and the daily life of hundreds of thousands of youth. It is clear that large numbers of teen e-cigarette users are struggling with nicotine addiction and withdrawal. Last year, the *San Francisco Chronicle* profiled a California teen addicted to JUUL, who said he used the device dozens of times a day and that, "He says he wants to quit. But when he goes without a hit for too long, he gets a headache and body aches. He gets irritable."[24] He is not alone. The problem is so bad that FDA convened a public hearing to gather input on how to help youth addicted to the nicotine in e-cigarettes. No one is quite sure how to help these youth quit. Banning the sale of flavored e-cigarettes will prevent teens in Los Angeles from ever getting hooked.

**Youth E-Cigarette Users Are At Increased Risk of Smoking Cigarettes**

Evidence continues to build that for young people, using e-cigarettes increases the likelihood of smoking cigarettes.

- In 2016, the Surgeon General concluded that while more research is needed, evidence from several longitudinal studies suggests that e-cigarette use is "strongly associated" with the use of other tobacco products among youth and young adults, including conventional cigarettes.[25]

- Last year, the National Academies of Science, Engineering & Medicine (NASEM) released a comprehensive report finding substantial evidence that e-cigarette use increases risk of ever using cigarettes among youth and young adults.[26]

- From 2013 to 2016, youth (ages 12-15) e-cigarette use was associated with more than four times the odds of trying cigarettes and nearly three times the odds of current cigarette use. This translates to over 43,000 current youth cigarette smokers who might not have become smokers without e-cigarettes.[27]

- The risk of progressing to smoking regular cigarettes is not just for youth who were already at risk for smoking. In fact, several studies find that the link between e-cigarette use and smoking initiation is stronger for those who had *lower* risk factors for smoking at baseline.[28]

**Limiting Sale of Flavored E-Cigarettes to Adult-Only Retailers is Insufficient to Curb the Youth Epidemic**

California took an important step in reducing youth access to tobacco products by raising the age of sale to 21. However, raising the age of sale is not enough on its own to reduce youth access as evidenced by the persistent high rates of e-cigarette use among California teens. Likewise, limiting sales of flavored tobacco products to certain types of stores is insufficient. There is no evidence that "adult-only tobacco retailers" are more effective at preventing sales to minors. In fact, a recent study found that vape and tobacco shops, many of which purport to be adult-only facilities, have the highest rate of sales to minors violations in California. Compliance checks in retailers across California found sales to minors violations in 19.1% of retailers; violations were found in 34.9% of tobacco and vape shops.

Nationally, more than 60% of 10th grade students say it is easy to get vaping devices and e-liquids.[29] According to the 2018 National Youth Tobacco Survey (NYTS), 14.8% of middle and high school e-cigarette users under 18 report obtaining e-cigarettes from a vape shop in the past month and 8.4% from a gas station or convenience store.[30] Prohibiting the sale of the tobacco products that are most popular among youth—flavored tobacco products—in *all* retailers is a critical step to reducing youth access and use of tobacco.

Moreover, only 0.8% of California adults over age 30 use flavored e-cigarettes.[31] That a fraction of these 0.8% might succeed in quitting smoking using flavored e-cigarettes is not sufficient justification to allow these products to continue to fuel an epidemic of use among California's youth. This is especially true given the limited evidence that e-cigarettes are an effective cessation tool. The U.S. Preventive Services Task Force, which makes recommendations about the effectiveness of specific preventive care services after a thorough assessment of the science, concluded that "the current evidence is insufficient to recommend electronic nicotine delivery systems for tobacco cessation..."[32] According to researchers from the CDC, "There is currently no conclusive scientific evidence that e-cigarettes promote long-term cessation, and e-cigarettes are not included as a recommended smoking cessation method by the U.S. Public Health Service."[33]

Any potential benefit of flavors to adult smokers must be weighed against the role that these flavors play in the current epidemic of e-cigarette use among youth.

**Menthol Cigarettes Increase Youth Tobacco Use and Use Among African-Americans**

No single product contributes more to the death and disease caused by tobacco use than menthol cigarettes. The scientific evidence leaves no doubt that menthol cigarettes increase the number of people, particularly kids, and especially African-American kids, who try the product, become addicted and die a premature death as a result.

As we note, the tobacco industry has targeted the African-American community for decades with its marketing. The net result has contributed to African-Americans suffering unfairly and disproportionately from tobacco related diseases.

Menthol cigarettes pose a tremendous public health threat. A 2013 Food and Drug Administration (FDA) report on the health impact of menthol cigarettes determined that menthol cigarettes lead to increased smoking initiation among youth and young adults, greater addiction and decreased success in quitting smoking.[34] Further, FDA's Tobacco Products Scientific Advisory Committee[1] concluded, "Removal of menthol cigarettes from the marketplace would benefit public health in the United States."[35] They projected that by 2020, about 17,000 premature deaths will be attributable to menthol cigarettes and about 2.3 million people will have started smoking because of menthol cigarettes.[36]

Menthol is a chemical compound that cools and numbs the throat, reducing the harshness of cigarette smoke, making menthol cigarettes more appealing to youth who are initiating tobacco use.[37] Tobacco companies have long known that menthol cigarettes reduce the harshness of their products and make them easier to use by new users, almost all of whom are under age 18. [38] FDA's Tobacco Products Scientific Advisory Committee concluded that menthol cigarettes increase the number of children who experiment with cigarettes and the number of children who become regular smokers, increasing overall youth smoking. Further, they found that people who initiate smoking using menthol cigarettes are more likely to become addicted and become long-term daily smokers.[39]

Just like other flavored tobacco products, youth smokers are more likely to use menthol cigarettes than any other age group. Half (50.1%) of youth who have ever tried smoking initiated with menthol flavored cigarettes.[40] Over half (54 percent) of current youth smokers ages 12-17 continue to use menthol cigarettes, compared to less than one-third of smokers ages 35 and older.[41] Prevalence of menthol use is even higher among African American youth: seven out of ten African-American youth smokers smoke menthol cigarettes.[42]

**Menthol Cigarettes Have a Devastating Impact on the Health of African Americans and Are a Major Cause of Tobacco-Related Health Disparities**

Nationally, sales of menthol cigarettes increased from 2011 to 2015, at a time when overall cigarette sales have been gradually decreasing.[43] Data from the Federal Trade Commission (FTC) show that in 2017, menthol cigarettes comprised 36 percent of the U.S. market, the highest proportion on record since FTC began collecting this data in 1963.[44] The continued availability of menthol cigarettes threatens the progress we have made in reducing adult smoking, particularly among African Americans. Prevalence of menthol use is highest among African Americans - 85 percent of all African-American smokers smoke menthol cigarettes, compared to 29 percent of Whites.[45]

Both TPSAC's and FDA's own scientific analyses conclude that menthol cigarettes are associated with increased nicotine dependence and reduced success in smoking cessation.[46] The impact is greatest for African Americans, who predominantly smoke menthol cigarettes. African Americans generally have higher levels of nicotine dependence as a consequence of their preference for mentholated cigarettes.[47] While research shows that African American smokers are highly motivated to quit smoking and are more likely than White smokers to have made a quit attempt and used counseling services in the previous year, they are less likely than White smokers to successfully quit smoking.[48] Data from the 2015 National Health Interview Survey show that, among smokers who made a quit attempt in the past year, only 4.9 percent of African Americans remained abstinent after 6 months, compared to 7.1 percent of Whites.[49]

Smoking kills 45,000 African American each year. [50] Lung cancer is the second most common cancer in both African-American men and women, but it kills more African Americans than any other type of cancer.[51] While the gap has been narrowing, from 2011-2016 the average incidence rate of lung and

[1] TPSAC is a group of scientific experts charged with advising the Commissioner of Food and Drugs on safety, dependence, and health issues relating to tobacco. See https://www.fda.gov/advisoryCommittees/CommitteesMeetingMaterials/tobaccoproductsScientificAdvisoryCommittee/default.htm for more details.

bronchial cancers was still 15 percent higher in African-American men compared to white men and the average death rate was 18 percent higher in African-American men compared to white men.[52] If current smoking rates persist, an estimated 1.6 million black Americans alive today under the age of 18 will become regular smokers, and about 500,000 will die prematurely from a tobacco-related disease.[53] In 2011, TPSAC estimated that by 2020, 4,700 excess deaths in the African American community will be attributable to menthol in cigarettes, and over 460,000 African Americans will have started smoking because of menthol in cigarettes. [54]

**The Tobacco Industry Targets African Americans and Youth with Menthol Cigarette Marketing**

It is no “accident” that African Americans and youth smoke menthol at higher rates than other demographic groups. It is a direct result of a decades-long marketing campaign by the tobacco industry. The tobacco industry’s “investment” in the African-American community has had a devastating impact.

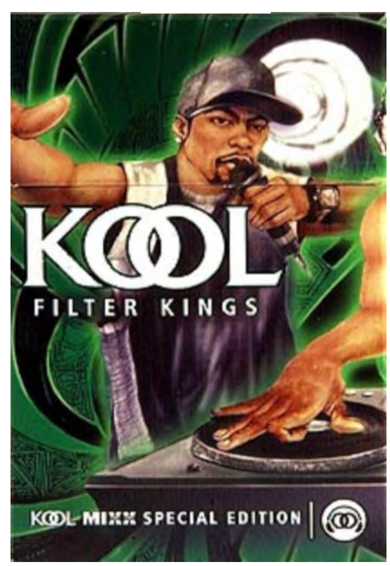
Decades of research and the tobacco industry’s internal documents demonstrate that the industry employed campaigns and strategies to aggressively target African Americans. Dating back to the 1950s, the tobacco industry has targeted these communities with marketing for menthol cigarettes through sponsorship of community and music events, free sampling, targeted magazine advertising, youthful imagery, and marketing in the retail environment. Many of these efforts targeted African American neighborhoods right here in Los Angeles, including the Kool Inner City Music Program, the Newport Pleasure Van, which distributed free cigarettes, and the Benson & Hedges Inner City Program.[55]

The tobacco industry has used popular African American magazines like *Ebony* and *Jet* to advertise menthol cigarettes to African Americans since the 1960s, and this practice continues today. From 1998 to 2002, *Ebony,* a magazine tailored to the African American culture, was 9.8 times more likely than *People* to contain ads for menthol cigarettes.[56] An assessment of menthol cigarette ads run from June 2012 to February 2013 found that the tobacco industry spent an estimated $31 million on menthol cigarette direct mail, email, print and online advertisements in just a 9-month period. During this time, 61 percent of Newport print ads featured at least one African-American model. These ads ran in twenty publications, including *Jet*, *Ebony*, and *Essence*, which have predominantly African-American readership.[57]

**1966**


**1984**

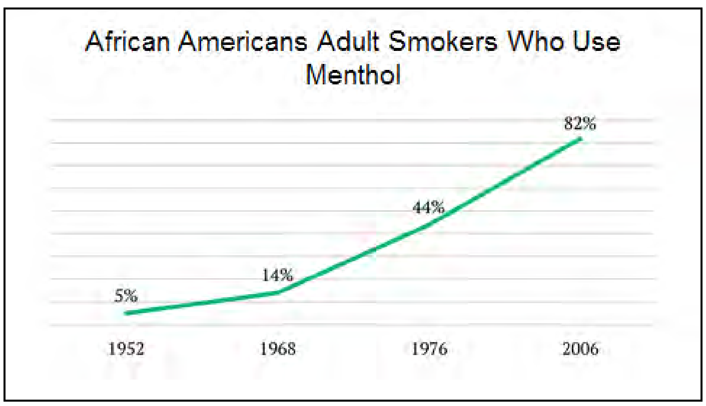

**2004**



**Images courtesy of Stanford Research Into the Impact of Advertising (SRITA) and TrinketsandTrash.Org.**

In magazines and other marketing materials, the industry used advertisements characterized by slogans, relevant and specific messages, or images that have a great appeal among those in the black community or depict African Americans in an appealing light.[58] In 2004, Brown & Williamson started an ad campaign for their Kool brand cigarettes clearly aimed at youth—and African-American youth, in particular. The Kool Mixx campaign featured images of young rappers, disc jockeys and dancers on cigarette packs and in advertising. The campaign also included radio giveaways with cigarette purchases and a Hip-Hop disc jockey competition in major cities around the country. The themes, images, radio giveaways and music involved in the campaign all clearly have tremendous appeal to youth, especially African-American youth. Attorneys General from several states, including New York, promptly filed motions against Brown & Williamson for violating the Master Settlement Agreement. [59]

The overwhelming preference for menthol cigarettes among African Americans seen today is no coincidence. The tobacco industry deliberately targeted the African American community to create this disparity. Just 5 percent of African-Americans smoked menthol cigarettes in the early 1950's, by 1968 the number had risen to 14 percent, and today the number is now well over 80 percent.[60] Make no mistake this is a crisis that is the direct result of the conscious decisions of the major tobacco companies.

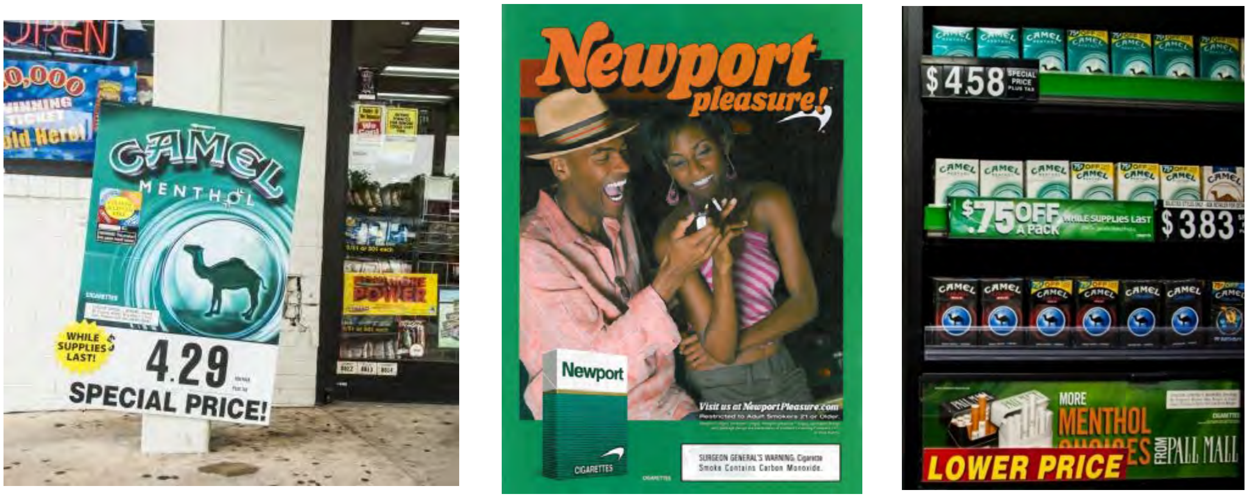



Slide Courtesy of Phillip S. Gardiner
http://www.acbhcs.org/tobacco/docs/conference/Dr_Gardiner_Tob_Industry_AA_Me

This targeting continues today: magazine advertisements continue to target African Americans and menthol cigarettes continue to be heavily advertised, widely available, and priced cheaper in certain African American communities, making them more appealing, particularly to price-sensitive youth. [61] In California, African-American neighborhoods have more price discounts for Newport cigarettes and more marketing for menthol cigarettes:

- The 2011 California Tobacco Advertising Survey reports that there were significantly more menthol advertisements at stores in neighborhoods with a higher proportion of African-American residents and in low-income neighborhoods.[62]

- Another California study found that as the proportion of African-American high school students in a neighborhood rose, the proportion of menthol advertising increased, the odds of a Newport promotion were higher, and the cost of Newport cigarettes was lower.[63]




**Current marketing strategies: Menthol marketing and price promotion strategies at the point of sale. 2016 magazine advertising for Newport cigarettes. Images courtesy of CounterTobacco.Org and TrinketsandTrash.Org**

**Cigars Remain Popular Among Youth Due to Surge in Candy-Flavored Products**

Sales of flavored cigars have increased by nearly 50 percent since 2008, and flavored cigars made up more than half (52.1%) of the U.S. cigar market in 2015, according to Nielsen convenience store market scanner data.[64] The number of unique cigar flavor names more than doubled from 2008 to 2015, from 108 to 250.[65] These products are often colorfully packaged and much cheaper than cigarettes; for instance, cigarillos can be priced as low as 3 or 4 for 99 cents, making them even more appealing to price-sensitive youth.

Youth and young adults prefer cigar brands that come in a variety of flavors, and that preference declines significantly with age.[66] 71.7 percent of current youth cigar smokers had used a flavored product in the last month and that 73.8 percent smoked cigars "because they come in flavors I like."[67] In California, little cigars and cigarillos are more popular among high school students than cigarettes (2.3% vs. 2.0%).[68] These cheap, sweet cigars can serve as an entry product for kids to a lifetime of smoking.

The scientific evidence leaves no doubt that flavored tobacco products – including menthol cigarettes – have a profound adverse impact on public health in the United States, resulting in more tobacco use and subsequently more death and disease. The research also demonstrates that the tobacco industry is responsible for the health disparities caused by menthol cigarettes because of its targeted marketing to children and African-American communities.

Strong laws banning the sale of flavored tobacco products can protect youth from accessing flavored and cheap tobacco products, and are crucial to preventing a lifetime of tobacco addiction. Thank you for putting the health and lives of our children before tobacco industry profits, and ensuring that all of Los Angeles' children get to have the healthy and prosperous lives they deserve.

---

[1] Centers for Disease Control and Prevention (CDC), "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *Morbidity and Mortality Weekly Report (MMWR*), 67(45): 1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.

[2] University of Michigan, Monitoring the Future Study, 2018. http://monitoringthefuture.org/data/18data/18drtbl3.pdf

[3] Centers for Disease Control and Prevention (CDC), "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *Morbidity and Mortality Weekly Report (MMWR*), 67(45): 1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.

[4] California Department of Public Health, *California Tobacco Facts and Figures 2019,* May 2019, https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/ResearchandEvaluation/FactsandFigures/CATobaccoFactsandFigures2019.pdf.

[5] CDC, "Youth Risk Behavior Surveillance—United States, 2017," *MMWR,* 67(8), June 15, 2018. https://www.cdc.gov/healthyyouth/data/yrbs/pdf/2017/ss6708.pdf.

[6] CDC, "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *Morbidity and Mortality Weekly Report (MMWR*), 67(45):1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.

[7] Truth Initiative, "Monitoring the Future reveals good and bad news underscoring need for education and regulation," December 14, 2017, https://truthinitiative.org/news/monitoring-future-reveals-good-and-bad-news-underscoring-need-education-and-regulation.

[8] HHS, *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.

[9] Zhu, S-H, et al., "Evolution of Electronic Cigarette Brands from 2013-2014 to 2016-2017: Analysis of Brand Websites," Journal of Medical Internet Research, 20(3), published online March 12, 2018.

[10] FDA, "Modifications to Compliance Policy for Certain Deemed Products: Guidance for Industry, Draft Guidance," March 13, 2019, https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM633281.pdf.

[11] CDC, "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *MMWR*, 67(45): 1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.

[12] California Department of Public Health, *California Tobacco Facts and Figures 2019,* May 2019, https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/ResearchandEvaluation/FactsandFigures/CATobaccoFactsandFigures2019.pdf.

[13] Marynak, K., et al., "Exposure to Electronic Cigarette Advertising Among Middle and High School Students—United States, 2014-2016," *MMWR* 67(10: 294-299, March 16, 2018, https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6710a3-H.pdf.

[14] Chu, KH, et al., "JUUL: Spreading Online and Offline," *Journal of Adolescent Health* 63(5):582-586, 2018.

[15] Centers for Disease Control and Prevention (CDC), "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *Morbidity and Mortality Weekly Report (MMWR*), 67(45): 1276-1277.

[16] CDC, Office of the Surgeon General, "Health Care Professionals: Educate Your Young Patients About the Risks of E-cigarettes," https://e-cigarettes.surgeongeneral.gov/documents/SGR_E-Cig_Health_Care_Provider_Card_508.pdf

[17] CDC, Office of the Surgeon General, "Know the Risks: E-Cigarettes and Young People, Frequently Asked Questions," https://e-cigarettes.surgeongeneral.gov/documents/2016_SGR_ECig_FAQ_508.pdf

[18] Jackler, RK, Ramamurthi, D, "Nicotine arms race: JUUL and the high-nicotine product market" *Tobacco Control*, published online February 6, 2019.

[19] Jackler, RK, Ramamurthi, D, "Nicotine arms race: JUUL and the high-nicotine product market" *Tobacco Control*, published online February 6, 2019.

[20] Pax Labs, Inc. (former name of JUUL Labs), *Pax Labs, Inc. Granted U.S. Patent for Nicotine Salt E-Cigarette*, December 22, 2015, https://www.juulvapor.com/media/wysiwyg/JUUL/JUUL_USPTO_Patent_Press_Release_15-1216.pdf.

[21] Office of the Surgeon General, "Surgeon General's Advisory on E-Cigarette Use Among Youth," December 18, 2018, https://e-cigarettes.surgeongeneral.gov/documents/surgeon-generals-advisory-on-e-cigarette-use-among-youth-2018.pdf.

[22] US Department of Health and Human Services (HHS), *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.
[23] Jackler, RK, Ramamurthi, D, "Nicotine arms race: JUUL and the high-nicotine product market" *Tobacco Control*, published online February 6, 2019.
[24] Tucker, J, "As Juul vaping surges among teens, health concerns grow," *San Francisco Chronicle*, May 27, 2018, https://www.sfchronicle.com/bayarea/article/As-Juul-vaping-surges-among-teens-health-12946713.php.
[25] HHS, *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016. See also, Leventhal, AM, et al., "Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence," *Journal of the American Medicine Association*, 314(7): 700-707, 2015. Wills, Thomas A, et al., "Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii," Tobacco Control, published online first January 25, 2016. Wills, TA, et al., "E-cigarette use is differentially related to smoking onset among lower risk adolescents," *Tobacco Control*, published online August 19, 2016. Barrington-Trimis, JL, et al., "E-Cigarettes and Future Cigarette Use," *Pediatrics*, 138(1), published online July 2016.
[25] Barrington-Trimis, JL, et al., "E-Cigarettes and Future Cigarette Use," *Pediatrics*, 138(1), published online July 2016. Wills, TA, et al., "E-cigarette use is differentially related to smoking onset among lower risk adolescents," *Tobacco Control*, published online August 19, 2016.
[26] National Academies of Sciences, Engineering, and Medicine. 2018. *Public health consequences of e-cigarettes*. Washington, DC: The National Academies Press. http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx .
[27] Berry, KM, et al., "Association of Electronic Cigarette Use with Subsequent Initiation of Tobacco Cigarettes in US Youths," *JAMA Network Open*, 2(2), published online February 1, 2019.
[28] Barrington-Trimis, JL, et al., "E-Cigarettes and Future Cigarette Use," *Pediatrics*, 138(1), published online July 2016. Wills, TA, et al., "E-cigarette use is differentially related to smoking onset among lower risk adolescents," *Tobacco Control*, published online August 19, 2016.
[29] University of Michigan, 2018 Monitoring the Future Study, *Trends in Availability – Tables 15-17.* See http://monitoringthefuture.org/data/18data/18drtbl15.pdf and http://monitoringthefuture.org/data/18data/18drtbl16.pdf.
[30] FDA, "Modifications to Compliance Policy for Certain Deemed Products: Guidance for Industry, Draft Guidance," March 13, 2019, https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM633281.pdf.
[31] California Department of Public Health, *California Tobacco Facts and Figures 2019,* May 2019, https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/ResearchandEvaluation/FactsandFigures/CATobaccoFactsandFigures2019.pdf.
[32] U.S. Preventive Services Task Force, *Final Recommendation Statement: Tobacco Smoking Cessation in Adults, Including Pregnant Women: Behavioral and Pharmacotherapy Interventions*, May 2019, https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions1.
[33] King, BA, et al., "Awareness and Ever Use of Electronic Cigarettes Among U.S. Adults, 2010-2011," *Nicotine & Tobacco Research*, 15(9):1623-7, 2013. See also, King, BA, et al., "Trends in Awareness and Use of Electronic Cigarettes among U.S. Adults, 2010-2013," *Nicotine & Tobacco Research*, first published online September 19, 2014 and Fiore, MC, et al., Treating Tobacco Use and Dependence: 2008 Update, U.S. Public Health Service Clinical Practice Guideline, May 2008, http://www.surgeongeneral.gov/tobacco/treating_tobacco_use08.pdf.
[34] FDA. *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes* (2013).
[35] Tobacco Products Scientific Advisory Committee (TPSAC), FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[36] TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf
[37] FDA. *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes* (2013).
[38] HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.cdc.gov/Features/YouthTobaccoUse/.
[39] TPSAC, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[40] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.
[41] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[42] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[43] Kuiper, NM, et al., "Trends in sales of flavored and menthol tobacco products in the United States during 2011-2015," *Nicotine & Tobacco Research*, published online June 1, 2017.

44 U.S. Federal Trade Commission (FTC), *Cigarette Report for 2017*, 2019, https://www.ftc.gov/system/files/documents/reports/federal-trade-commission-cigarette-report-2017-federal-trade-commission-smokeless-tobacco-report/ftc_cigarette_report_2017.pdf [data for top 5 manufacturers only].

45 Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016

46 TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf

47 FDA, "Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes," http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PeerReviewofScientificInformationandAssessments/UCM361598.pdf, 2013; Tobacco Products Scientific Advisory Committee, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697;pdf.; Alexander, LA, et al., "Why we must continue to investigate menthol's role in the African American smoking paradox," *Nicotine & Tobacco Research, 18(S1):* S91-S101, 2016;

48 See e.g., CDC, "Quitting Smoking Among Adults—United States, 2000-2015," *MMWR*, 65(52): 1457-1464, January 6, 2017, https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6552a1.pdf. Royce, J, et al., "Smoking cessation factors among African Americans and Whites: COMMIT Research Group," *American Journal of Public Health* 83(2):220-6, February 1993. https://www.fda.gov/advisoryCommittees/CommitteesMeetingMaterials/tobaccoproductsScientificAdvisoryCommittee/default.htm

49 CDC, "Quitting Smoking Among Adults—United States, 2000-2015," *MMWR*, 65(52): 1457-1464, January 6, 2017, https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6552a1.pdf.

50 US Department of Health and Human Services (HHS), "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.

51 American Cancer Society, "Cancer Facts & Figures for African Americans, 2016-2018," 2016, http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-047403.pdf.

52 American Cancer Society, *Cancer Facts & Figures 2019*, https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf.

53 HHS, "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.

54 TPSAC, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.

55 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

56 Landrine, H, et al., "Cigarette advertising in Black, Latino and White magazines, 1998-2002: An exploratory investigation," *Ethnic Disparities* 15(1):63-7, 2005.

57 Richardson, A, et al., "How the industry is marketing menthol cigarettes: the audience, the message, and the medium," *Tobacco Control*, 24: 594-600, 2015.

58 Hutchinson, EO, "Joe Camel Dominants More Than Billboards in Black America," June 23, 1997, http://www.pacificnews.org/jinn/stories/3.13/970623-cigarettes.html

59 Hafez, N, & Ling, P, "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control*, 15: 359-366, 2006.

60 Slide credit: Phillip S. Gardiner http://www.acbhcs.org/tobacco/docs/conference/Dr_Gardiner_Tob_Industry_AA_Menthol.pdf Sources include: Gardiner, PS, "The African Americanization of menthol cigarette use in the United States," Nicotine & Tobacco Research, February 2004; Roper, B.W. (1953). A Study of People's Cigarette Smoking Habits and Attitudes Volume I. Philip Morris, Bates No. 2022239249; MSA, Inc. (1978) The Growth of Menthols, 1933 -1977; Brown & Williamson, Bates No. 670586709-785; National Survey on Drug Use and Health,, 2004-2008.

61 Rodriguez, D, et al., "Predictors of tobacco outlet density nationwide: a geographic analysis," *Tobacco Control* 22(5):349-55, 2013. See also Lee, JG, et al., "Inequalities in tobacco outlet density by race, ethnicity and socioeconomic status, 2012, USA: results from the ASPIRE Study," *Journal of Epidemiology and Community Health* 71(5):487-492, 2017. Henriksen, L, et al., "Targeted Advertising, Promotion, and Price for Menthol Cigarettes in California High School Neighborhoods," *Nicotine & Tobacco Research* 14(1):116-21, 2012.

62 Schleicher, N, et al., "Tobacco Marketing in California's Retail Environment (2008-2011), Final report for the California Tobacco Advertising Survey. Stanford, CA: Stanford Prevention Research Center, July 2013.

63 Henriksen, L., et al., "Targeted Advertising, Promotion, and Price for Menthol Cigarettes in California High School Neighborhoods," Nicotine & Tobacco Research, June 24, 2011.

64 Delnevo, CD, et al., "Changes in the mass-merchandise cigar market since the Tobacco Control Act," *Tobacco Regulatory Science,* 3(2 Suppl 1): S8-S16, 2017.

65 Delnevo, CD, et al., "Changes in the mass-merchandise cigar market since the Tobacco Control Act," *Tobacco Regulatory Science,* 3(2 Suppl 1): S8-S16, 2017.

[66] Delnevo, C, et al., "Preference for flavoured cigar brands among youth, young adults and adults in the USA," *Tobacco Control* 24(4):389-94, 2015

[67] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.

[68] California Department of Public Health, *California Tobacco Facts and Figures 2019,* May 2019, https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/ResearchandEvaluation/FactsandFigures/CATobaccoFactsandFigures2019.pdf.

## KEY SCIENTIFIC FINDINGS ON MENTHOL FROM THE FOOD AND DRUG ADMINISTRATION (FDA) AND FDA'S TOBACCO PRODUCT SCIENTIFIC ADVISORY COMMITTEE

### 2011 Report of the Tobacco Products Scientific Advisory Committee (TPSAC) of the Center for Tobacco Products of the Food and Drug Administration (FDA)

Overall Conclusions

- **"Removal of menthol cigarettes from the marketplace would benefit public health in the United States."**
- "Menthol cigarettes have an adverse impact on public health in the United States."
- "There are no public health benefits of menthol compared to non-menthol cigarettes."
- "The availability of menthol cigarettes increases initiation and reduces cessation, thereby increasing the number of people who are smoking. This increase in the number of smokers represents an adverse impact of the availability of menthol cigarettes on public health."
- "Assuming the best estimates, by 2020 about 17,000 premature deaths will occur and about 2.3 million people will have started smoking, beyond what would have occurred absent availability of menthol cigarettes."

Smoking Prevalence

- "Although cigarette smoking is becoming less prevalent, the evidence is sufficient to conclude that menthol cigarette smoking is declining at a slower rate than non-menthol cigarette smoking."

Initiation

- "The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases experimentation and regular smoking. (Above Equipoise)
- "The evidence is sufficient to conclude that it is more likely than not that the availability of menthol cigarettes increases the likelihood of experimentation and regular smoking beyond the anticipated prevalence if such cigarettes were not available, in the general population and particularly in African Americans. The evidence is sufficient to conclude that it is more likely than not there is a causal relationship between the availability of menthol cigarettes and regular smoking among youth. (Above Equipoise)"

Menthol Physiology

- "Menthol is not simply a flavoring agent but has drug-like characteristics that modulate the effect of nicotine on the smoker. The consequences of these effects for menthol cigarette smokers are twofold: the sensory stimulation from the "throat grab" of menthol could provide greater reinforcement of smoking behavior, and the reduced irritation provided by lower levels of menthol could lessen aversion to initial self-administration of nicotine among novice smokers, thereby facilitating continued smoking that leads to addiction."
- "The evidence is sufficient to conclude that menthol has cooling and anesthetic effects that reduce the harshness of cigarette smoke. Research indicates that menthol acts on both thermal and nociceptive receptors. This dual action results in both cooling and counter-irritant effects. Menthol desensitizes receptors by which nicotine produces irritant effects, thereby, reducing the irritation from nicotine in tobacco smoke."

Addiction and Dependence

- "The evidence is sufficient to conclude that it is biologically plausible that menthol makes cigarette smoking more addictive."
- "The currently presented evidence is persuasive in demonstrating that initiating with menthol cigarettes is associated with increased risk for transitioning to more established smoking**."**

- **“**There is strong evidence indicating that adolescent menthol cigarette smokers are more dependent on nicotine than adolescent non-menthol cigarette smokers.”
- **“**Among youth, there is sufficient evidence to indicate that those who smoke menthol cigarettes tend to be more dependent than those who smoke non-menthol cigarettes as reflected by the number of cigarettes smoked and dependence measures. Thus, this population seems to be particularly vulnerable to the effects of menthol cigarette smoking.”
- “The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases the likelihood of addiction and the degree of addiction in youth smokers.”

Cessation

- “The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes results in lower likelihood of smoking cessation success in African Americans, compared to smoking non-menthol cigarettes. (Above Equipoise)”

Marketing

- “The evidence is sufficient to conclude that other menthol marketing messages feature youthful imagery and themes to appeal to youthful audiences, as well as socially and culturally relevant messages about in-group identity to appeal to different market segments”
- The evidence is sufficient to conclude that menthol cigarettes have been and continue to be marketed with a set of associated branding elements and labels that connote health benefits.”
- “The evidence is sufficient to conclude that, consistent with marketing claims, consumers hold beliefs about the medicinal benefits of menthol and beliefs about other implicit health benefits, and that this is especially the case among African Americans.”
- “The evidence is sufficient to conclude that menthol cigarettes are disproportionately marketed per capita to African Americans. African Americans have been the subjects of specifically tailored menthol marketing strategies and messages. Billboard advertising and point-of-sale advertising for menthol cigarettes has been over-represented in neighborhoods with a high percentage of African Americans and in magazines with high African American readership, and more so than non-menthol cigarette advertising. Consistent with these targeted marketing efforts, menthol cigarettes are disproportionately smoked by African American smokers.”

**2013 FDA Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes**

Overall Conclusions

- “While there is little evidence to suggest that menthol cigarettes are more or less toxic or contribute to more disease risk to the user than nonmenthol cigarettes, adequate data suggest that menthol use is likely associated with increased smoking initiation by youth and young adults. Further, the data indicate that menthol in cigarettes is likely associated with greater addiction. Menthol smokers show greater signs of nicotine dependence and are less likely to successfully quit smoking. These findings, combined with the evidence indicating that menthol’s cooling and anesthetic properties can reduce the harshness of cigarette smoke and the evidence indicating that menthol cigarettes are marketed as a smoother alternative to nonmenthol cigarettes, make it likely that menthol cigarettes pose a public health risk above that seen with nonmenthol cigarettes.”
- “Data support that (1) a majority of African American smokers reported menthol cigarette use and other minority groups were more likely to smoke menthol cigarettes than White smokers, (2) younger smokers had the highest rate of smoking menthol cigarettes, (3) female smokers were more likely to smoke menthol cigarettes, and (4) menthol smokers were more likely to have lower education levels and lower incomes compared with nonmenthol smokers.”

Menthol Physiology

- “Menthol generates a minty taste and a cooling sensation. At lower concentrations menthol has a soothing effect, while it is irritating at high concentrations. Smokers experience the cooling sensation of menthol in cigarettes, and menthol is perceived as reducing the irritation and harshness of smoking. Several in vitro and in vivo studies investigated the sensory effects of menthol and discussed mechanisms for these effects. In addition, a few studies suggested that menthol might have a role on exposure and metabolism of nicotine and TSNAs. Due primarily to menthol’s sensory effects, the weight of evidence supports the conclusion that menthol in cigarettes in likely associated with altered physiological responses to tobacco smoke.”

Initiation

- “From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased initiation and progression to regular of cigarette smoking.”
- “Younger, newer smokers prefer menthol at levels far above that of the general population, a finding that is generally consistent across racial or ethnic groups. The data that support the finding that those of younger age have greater menthol preference are consistent. This suggests that as smokers grow older, menthol preferences change. Additionally, while this is not a direct measure of individual initiation, it tracks very well to the ages that initiation typically occurs.”

Addiction and Dependence

- “From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased dependence.”
- “The data indicate that menthol in cigarettes is likely associated with greater addiction. Menthol smokers show greater signs of nicotine dependence and are less likely to successfully quit smoking.”
- “Based on the findings of TTFC, non-FTND scales of dependence, craving measures, and waking at night to smoke, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased dependence.”

Cessation

- “From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with reduced success in smoking cessation, especially among African American menthol smokers”
- “The data indicate that menthol in cigarettes is likely associated with greater addiction. Menthol smokers show greater signs of nicotine dependence and are less likely to successfully quit smoking.”

Marketing

- “The marketing of menthol cigarettes is associated with menthol brand preference among adolescents and the African American community.”

## Response to JUUL Research Related to Cessation

### Existing Research on the Effectiveness of E-cigarettes for Cessation is Limited

JUUL's research should be weighed against the existing body of research on e-cigarettes and cessation. The evidence to date that e-cigarettes are effective at helping smokers quit completely is limited and inconsistent and no e-cigarette has been approved or even reviewed for smoking cessation purposes by the Food and Drug Administration. Public health authorities in the U.S., including the CDC and the U.S. Preventive Services Task Force, have found that there is not enough evidence to recommend e-cigarettes for tobacco cessation.

- The US Preventive Services Task Force concluded that "the current evidence is insufficient to recommend electronic nicotine delivery systems for tobacco cessation..."[1]

- The 2018 National Academies of Sciences, Engineering, and Medicine report concluded, "Overall, there is limited evidence that e-cigarettes may be effective aids to promote smoking cessation."[2]

- Researchers from the CDC said, "There is currently no conclusive scientific evidence that e-cigarettes promote long-term cessation, and e-cigarettes are not included as a recommended smoking cessation method by the U.S. Public Health Service."[3]

A recent study from the U.S. also raises questions about the effectiveness of e-cigarettes to help smokers quit: Weaver, et. al., did not find any evidence that ENDS help adult smokers quit at a higher rate than smokers who did not use these products despite ENDS users being more likely to make a quit attempt. In fact, the authors state that "findings indicate that, at the time of this study, ENDS under "real world" use and conditions may have suppressed or delayed quitting among some adult smokers." Specifically, of the 27 percent of smokers who reported using ENDS at baseline, about 90 percent were still smoking at one-year follow-up (53.5% continued to smoke and use ENDS and 37.4% were smoking but not using ENDS) and 9.2 percent had quit smoking (2.5% quit smoking and were using ENDS and 6.7% quit smoking and quit ENDS). Moreover, the study found that ENDS users quit at a lower rate than non-ENDS users regardless of frequency or duration of ENDS use, device type, quitting as reason for use, or e-liquid flavor.[4]

**<u>Analysis of JUUL's Research on Switching from Cigarettes to JUUL</u>**

**Russell, C, et al., "Factors associated with past 30-day abstinence from cigarette smoking in a non-probabilistic sample of 15,456 adult established current smokers in the United States who used JUUL vapor products for three months,"** ***Harm Reduction Journal*****, 16(22), 2019.**

This study recruited 15,456 US adult (21+) smokers who had purchased JUUL starter kits in a retail store or through the JUUL website between April and June of 2018, assessing smoking and JUUL use monthly for 3 months. Researchers found that 28.3% of JUUL users had not smoked in the past 30 days at the 3-month survey. Abstinence was higher among those who purchased at a retailer (vs. online); those who primarily used Mint or Mango JUULpods; those who purchased JUUL with the intention to quit; lighter and less frequent smokers; younger smokers; and daily users of JUUL. There was no difference in abstinence among primary users of Virginia Tobacco, Crème, Fruit, Cucumber and Menthol pods.

**Goldenson, N, et al., "Association of Flavored Nicotine Salt Pod System Use and Subsequent Switching Behavior," Poster presented at the 2nd Scientific Summit on Tobacco Harm Reduction, May 29, 2019.**

The study recruited 19,595 US adult smokers who had purchased JUUL starter kits in a retail store or through the JUUL website, assessing smoking and JUUL use monthly for 6 months. Researchers found that 56.1% of JUUL users who completed the six-month survey had not smoked in the past 30 days.

Across follow-up time-points, JUUL users who used non-tobacco or menthol flavor pods were more likely to have switched from cigarettes to JUUL.

**Goldenson, N, et al., "Flavored JUUL Use and Smoking Abstention Among Adult Smokers," Poster presented at the 6th Annual Global Forum on Nicotine, June 14, 2019.**

The study recruited 21,332 US adult (21+) smokers who had purchased JUUL starter kits in a retail store or through the JUUL website, assessing smoking and JUUL use monthly for 6 months. Use of flavored JUUL pods other than tobacco, menthol or mint were more likely to have switched from cigarettes to JUUL.

There are significant limitations to JUUL's research findings:

- **Longitudinal studies cannot provide causal evidence that JUUL is effective for smoking cessation.** The best type of study to answer this question is a randomized controlled trial.
    - To quote the Russell 2019 study, "The uncontrolled nature of our study design means we cannot know what proportion of those quitters who were retailer purchasers and primary users of Mango flavored JUUL-pods would have used JUULpods in tobacco or mint/menthol flavors and quit smoking even if Mango flavored JUULpods had been unavailable for purchase in retail stores during this study"
- **These studies are not generalizable to all smokers or e-cigarette users.**
    - All study participants were self-selected established adult smokers who very recently started using a JUUL device. Recruitment efforts were geared towards outlets where new JUUL users would be found.
    - All studies used a non-probability sample.
    - The samples were not representative to the US smoking population, generally recruiting a higher income, higher educated, younger and less diverse population. As a result, these findings are not generalizable to the US smoking population.
        - Russell study: 66.6% were 34 or younger; 77.1% had some college or bachelor's degree; 6.6% had only a high school degree or GED; 52.3% smoked 1-9 cigarettes per day; 51% were daily smokers; 10.3% were Asian, Hawaiian or Pacific Islander; 3.1% were African American.
        - May 2019 Goldenson poster: 40.5% were college graduates, 44.9% had an income >$50,000
        - June 2019 Goldenson poster: 40.9% were college graduates, 59.7% had an income >$50,000
- **These studies do not account for participant drop-out rate.**
    - None of these studies report any analysis as to whether participants who dropped out were different than those who remained in the study. It is standard practice to use "intent-to-treat analysis" in this type of study, which assumes that those who drop out continued to smoke. JUUL advertises an inflated switching rate.
    - Russell study: JUUL's press release advertised the study as finding that 47.1 percent were abstinent at 3 months. However, 40 percent of participants had dropped out and did not complete the 3 month survey. In the intent-to-treat analysis, the authors found that 28.3 percent were abstinent at 3 months.
    - May 2019 Goldenson poster: JUUL's poster highlights a 56.1% switching rate at 6 months. However, based on the sample size provided at the 6 month survey, one can calculate that an intent-to-treat analysis would yield a 34% switching rate.
- **Measurement of flavor use is inadequate to determine impact of specific flavors on switching.**
    - These studies categorized flavor use by primary use or flavor used most in the past month, defined as using a specific flavor more than any other flavor, meaning that a

"primary Mango user" could be using other flavor pods. In the Russell study, one-fifth of the sample did not have a primary flavor (used two or more flavors equally). Flavor data was missing for another fifth of the sample. The authors did not report what proportion of the total sample had used multiple JUUL flavors in the past month. 25 percent of users were using tobacco-flavored JUULpods at the 3-month survey (alone or in addition to JUULpods with characterizing flavors).

  - In addition to the fact that these are not randomized controlled studies, these limitations prevent any conclusions about the impact of specific flavors on switching. They cannot answer whether primary users of Mint or Mango would have switched if only tobacco-flavored pods were available.

In addition to methodological limitations, there are important questions that remain unanswered:

- *What is the impact of JUUL use among former smokers and never smokers on subsequent smoking behavior (relapse or initiation)?* These studies only recruited current smokers. A previous study of 19,000 adult JUUL users found that 25 percent were former smokers when they started using JUUL and 12.7 percent were never smokers.[5]

- *What is the long-term impact of JUUL use on smoking behavior and nicotine use (e.g., will smokers relapse to cigarette smoking only or dual use, will users quit nicotine altogether, or will they become long-term JUUL users)?*

  - As the authors of the Russell study note, "Short-term self-reported smoking outcome data reported here should not be taken as evidence that using a JUUL vaporizer can be effective for helping smokers to quit in the long-term"

  - Studies indicate that e-cigarettes will have a public health benefit only if specific products are shown to be effective at helping smokers stop using cigarettes completely. Up to now, the large majority of e-cigarette users in the U.S. also continue to smoke cigarettes, and studies indicate these "dual users" actually reduced their likelihood of quitting.

- *Would primary users of non-tobacco flavored JUULpods quit smoking if only tobacco-flavored JUULpods were available?* These studies are not able to answer this question since users self-selected their flavors. The benefit of flavored JUULpods to adult smokers must also be weighed against the role that these flavors play in the current epidemic of e-cigarette use among youth.

- *Would smokers have been able to quit on their own or with FDA-approved cessation treatments?* In a randomized controlled trial, it would be appropriate to compare the impact of JUUL to currently available cessation treatments.

  - As the authors of the Russell study note, "Given that lighter smokers may have been comparably likely to try and succeed in quitting smoking with non-pharmacological interventions, and given that long-term inhalation of vapor from a JUUL vaporizers is unlikely to be without some health risks, the potential benefits of switching from light smoking to regular use of JUUL vaporizer need to be weighed against the potential risks that could be incurred through prolonged exposure to daily, high doses of nicotine and varying levels of other harmful and potentially harmful constituents of vapor if theses switchers were to go on to become long-term or lifelong JUUL users"

- *What are the long-term health effects of sustained use of JUUL?*

[1] U.S. Preventive Services Task Force, *Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women:* U.S. Preventive Services Task Force Recommendation Statement*, Annals of Internal Medicine, Vol.*

*163, No. 8, October 2015* , http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions1.
[2] National Academies of Sciences, Engineering, and Medicine (NASEM), *Public Health Consequences of E-Cigarettes*, Washington, DC: The National Academies Press, 2018, http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx
[3] King, BA, et al., "Awareness and Ever Use of Electronic Cigarettes Among U.S. Adults, 2010-2011," *Nicotine & Tobacco Research*, 15(9):1623-7, 2013. See also, King, BA, et al., "Trends in Awareness and Use of Electronic Cigarettes among U.S. Adults, 2010-2013," *Nicotine & Tobacco Research*, first published online September 19, 2014.
[4] Weaver, SR, et al., "Are electronic nicotine delivery systems helping cigarette smokers quit? Evidence from a prospective cohort study US adult smokers, 2015-2016," *PLOS One* 13(7), July 9, 2018.
[5] Russell, C, et al., "Transitions in Cigarette Smoking Associated with Use of the JUUL Vaping Device Among 18,799 Adults in the United States," 2018. Centre for Substance Use Research: Glasgow, UK.

# FLAVORED TOBACCO PRODUCTS ATTRACT KIDS

Cigarettes with specific characterizing flavors were prohibited in the U.S. on September 22, 2009, as part of the Family Smoking Prevention and Tobacco Control Act (TCA) that gave the U.S. Food and Drug Administration (FDA) authority over tobacco products.[1] However, before that, tobacco companies marketed cigarettes with flavors, images, and names that appealed to a young audience. Despite the FDA's ban on flavored cigarettes, the overall market for flavored tobacco products is growing. Continuing a long tradition of designing products that appeal explicitly to new users, tobacco companies in recent years have significantly stepped up the introduction and marketing of flavored other tobacco products (OTPs), particularly e-cigarettes and cigars, as well as smokeless tobacco and hookah. With their colorful packaging and sweet flavors, today's flavored tobacco products are often hard to distinguish from the candy displays near which they are frequently placed in retail outlets. Although tobacco companies claim to be responding to adult tobacco users' demand for variety, flavored tobacco products play a key role in enticing new users, particularly kids, to a lifetime of addiction. This growing market for flavored tobacco products is undermining the nation's overall progress in reducing youth tobacco use.

**Flavored Tobacco Products are on the Rise**

Tobacco companies market products in many kid-friendly flavors such as gummy bear, berry blend, chocolate, peach, cotton candy, strawberry, and grape, and more seem inevitable. "Candy-flavored" is, in fact, an appropriate way to describe these products since a recent chemical analysis has shown that the same flavor chemicals used in sweet-flavored cigars of various sizes and smokeless tobacco products are also used in popular candy and drink products such as LifeSavers, Jolly Ranchers, and Kool-Aid.[2] A 2013 survey of internet tobacco retailers found that more than 40 percent of cigarette-sized cigars, machine-made cigars, moist snuff, and dry snuff tobacco products were flavored, including fruit, sweet, and mint/menthol.[3] An article in *Convenience Store News* stated, "flavored tobacco is offering a bright spot in the category," referring to the increased tobacco sales – and number of consumers – in stores that sell such products.[4]

***Cigars*.** Historically, cigar manufacturers designed flavored cigars to serve as "starter" smokes for youth and young adults because the flavorings helped mask the harshness, making the products easier to smoke.[5] Recently, there has been an explosion of cheap, flavored cigars. Sales of all cigars (i.e., large cigars, cigarillos and small cigars) more than doubled between 2000 and 2017, from 6.1 billion cigars to 13.3 billion cigars, and sales have been generally increasing at a time when cigarette sales have been declining.[6]

Much of the growth in cigar sales can be attributed to smaller types of cigars, many of them flavored. An industry publication stated, "While different cigars target a variety of markets, all flavored tobacco products tend to appeal primarily to younger consumers."[7] These products are often colorfully packaged and much cheaper than cigarettes; for instance, cigarillos can be priced as low as 3 or 4 for 99 cents, making them even more appealing to price-sensitive youth.

- There has been an explosive growth in flavor options for cigars, such as candy, fruit, chocolate, and various other kid-attracting tastes. The vice president of one distributor commented, "For a while it felt as if we were operating a Baskin-Robbins ice cream store" in reference to the huge variety of cigar flavors available – and, no doubt, an allusion to flavors that would appeal to kids.[8]
- Flavored cigars have made a substantial contribution to the overall growth of the cigar market. 2015 Nielsen convenience store market scanner data show that sales of flavored cigars increased by nearly 50 percent since 2008. As a proportion of all cigar sales in these stores, the share of flavored cigars rose from 43.6 percent in 2008 to 52.1 percent in 2015. Among flavored cigars sold in these stores in 2015, the most popular flavors were fruit (38.8 percent), sweet or candy (21.2 percent), and wine (17.0 percent). Further, the number of unique cigar flavor names more than doubled from 2008

to 2015, from 108 to 250.[9] Including additional store types, Nielsen data showed that flavored cigars made up 43 percent of cigar sales in 2015, an increase from 2011.[10]

- The top five most popular cigar brands among 12- to 17-year olds who have used cigars – Swisher Sweets, Black & Mild, Backwoods, White Owl, and Dutch Masters – all come in flavor varieties.[11] For example, Black & Mild cigars come in flavors such as apple and cherry; Swisher Sweets comes in a huge variety of flavors such as tropical fusion, Maui pineapple, twisted berry, cherry dynamite and banana smash; and White Owl has flavors such as mango, tropical twist, strawberry kiwi and peach. Altria, the nation's largest tobacco manufacturer and parent company of Philip Morris USA, expanded its business to the cigar category in 2007 by acquiring John Middleton, Inc., which sells Black & Mild.
- Nielsen convenience store market scanner data also show an increasing number of products with names that do not explicitly identify a flavor, such as Swisher's "Wild Rush" and Altria's "Jazz," even though they are flavored. From 2012 to 2016, the proportion of all cigar sales comprised by these products (which researchers call "concept flavors") increased from 9 percent to 15 percent. The increase was greatest among cigarillos, among which the number of unique concept flavors more than doubled, from 17 to 46.[12] This strategy could be an attempt by cigar manufacturers to circumvent or complicate enforcement of local sales restrictions on characterizing flavors, some of which rely on definitions that describe flavors.

Since the Tobacco Control Act prohibited flavored cigarettes in 2009, cigarette makers have manipulated their products to qualify as "little" or "filtered" cigars.[13] For instance, the 2012 Surgeon General's report, *Preventing Tobacco Use Among Youth and Young Adults*, noted that flavored cigarettes such as Sweet Dreams re-emerged as Sweet Dreams flavored cigars after the federal restriction on flavored cigarettes went into effect.[14] In October 2009, U.S. Representatives Henry Waxman and Bart Stupak sent letters to two flavored cigarette companies, Cheyenne International and Kretek International, that began making little cigars shortly after the federal flavored cigarette ban went into effect.[15] Rep. Waxman discovered that Kretek International intentionally changed their cigarettes to cigars to exploit a loophole in the TCA.[16] In December 2016, the FDA issued warning letters to four tobacco manufacturers – Swisher International, Inc., Cheyenne International LLC, Prime Time International Co. and Southern Cross Tobacco Company Inc. – for marketing and selling fruit-flavored cigarettes labeled as cigars, in violation of the 2009 Tobacco Control Act.[17]

***Electronic Cigarettes*****.** Although these products are relatively new to the market, the variety of flavors available for use in e-cigarettes has grown exponentially. E-cigarette marketing employs many of the same strategies used for years by cigarette manufacturers that proved so effective in reaching kids, such as celebrity endorsements, slick TV and magazine advertisements, and sports and music sponsorships. Another strategy has been the widespread marketing of e-cigarettes and nicotine "e-juice" with a wild assortment of candy, fruit and other flavors. Flavors are not just a critical part of the product design, but are a key marketing ploy for the industry. The 2016 Surgeon General Report on e-cigarettes concluded that, **"E-cigarettes are marketed by promoting flavors and using a wide variety of media channels and approaches that have been used in the past for marketing conventional tobacco products to youth and young adults."**[18]

- As of 2017, researchers had identified more than 15,500 unique e-cigarette flavors available online.[19] An earlier study of e-cigarette flavors found that among the more than 400 brands available online in 2014, 84 percent offered fruit flavors and 80 percent offered candy and dessert flavors.[20]
- In addition to the more traditional candy and fruit flavors like cherry and chocolate, the liquid nicotine solutions are also being sold in such kid-friendly options as cotton candy, root beer float, and banana split. One study even uncovered over twenty different types of unicorn-flavored e-liquid, often paired with cartoon imagery, undoubtedly appealing to kids.[21]
- The top three cigarette manufacturers now sell e-cigarettes in a variety of flavors other than tobacco. Altria's MarkTen brand e-cigarettes come in flavors such as Apple Cider, Strawberry Brulee, "Mardi Gras" and "Caribbean Oasis" varieties. Reynolds American's Vuse product comes in flavors such as Melon, Nectar, Berry, Mint and Chai, while ITG Brand's blu e-cigarette features such flavors as Berry Cobbler, Blueberry, Cherry Crush, Strawberry Mint, Mango Apricot and Green Apple. JUUL, an independent company that has rapidly emerged as the market leader among tracked retailers as of late 2017, comes in eight flavors, including Mango, Fruit and Cucumber.

- “Vape shops,” which are specialty e-cigarette retail stores, offer an even wider assortment of flavors. In addition to the pre-made options, these stores allow patrons to mix their own preferred flavor combinations.[22]

The use of flavors in e-cigarette products is of even greater concern because e-cigarettes are the subject of extensive advertising campaigns, and there is evidence that young people are exposed to significant amounts of e-cigarette advertising. In 2012, e-cigarette companies began airing media campaigns on television. One study found that exposure of youth aged 12-17 to television e-cigarette advertising increased 256 percent from 2011 to 2013 and that e-cigarette companies advertise their products to a broad audience that includes 24 million youth.[23] Ads for the blu brand (then owned by Lorillard) accounted for 81 percent of the youth exposure.[24] The 2016 National Youth Tobacco Survey found that 78.2 percent of middle and high school students—20.5 million youth—had been exposed to e-cigarette advertisements from at least one source, an increase from 68.9 percent in 2014.[25]

***Smokeless Tobacco*.** The variety of flavored smokeless tobacco products has grown over time and continues to grow.

- U.S. Smokeless Tobacco Company (UST, owned by Philip Morris USA’s parent company, Altria) increased the number of its sub-brands—including flavored products—by 140 percent from 2000 to 2006 in order to “cast a wide net” and appeal to as many potential users as possible.[26] In 2011, more than 80 percent of Skoal smokeless tobacco sold in convenience stores was flavored; and more than one out of five (21.1%) were fruit-flavored.[27] Current Skoal flavors include kid-friendly peach, citrus, cherry, berry, and apple.
- Between 2005 and 2011, sales of moist snuff increased by more than two-thirds; increases in the sale of *flavored* moist snuff accounted for about 60 percent of this growth.[28] In 2012, flavored products made up more than half (58%) of all smokeless tobacco sales. Menthol and mint flavors are most popular, followed by fruit flavors.[29]
- In 2015, flavored products made up more than half of all smokeless tobacco sales. Menthol and mint flavors were by far the most popular.[30]
- A trade publication for convenience stores quoted one retailer stating, “In the case of smokeless tobacco, you get a new flavor once every quarter.”[31]

***Hookah.*** Hookahs (water pipes) originate from Middle Eastern countries, but their use has rapidly increased in the U.S. The tobacco used in hookah often has flavorings or sweeteners added to enhance the taste and aroma. In the U.S., even more kid-friendly flavors are available, such as watermelon, tropical fruit, orange cream, caramel, chocolate, tutti frutti, vanilla and strawberry.[32]

***Cigarettes*.** Menthol cigarettes, the only remaining flavored cigarette, maintain a significant market share. While overall cigarette sales have been declining, the proportion of smokers using *menthol* cigarettes has been increasing.[33]

- Data from the Federal Trade Commission (FTC) show that in 2017 (the most recent year for which data are available), menthol cigarettes comprised 36 percent of the market, the highest proportion on record since FTC began collecting this data in 1963.[34]
- Before cigarettes with specific characterizing flavors were prohibited by the Tobacco Control Act, R.J. Reynolds’ “Camel Exotic Blends” came in flavors such as Twista Lime, Kauai Kolada, Warm Winter Toffee and Winter Mocha Mint, among others. Bright, colorful and alluring ads for these cigarettes have appeared in magazines popular with kids, including *Rolling Stone*, *Cosmopolitan* and *Sports Illustrated*.
- Using data from the 1999-2013 Youth Tobacco Surveys, a 2017 study analyzed the impact of the 2009 ban on characterizing flavors in cigarettes on youth tobacco use. The researchers found that cigarette use declined significantly after the ban, whereas cigar and pipe tobacco use significantly increased. Further, use of menthol cigarettes, the only remaining flavored cigarette, increased significantly after the ban.[35]

**Flavored Products Appeal to Youth and Young Adults**

Research shows that flavored products – no matter what the tobacco product – appeal to youth and young adults. Data from the 2013-2014 Population Assessment of Tobacco and Health (PATH) study found that 80.8 percent of 12-17 year olds who had ever used a tobacco product initiated tobacco use with a flavored product, and that 79.8 percent of current tobacco users had used a flavored tobacco product in the past month.[36] Moreover, for each tobacco product, at least two-thirds of youth reported using these products "because they come in flavors I like."[37]

Additional national data from the 2017 National Youth Tobacco Survey (NYTS) found that 63.6 percent of current middle and high school tobacco users had used a flavored tobacco product in the past month. [38] According to the NYTS, youth who use flavored tobacco products are also more likely to be dual or poly tobacco users. Use of multiple tobacco products is associated with increased risk of addiction and long-term tobacco use.[39] Another national study found that 18.5 percent of young adult tobacco users (18-34 years old) currently use a flavored tobacco product, with younger age being a predictor of flavored tobacco product use. In fact, the study found that those aged 18-24 years old had an 89 percent increased odds of using a flavored tobacco product compared to those aged 25-34 years old.[40]

According to the 2012 Surgeon General Report, "Much of the growing popularity of small cigars and smokeless tobacco is among younger adult consumers (aged <30 years) and appears to be linked to the marketing of flavored tobacco products that, like cigarettes, might be expected to be attractive to youth."[41] The 2016 Surgeon General Report on e-cigarettes concluded that flavors are among the most commonly cited reasons for using e-cigarettes among youth and young adults.[42]

***Cigars.*** More than 2,100 children under age 18 try cigar smoking for the first time every day.[43] Teens and young adults are much more likely than adults 25 years and older to report smoking cigars.[44] Research demonstrates that flavored cigars are driving much of this usage and not surprisingly, flavored cigars are the most popular among youth. Cheap, sweet cigars can serve as an entry product for kids to a lifetime of smoking.

- The 2016-2017 wave of the PATH study found that 56.8 percent of 12-17 year olds who had ever smoked cigarillos started with a flavored product.[45] Older data from the 2013-2014 wave of the PATH study, which assessed use of all cigar types, found that 71.7 percent of current youth cigar smokers had used a flavored product in the last month and that 73.8 percent smoked cigars "because they come in flavors I like."[46]
- While the methodology is not comparable to the PATH study, the 2017 NYTS found that half (49.0%) of middle and high school cigar smokers had smoked a flavored cigar in the past month.[47]
- National data suggest that flavored cigar products are driving cigar use among adults, particularly young adults. With few exceptions, use of flavored cigars among adult cigar smokers is highest among those groups with the highest overall cigar use rates, including young adults aged 18-24 (57.1%), income below $20,000 (51.7%), and non-Hispanic others (62.4%).[48]
- Data from the National Adult Tobacco Survey indicate that use of flavored cigars decreases with age. Flavored cigar use among cigar smokers was 57.1 percent among 18-24 year olds, 43.2 percent among 25-44 year olds, 28.9 percent among 45-64 year olds and 13.4 percent among those ages 65 and older.[49]
- Youth and young adults prefer brands that come in a variety of flavors, and that preference declines significantly with age – in one study, 95 percent of 12-17 year old cigar smokers reported a usual brand that makes flavored cigars compared with 63 percent of cigar smokers aged 35 and older.[50]

***E-Cigarettes.*** Given the dramatic growth in the availability and marketing of flavored e-cigarettes, it's no surprise that e-cigarettes have been the most commonly used tobacco product among youth since 2014. Among high school students, e-cigarette use increased from 1.5 percent in 2011 to 20.8 percent in 2018, including a 78 percent increase from 2017 to 2018. More than 3.6 million middle and high school students were current e-cigarette users in 2018.[51]

One tobacco company has even acknowledged that youth are attracted to sweet flavored products. Lorillard Inc.'s Youth Smoking Prevention Program posted a page on e-cigarettes on its "Real Parents

Real Questions” website that stated: “Kids may be particularly vulnerable to trying e-cigarettes due to an abundance of fun flavors such as cherry, vanilla, piña-colada and berry.”[52]

- Data from the 2016-2017 wave of the PATH study found that 96.1 percent of 12-17 year olds who had initiated e-cigarette use since the last survey wave started with a flavored product. Additionally, it found that 97 percent of current youth e-cigarette users had used a flavored e-cigarette in the past month and 70.3 percent say they use e-cigarettes “because they come in flavors I like.”[53]
- The 2018 NYTS found that 67.8 percent of high school e-cigarette users had used a flavored e-cigarette in the past month, an increase from 60.9 percent in 2017. Current use of menthol or mint flavored e-cigarettes among high school e-cigarette users also increased from 42.3 percent in 2017 to 51.2 percent in 2018.[54]
- The 2013-2014 National Adult Tobacco Survey found that use of flavored e-cigarettes was highest among young adults (ages 18-24), compared to those over age 25, and that flavored e-cigarettes were most popular among adults who were never cigarette smokers.[55]
- A national phone survey found that youth (ages 13-17) were more likely to report interest in trying an e-cigarette offered by a friend if it were flavored like fruit, candy or menthol, compared to tobacco. This study also found that youth believed that fruit-flavored e-cigarettes were less harmful than tobacco-flavored e-cigarettes.[56]
- Another study found that compared to college students, high school students were more likely to report experimenting with e-cigarettes because of appealing flavors (47 percent vs. 33 percent).[57]

***Smokeless Tobacco.*** As with cigarettes, characterizing flavors in other tobacco products (OTPs) mask the tobacco flavor, and can make the products appealing to youth. Smokeless (or spit) tobacco companies, particularly the U.S. Smokeless Tobacco Company (UST), have a long history of creating new products that appeal to kids and marketing them aggressively to children in order to “graduate” them to more potent smokeless tobacco varieties.[58]

Although cigarette smoking among youth in the U.S. has declined rapidly since the Tobacco Control Act went into effect, use of smokeless tobacco among youth has not followed that same trend, and among boys the prevalence of smokeless tobacco use is now slightly higher than that of cigarettes (7.7% vs. 7.6%).[59]

- The 2013-2014 PATH study found that 68.9 percent of 12-17 year olds who had ever used smokeless tobacco used flavored smokeless tobacco the first time they tried the product, and 81 percent of current smokeless tobacco users had used a flavored product in the last month. [60]
- The 2017 NYTS found that 44.5 percent of middle and high school smokeless tobacco users had used flavored smokeless tobacco in the past month.[61]

***Hookah.*** Research shows that many youth and young adults perceive hookah to be safer than other combustible tobacco products.[62] However, according to the CDC, using a hookah to smoke tobacco poses serious health risks to smokers and others exposed to the smoke from the hookah.[63] Because the flavors and the smoking technique create a more soothing (“smooth”) experience, hookah smokers can inhale more deeply and spend more time in a “hookah session,” which typically lasts for 40 to 45 minutes (three to four times longer than it takes to smoke a cigarette). While a typical cigarette requires about 20 puffs, an hour-long hookah session may involve 100 to 200 puffs[64], potentially exposing the user to more smoke over a greater period of time than what occurs when smoking a regular cigarette.[65] The appeal of flavored hookah undoubtedly contributes to its popularity among youth and young adults.

- The 2013-2014 PATH study found that 88.7 percent of 12-17 year olds who had ever smoked hookah used flavored hookah the first time they tried the product, and 89 percent of current hookah users had used a flavored product in the last month.[66]
- According to the PATH study, use of flavored tobacco is highest for users of hookah than for any other tobacco product, and more than three-quarters (78.9 percent) of youth hookah users reported that they use hookah “because they come in flavors I like.”[67]

- The 2017 NYTS found that 30.6 percent of middle and high school hookah users had used flavored hookah in the past month.[68]

***Cigarettes.*** As the only flavored cigarette left on the market, it is no surprise that menthol cigarettes are popular among youth. Menthol cools and numbs the throat, reducing the harshness of cigarette smoke, thereby making menthol cigarettes more appealing to youth who are initiating tobacco use. [69]

- Over half (54 percent) of youth smokers ages 12-17 use menthol cigarettes compared to one-third (32 percent) of older adult smokers.[70] Prevalence of menthol use is even higher among African Americans: 85 percent of all African-American smokers smoke menthol cigarettes and seven out of ten African-American youth smokers smoke menthol cigarettes.[71]
- The popularity of menthol flavored cigarettes is also evidenced by brand preference among youth. According to data from the 2016 National Survey on Drug Use and Health, about one in five (18.9%) smokers ages 12-17 prefers Newport cigarettes, a heavily marketed menthol cigarette brand. Preference for Newport is even higher among African-American youth smokers (70.9 percent) because of targeted marketing by the tobacco industry. [72]
- Daily menthol cigarette smokers have higher odds of also using flavored little cigars/cigarillos compared to occasional non-menthol smokers.[73]

According to FDA's Tobacco Product Scientific Advisory Committee (TPSAC):[74]

- Menthol cigarettes increase the number of children who experiment with cigarettes and the number of children who become regular smokers, increasing overall youth smoking.
- Young people who initiate using menthol cigarettes are more likely to become addicted and become long-term daily smokers.
- The availability of menthol cigarettes reduces smoking cessation, especially among African-Americans, and increases the overall prevalence of smoking among African Americans.

FDA's own scientific analysis concluded that menthol cigarettes lead to increased smoking initiation among youth and young adults, greater addiction and decreased success in quitting smoking.[75] Although they are no longer on the market, older studies on flavored cigarettes other than menthol are still relevant to reinforce the general appeal of flavors to youth and young adults. When they were available, flavored cigarettes were being tried and used primarily by the young.[76] Candy-flavored cigarettes clearly had their greatest appeal to new smokers, 90 percent of whom were teens or younger. Research indicated that youth and young adults were more likely to notice flavored tobacco products and their ads, and this awareness translated into higher use rates among young smokers.

- Older adolescents and young adults aged 17 to 19 years old were more than twice as likely to report using flavored cigarettes (specifically Camel Exotic blends, Kool Smooth Fusion or Salem Silver Label brands) in the past 30 days compared to those aged 22 years or older.[77]
- A significant gradient in flavored cigarette use was seen across age, with the highest rates of utilization among 17 year old smokers (22.8%) and 18-19 year old smokers (21.7%). Nine percent of 24-26 year olds reported flavored cigarette use.[78]

**Tobacco Companies Have Long Recognized that Flavored Products Appeal to Youth**

The tobacco companies know that almost all new tobacco users begin their addiction as kids, but they also know that to novice smokers, tobacco can be harsh and unappealing. Internal tobacco industry documents show that tobacco companies have a long history of using flavors to reduce the harshness of their products to make them more appealing to new users, almost all of whom are under age 18.[79] By masking the harshness and soothing the irritation caused by tobacco smoke, flavors make it easier for beginners – primarily kids – to try the product and ultimately become addicted. As early as the 1970s, the tobacco companies were discussing the "benefits" of sweet flavors. Their internal documents and public statements show that the tobacco industry's use of sweet flavors goes beyond just encouraging current smokers to switch brands, but rather to attract new users, mostly kids.

- As early as 1972, advisors to Brown & Williamson reviewed new concepts for a "*youth cigarette,*" including cola and apple flavors, and a "*sweet flavor cigarette,*" stating, "*It's a well-known fact that teenagers like sweet products. Honey might be considered.*"[80]
- A 1974 summary of an RJR meeting discussed cigarettes designed for beginning smokers, noting that such a cigarette should be "*low in irritation and possibly contain added flavors to make it easier for those who never smoked before to acquire the taste of it more quickly.*"[81]
- An RJR interoffice memo revealed ideas for new products: "*Make a cigarette which is obviously youth oriented. This could involve cigarette name, blend, flavor and marketing technique....for example, a flavor which would be candy-like but give the satisfaction of a cigarette.*"[82]
- A Lorillard report summarizing the test results from new cigarette flavors, included smokers' description of "Tutti Frutti" flavored cigarettes as "*for younger people, beginner cigarette smokers, teenagers . . . when you feel like a light smoke, want to be reminded of bubblegum*."[83]
- A UST document called "The graduation theory" stated: "*New users of smokeless tobacco – attracted to the product for a variety of reasons – are most likely to begin with products that are milder tasting, more flavored, and/or easier to control in the mouth. After a period of time, there is a natural progression of product switching to brands that are more full-bodied, less flavored, have more concentrated 'tobacco taste' than the entry brand.*"[84]
- A former UST sales representative revealed that, "*Cherry Skoal is for somebody who likes the taste of candy, if you know what I'm saying*."[85]

**What States and Localities Can Do**

In addition to the federal ban on flavored cigarettes, states and localities can implement additional sales restrictions to address the remaining flavored tobacco products on the market, including menthol cigarettes, and their appeal to youth and young adults.

Despite inevitable pushback from the tobacco companies, states and localities have clear authority to restrict the sale of flavored tobacco products to reduce tobacco use and its harms to its citizens. Courts have held that state and local governments can prohibit or restrict the sale of flavored tobacco products and have rejected the argument that a prohibition on the sale or distribution of flavored products raises First Amendment issues.[86]

At least two states and over 180 localities restrict sales of flavored tobacco products, although laws differ in their application to specific products and store types. At least a dozen of these localities restrict the sale of menthol cigarettes.

For a list of state and localities that have passed restrictions on the sale of flavored tobacco products, visit: https://www.tobaccofreekids.org/assets/factsheets/0398.pdf.

***Campaign for Tobacco-Free Kids, May 3, 2019 / Laura Bach***

[1] See U.S. Food and Drug Administration's (FDA) Flavored Tobacco webpage at http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/FlavoredTobacco/default.htm.
[2] Brown, JE, et al., "Candy Flavorings in Tobacco," *New England Journal of Medicine*, DOI: 10.1056/NEJMc1403015, May 7, 2014, http://www.nejm.org/doi/full/10.1056/NEJMc1403015.
[3] Morris, DS, Fiala, SC, "Flavoured, non-cigarette tobacco for sale in the USA: an inventory analysis of Internet retailers," *Tobacco Control* [Epub ahead of print] doi: 10.1136/tobaccocontrol-2013-051059, August 8, 2013.
[4] "Flavors Add New Dimension to Tobacco," *Convenience Store News*, October 1, 2007.
[5] Kostygina, G, Glantz, S, & Ling, PM, "Tobacco industry use of flavours to recruit new users of little cigars and cigarillos," *Tobacco Control* 25(1):66-74, January 2016.
[6] U.S. Alcohol and Tobacco Tax and Trade Bureau (TTB), Tobacco Statistics. December 2000 & December 2017, https://www.ttb.gov/tobacco/tobacco-stats.shtml.
[7] Niksic, M, "Flavored Smokes: Mmmmm...More Profits?"*Tobacco Retailer*, April 2007, http://tobacco-retailer.com/uploads/Features/2007/0407_flavored_smokes.asp.

[8] Niksic, M, "Flavored Smokes: Mmmmm...More Profits?" *Tobacco Retailer*, April 2007, http://tobacco-retailer.com/uploads/Features/2007/0407_flavored_smokes.asp.
[9] Delnevo, CD, et al., "Changes in the mass-merchandise cigar market since the Tobacco Control Act," *Tobacco Regulatory Science,* 3(2 Suppl 1): S8-S16, 2017.
[10] Kuiper, NM, et al., "Trends in sales of flavored and menthol tobacco products in the United States during 2011-2015," *Nicotine & Tobacco Research*, published online June 1, 2017.
[11] SAMHSA's public online data analysis system (PDAS). National Survey on Drug Use and Health, 2016, https://pdas.samhsa.gov/#/survey/NSDUH-2016-DS0001?column=CATAG2&results_received=true&row=CGR30BR2&weight=ANALWT_C.
[12] Gammon, DG, et al., "National and state patterns of concept-flavoured cigar sales, USA, 2012-2016," *Tobacco Control*, published online August 1, 2018. See also Viola, AS, et al., "A cigar by any other name would taste as sweet," *Tobacco Control*, published online October 1, 2015. Delnevo, CD, et al., "Changes in the mass-merchandise cigar market since the Tobacco Control Act," *Tobacco Regulatory Science,* 3(2 Suppl 1): S8-S16, 2017.
[13] Delnevo, CD, et al., "Close, but no cigar: certain cigars are pseudo-cigarettes designed to evade regulation," *Tobacco Control*, Online first, doi:10.1136/tobaccocontrol-2016-052935, May 24, 2016.
[14] HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.cdc.gov/Features/YouthTobaccoUse/.
[15] House Committee on Energy & Commerce, "Energy and Commerce Committee Requests Information on Sales and Marketing of Flavored Tobacco Products," October 2, 2009, accessed April 18, 2012 at http://democrats.energycommerce.house.gov/index.php?q=news/energy-and-commerce-committee-requests-information-on-sales-and-marketing-of-flavored-tobacco-p.
[16] Representative Henry A. Waxman, "Rep. Waxman Urges FDA to Ban Clove-Flavored Cigars," Letter to FDA Commissioner Margaret Hamburg, March 28, 2011, accessed April 18, 2012 at http://democrats.energycommerce.house.gov/index.php?q=news/rep-waxman-urges-fda-to-ban-clove-flavored-cigars.
[17] FDA, Center for Tobacco Products, "FDA takes action against four tobacco manufacturers for illegal sales of flavored cigarettes labeled as little cigars or cigars," December 9, 2016, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm532563.htm.
[18] HHS, *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.
[19] Zhu, S-H, et al., "Evolution of Electronic Cigarette Brands from 2013-2014 to 2016-2017: Analysis of Brand Websites," Journal of Medical Internet Research, 20(3), published online March 12, 2018.
[20] Zhu, S-H, et al., "Four Hundred and Sixty Brands of E-cigarettes and Counting: Implications for Product Regulation," *Tobacco Control*, 23(Suppl 3):iii3-iii9, 2014.
[21] Jackler, RK, and Ramamurthi, D. "Unicorn cartoons: marketing sweet and creamy e-juice to youth," *Tobacco Control*, published online August 19, 2016.
[22] Johnson, A, "Up in smoke? Alamance e-cigarette store operators concerned about proposed regulations," Times-News, April 30, 3014, http://www.thetimesnews.com/news/top-news/up-in-smoke-alamance-e-cigarette-store-operators-concerned-about-proposed-regulations-1.313005. The website for VapeRite ATL also boasts that customers can "mix well over 100,000 possible flavor and mix type combinations" [https://atlanta.vaperite.com/#vape-bar, accessed May 30, 2014].
[23] Duke, JC, et al., "Exposure to Electronic Cigarette Television Advertisements Among Youth and Young Adults," *Pediatrics,* June 2, 2014.
[24] Duke, JC, et al., "Exposure to Electronic Cigarette Television Advertisements Among Youth and Young Adults," *Pediatrics,* June 2, 2014
[25] CDC, "Exposure to Electronic Cigarette Advertising Among Middle and High School Students—United States, 2014-2016," *MMWR* 67(10): 294-299, March 16, 2018, https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6710a3-H.pdf.
[26] Alpert, HR, et al., "Free nicotine content and strategic marketing of moist snuff tobacco products in the United States: 2000-2006," *Tobacco Control* 17:332-338, 2008.
[27] Delnevo, C, et al., "Examining market trends in the United States smokeless tobacco use: 2005 – 2011," *Tobacco Control,* October 31, 2012, doi:10.1136/tobaccocontrol-2012-050739.
[28] Delnevo, CD, et al., "Examining market trends in the United States smokeless tobacco use: 2005-2011," *Tobacco Control*, 23: 107-112, 2014.
[29] Chaloupka, F, et al., Analysis of 2012 Nielsen Store Data, results forthcoming.
[30] Kuiper, NM, et al., "Trends in sales of flavored and menthol tobacco products in the United States during 2011-2015," *Nicotine & Tobacco Research*, published online June 1, 2017.
[31] "Flavors Add New Dimension to Tobacco," *Convenience Store News*, October 1, 2007.
[32] American Lung Association, *An Emerging Deadly Trend: Waterpipe Tobacco Use,* February 2007, http://www.lungusa2.org/embargo/slati/Trendalert_Waterpipes.pdf.
[33] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016.
[34] U.S. Federal Trade Commission (FTC), *Cigarette Report for 2017*, 2019, https://www.ftc.gov/system/files/documents/reports/federal-trade-commission-cigarette-report-2017-federal-trade-commission-smokeless-tobacco-report/ftc_cigarette_report_2017.pdf [data for top 5 manufacturers only].
[35] Courtemanche, CJ, et al., "Influence of the Flavored Cigarette Ban on Adolescent Tobacco Use," *American Journal of Preventive Medicine*, published online January 9, 2017.
[36] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.
[37] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.

[38] Dai, H, "Changes in Flavored Tobacco Product Use Among Current Youth Tobacco Users in the United States, 2014-2017," *JAMA Pediatrics*, published online January 7, 2019.
[39] Mantey, DS, et al., "Flavored tobacco use is associated with dual and poly tobacco use among adolescents," *Addictive* Behaviors, 92:84-88, 2019.
[40] Villanti, AC, et al., "Flavored Tobacco Product Use Among U.S. Young Adults," *American Journal of Preventive Medicine* 44(4):388-391, 2013.
[41] HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.cdc.gov/Features/YouthTobaccoUse/.
[42] HHS, *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.
[43] Substance Abuse and Mental Health Services Administration (SAMHSA), HHS, *Results from the 2015 National Survey on Drug Use and Health, NSDUH: Detailed Tables,* 2016. http://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf. Cigars are defined as cigars, cigarillos or little cigars.
[44] 2013 YRBS. King, BA, Dube, SR, & Tynan, MA, "Flavored Cigar Smoking Among U.S. Adults: Findings From the 2009–2010 National Adult Tobacco Survey," *Nicotine & Tobacco Research* 15(2):608-14, 2013, at 610, http://ntr.oxfordjournals.org/content/15/2/608.full.pdf+html.
[45] FDA, "Modifications to Compliance Policy for Certain Deemed Products: Guidance for Industry, Draft Guidance," March 13, 2019, https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM633281.pdf.
[46] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.
[47] Dai, H, "Changes in Flavored Tobacco Product Use Among Current Youth Tobacco Users in the United States, 2014-2017," *JAMA Pediatrics*, published online January 7, 2019.
[48] King, BA, Dube, SR, & Tynan, MA, "Flavored Cigar Smoking Among U.S. Adults: Findings From the 2009–2010 National Adult Tobacco Survey," *Nicotine & Tobacco Research*, August 27, 2012.
[49] King, BA, Dube, SR, & Tynan, MA, "Flavored Cigar Smoking Among U.S. Adults: Findings From the 2009–2010 National Adult Tobacco Survey," *Nicotine & Tobacco Research*, August 27, 2012.
[50] Delnevo, C, et al., "Preference for flavoured cigar brands among youth, young adults and adults in the USA," *Tobacco Control* 24(4):389-94, 2015.
[51] CDC, "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *Morbidity and Mortality Weekly Report (MMWR*), 67(45): 1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.
[52] Real Parents Real Answers, "What you need to know about e-cigarettes – Infographic," April 23, 2014, accessed November 7, 2014, http://www.realparentsrealanswers.com/what-you-need-to-know-about-e-cigarettes-infographic/.
[53] FDA, "Modifications to Compliance Policy for Certain Deemed Products: Guidance for Industry, Draft Guidance," March 13, 2019, https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM633281.pdf.
[54] CDC, "Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students—United States, 2011-2018," *MMWR*, 67(45): 1276-1277. https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm?s_cid=mm6745a5_w. Current use defined as any use in the past month.
[55] Bonhomme, MG, et al., "Flavoured non-cigarette tobacco product use among US adults: 2013-2014," *Tobacco Control*, 25: ii4-ii13, 2016.
[56] Pepper, JK, et al., "Adolescents' interest in trying flavoured e-cigarettes," *Tobacco Control*, 25:ii62-ii66, published online September 15, 2016.
[57] Kong, G, et al., "Reasons for Electronic Cigarette Experimentation and Discontinuation Among Adolescents and Young Adults," *Nicotine & Tobacco Research* 17(7):847-54, July 2015.
[58] Connolly, GN, "The Marketing of Nicotine Addiction by One Oral Snuff Manufacturer," *Tobacco Control* 4(1):73-79, Spring 1995.
[59] CDC, "Tobacco Use Among Middle and High School Students—United States, 2011-2017," MMWR, 67(22): 629-633, June 7, 2018, https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6722a3-H.pdf. CDC, "Tobacco Use Among Middle and High School Students—United States, 2000-2009," *MMWR*, 59(33): 1063-1068, https://www.cdc.gov/mmwr/pdf/wk/mm5933.pdf.
[60] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.
[61] Dai, H, "Changes in Flavored Tobacco Product Use Among Current Youth Tobacco Users in the United States, 2014-2017," *JAMA Pediatrics*, published online January 7, 2019.
[62] See e.g., Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015. Wackowski, OA and Delnevo, CD, "Young Adults' Risk Perceptions of Various Tobacco Products Relative to Cigarettes: Results from the National Young Adult Health Survey," *Health Education & Behavior*, published online August 24, 2015. Villanti, AC, et al., "Correlates of Hookah Use and Predictors of Hookah Trial in U.S. Young Adults," *American Journal of Preventive Medicine,* 48(6):742-746, 2015.
[63] CDC, "Hookahs." Available at http://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/hookahs/. Accessed March 4, 2016.
[64] CDC, "Dangers of Hookah Smoking." Available at http://www.cdc.gov/features/hookahsmoking/. Accessed March 4, 2016.
[65] World Health Organization. WHO Advisory Note: "WaterpipeTobacco Smoking: Health Effects, Research Needs and Recommended Actions by Regulators," WHO 2005; HHS, *Prevention Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/index.html; American Lung Association, *An Emerging Deadly Trend: Waterpipe Tobacco Use,* February 2007, http://www.lungusa2.org/embargo/slati/Trendalert_Waterpipes.pdf. American Lung Association, *Hookah Smoking: A Growing Threat to Public Health,* 2011, http://www.lung.org/assets/documents/tobacco/hookah-policy-brief-updated.pdf.

[66] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015. The 2014 NYTS found that 60.6 percent of middle and high school hookah smokers—totaling over 1 million youth—had used flavored hookah in the past month.
[67] Ambrose, BK, et al., "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014," *Journal of the American Medical Association*, published online October 26, 2015.
[68] Dai, H, "Changes in Flavored Tobacco Product Use Among Current Youth Tobacco Users in the United States, 2014-2017," *JAMA Pediatrics*, published online January 7, 2019.
[69] FDA, *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes,* 2013.
[70] Villanti, A, et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016.
[71] Villanti, A, et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[72] SAMHSA's public online data analysis system (PDAS), National Survey on Drug Use and Health, 2016. https://pdas.samhsa.gov/#/survey/NSDUH-2016-DS0001?column=CATAG3&results_received=true&row=CIG30BR2&weight=ANALWT_C and https://pdas.samhsa.gov/#/survey/NSDUH-2016-DS0001?column=CATAG3&control=NEWRACE2&results_received=true&row=CIG30BR2&weight=ANALWT_C.
[73] Sterling, K, et al., "Association between menthol-flavoured cigarette smoking and flavoured little cigar and cigarillo use among African-American, Hispanic, and white young and middle-aged adult smokers," *Tobacco Control* 25(Suppl 2):ii21-ii31, November 2016.
[74] Tobacco Products Scientific Advisory Committee, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf
[75] FDA, *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes,* 2013.
[76] Carpenter, CM, et al, "New Cigarette Brands with Flavors that Appeal to Youth: Tobacco Marketing Strategies," *Health Affairs* 24(6):1601-1610, Nov/Dec 2005. Lewis, M, et al., "Dealing with an Innovative Industry: A Look at Flavored Cigarettes Promoted by Mainstream Brands," *American Journal of Public Health* 96(2), February 2006.
[77] Klein, S, et al., Use of flavored cigarettes among older adolescent and adult smokers: United States, 2004 – 2005," *Nicotine and Tobacco Research*, Volume 10, Number 7, July 2008.
[78] Klein, S et al., Use of flavored cigarettes among older adolescent and adult smokers: United States, 2004 – 2005," *Nicotine and Tobacco Research*, Volume 10, Number 7, July 2008.
[79] HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.cdc.gov/Features/YouthTobaccoUse/.
[80] Marketing Innovations, "Youth Cigarette - New Concepts," Memo to Brown & Williamson, September 1972, Bates No. 170042014.
[81] R.J. Reynolds Tobacco Company, "Conference report #23," June 5, 1974, Bates No. 500254578-4580.
[82] R.J. Reynolds Inter-office Memorandum, May 9, 1974, Bates No. 511244297-4298.
[83] R.M. Manko Associates report for Lorillard, Summary Report: New Flavors Focus Group Sessions, August, 1978, Bates No. 85093450-3480.
[84] Connolly, GN, "The Marketing of Nicotine Addiction by One Oral Snuff Manufacturer," *Tobacco Control* 4(1):73-79, Spring 1995.
[85] "Juiced Up: How a Tobacco Giant Doctors Snuff Brands to Boost Their 'Kick,'" *The Wall Street Journal*, October 26, 1994.
[86] National Association of Tobacco Outlets v. City of Providence, 731 F.3d 71 (1st Cir. 2013); U.S. Smokeless Tobacco Company v. FDA , 708 F.3d 428 (2d Cir. 2013 ).

# IMPACT OF MENTHOL CIGARETTES ON YOUTH SMOKING INITIATION AND HEALTH DISPARITIES

Cigarettes with specific characterizing flavors were prohibited in the U.S. on September 22, 2009, as part of the Family Smoking Prevention and Tobacco Control Act (TCA) that gave the U.S. Food and Drug Administration (FDA) authority over tobacco products.[1] This provision excluded menthol cigarettes, which have subsequently increased their share of the cigarette market. Sales of menthol cigarettes increased from 2011 to 2015, at a time when overall cigarette sales have been gradually decreasing.[2] Data from the Federal Trade Commission (FTC) show that in 2017, menthol cigarettes comprised 36 percent of the market, the highest proportion on record since FTC began collecting this data in 1963.[3]

Menthol cigarettes pose a tremendous public health threat. A 2013 FDA report on the health impact of menthol cigarettes determined that menthol cigarettes lead to increased smoking initiation among youth and young adults, greater addiction and decreased success in quitting smoking.[4] Further, FDA's Tobacco Products Scientific Advisory Committee's (TPSAC)[*] concluded, "**Removal of menthol cigarettes from the marketplace would benefit public health in the United States**."[5] Ontario, Canada banned menthol cigarettes as of January 1, 2017 and initial evaluation results suggest that the law led to increased quit attempts and smoking cessation among adult menthol smokers.[6] The Canadian government subsequently banned menthol cigarettes nationwide in October 2017.

**Menthol Makes it Easier for Youth to Initiate Tobacco Use**

The tobacco companies know that almost all new tobacco users begin their addiction as kids, but they also know that to novice smokers, tobacco can be harsh and unappealing. Internal tobacco industry documents show that tobacco companies have a long history of using flavors to reduce the harshness of their products to make them more appealing to new users, almost all of whom are under age 18.[7] By masking the harshness and soothing the irritation caused by tobacco smoke, flavors make it easier for beginners – primarily kids – to experiment with the product and ultimately become addicted.
Menthol has particularly appealing qualities for novice smokers. Menthol is a chemical compound that cools and numbs the throat, reducing the harshness of cigarette smoke, thereby making menthol cigarettes more appealing to youth who are initiating tobacco use.[8] As TPSAC noted, "Menthol cannot be considered merely a flavoring additive to tobacco. Its pharmacological actions reduce the harshness of smoke and the irritation from nicotine."[9] According to TPSAC's conclusions:[10]

- Menthol cigarettes increase the number of children who experiment with cigarettes and the number of children who become regular smokers, increasing overall youth smoking.

- Young people who initiate using menthol cigarettes are more likely to become addicted and become long-term daily smokers.

As the only flavored cigarette left on the market, it is no surprise that menthol cigarettes remain popular among youth. In fact, a study analyzing the impact of the 2009 ban on characterizing flavors in cigarettes on youth tobacco use found that use of menthol cigarettes among high schoolers significantly increased

[*] TPSAC is a group of scientific experts charged with advising the Commissioner of Food and Drugs on safety, dependence, and health issues relating to tobacco. See https://www.fda.gov/advisoryCommittees/CommitteesMeetingMaterials/tobaccoproductsScientificAdvisoryCommittee/default.htm for more details.

after the ban.[11] Since the reports from FDA and TPSAC, research has continued to demonstrate the popularity of menthol cigarettes among youth and menthol's role in smoking initiation:

- Youth smokers are more likely to use menthol cigarettes than any other age group. Over half (54 percent) of youth smokers ages 12-17 use menthol cigarettes, compared to less than one-third of smokers ages 35 and older.[12]

- Prevalence of menthol use is even higher among African American youth: seven out of ten African-American youth smokers smoke menthol cigarettes.[13]

- The popularity of menthol flavored cigarettes is also evidenced by brand preference among youth. According to data from According to data from the 2015 National Survey on Drug Use and Health, one in five smokers ages 12-17 prefers Newport cigarettes, a heavily marketed menthol cigarette brand. Preference for Newport is even higher among African-American youth smokers (69.1 percent) because of targeted marketing by the tobacco industry. [14]

- Data from Wave 1 of the government's Population Assessment of Tobacco and Health (PATH) study found that youth menthol smokers are more likely to perceive menthol cigarettes as easier to smoke than regular cigarettes.[15]

- Data from Truth Initiative's Young Adult Cohort Study, a national study of 18-34 year olds, showed that 52 percent of new young adult smokers initiated with menthol cigarettes. Initiation with menthol cigarettes was higher among black smokers (93.1%) compared to white smokers (43.9%).[16]

**Menthol Increases Addiction and Makes it Harder for Smokers to Quit**

While the tobacco industry initially marketed menthol cigarettes as safer and healthier cigarettes, because of their cooling properties and reduced throat irritability, this could not be further from the truth.[17] In fact, because menthol cigarettes are less harsh, they are associated with increased initiation and greater addiction, and FDA found that it is "**likely that menthol cigarettes pose a public health risk above that seen with nonmenthol cigarettes**."[18]

Both TPSAC's and FDA's own scientific analyses conclude that menthol cigarettes are associated with increased nicotine dependence and reduced success in smoking cessation.[19] TPSAC projected that by 2020, about 17,000 premature deaths will be attributable to menthol cigarettes and about 2.3 million people will have started smoking because of menthol cigarettes.[20]

Research continues to bolster the findings of FDA and TPSAC. A 2014 randomized clinical trial of FDA-approved cessation treatments among 1,500 US adult smokers found that menthol smoking was associated with reduced likelihood of quitting, compared to non-menthol smoking. African American female smokers had the quit rates of all groups in the study.[21] A meta-analysis of findings from nearly 150,000 smokers found that among African Americans, menthol smokers have a 12% lower odds of smoking cessation compared to non-menthol smokers.[22]

The difficulty that menthol smokers have in quitting continues to be reflected in national smoking prevalence and sales trends. Between 2009 and 2016, sales of non-menthol cigarettes have declined by 25.8% nationally, while sales of menthol cigarettes have declined by only 2.2%.[23] While smoking rates have declined overall in recent years, use of menthol cigarettes has increased significantly. Menthol smoking rates have increased among young adults and remained constant among youth and adults, while non-menthol smoking has decreased in all three age groups.[24] Overall, nearly 40 percent (38.8%) of smokers use menthol cigarettes.

In recent years, use of menthol cigarettes has increased among White, Asian, and Hispanic smokers. Use of menthol cigarettes has remained constant among African-American smokers, who continue to use menthol cigarettes more than any other racial/ethnic group.[25] Research also shows that use of menthol cigarettes has perpetuated disparities among those with mental illness. Data from the 2008 and 2009 National Survey on Drug Use and Health show that smokers with severe psychological distress were significantly more likely to use menthol cigarettes than smokers with no or mild psychological distress.[26]

**Use of Menthol Cigarettes Leads to Health Disparities for African Americans**

Prevalence of menthol use is highest among African Americans - 85 percent of all African-American smokers smoke menthol cigarettes, compared to 29 percent of Whites.[27] The tobacco industry's "investment" in the African-American community has had a destructive impact. TPSAC's report and FDA's analysis conclude that African Americans are disproportionately burdened by the health harms of menthol cigarettes. Specifically, TPSAC concluded that the marketing and availability of menthol cigarettes increases the overall prevalence of smoking and reduces cessation among African Americans.[28]

- African Americans generally have higher levels of nicotine dependence as a consequence of their preference for mentholated cigarettes.[29] While research shows that African American smokers are highly motivated to quit smoking and are more likely than White smokers to have made a quit attempt and used counseling services in the previous year, they are less likely than White smokers to successfully quit smoking.[30]

- TPSAC estimated that by 2020, 4,700 excess deaths in the African-American community will be attributable to menthol cigarettes, and over 460,000 African Americans will have started smoking because of menthol cigarettes.[31]

- African Americans suffer the greatest burden of tobacco-related mortality of any racial or ethnic group in the United States. Each year, approximately 45,000 African Americans die from a smoking-caused illness. Unless action is taken, an estimated 1.6 million African Americans alive today, who are now under the age of 18, will become regular smokers; and about 500,000 of these will die prematurely from a tobacco-related disease.[32]

- Lung cancer is the second most common cancer in both African-American men and women, but it kills more African Americans than any other type of cancer.[33] Decreased cessation success due to the popularity of menthol cigarettes among African Americans likely contributes to this mortality disparity.[34]

**The Tobacco Industry Targets Minorities and Youth with Menthol Cigarette Marketing**

The greater popularity of menthol cigarettes among African Americans, youth, and other minorities is a direct result of a decades-long marketing campaign by the tobacco industry. In fact, TPSAC concluded that menthol cigarettes are marketed disproportionately to younger smokers and African Americans.[35] Dating back to the 1950s, the tobacco industry has targeted these communities with marketing for menthol cigarettes through sponsorship of community and music events, targeted magazine advertising, youthful imagery, and marketing in the retail environment.

***Music and Community Event Sponsorship.*** Beginning in the 1970s, the major tobacco companies competed for the African American market share by sponsoring music and community events like Brown & Williamson's "Kool Jazz Festival," R.J. Reynolds' "Salem Summer Street Scenes," and Phillip Morris's "Club Benson & Hedges" promotional bar nights.[36] Kool also sponsored Latin music festivals, including the branded "Kool Latino Festival," in the 1970s and 1980s.[37]

***Magazine Advertising.*** Expenditures for magazine advertising of mentholated cigarettes increased from 13 percent of total ad expenditures in 1998 to 76 percent in 2006.[38] During the two years after the Master Settlement Agreement (MSA) in November 1998, the average annual expenditures for Newport in magazines with high youth readership increased 13.2 percent (from $5.3 to $6.0 million).[39] Between 1998–2002, *Ebony,* a magazine tailored to African-American culture, was 9.8 times more likely than *People* to contain ads for menthols.[40] One study comparing the English and Spanish language versions of *Cosmopolitan* and *Glamour* from 1998-2002 found that 51 percent of the cigarette ads in the Spanish language versions were for menthol brands, compared to only 28 percent in the English language versions.[41]

***Youthful Imagery.*** The tobacco companies commonly use youthful imagery in its advertising to appeal to young consumers. As a R.J. Reynolds document from 1981 noted, "The benefit of smoking which has most frequently and most successfully been exploited by brand families appears to be Social Interaction. For example, some brands, such as Newport, have focused on the younger adult 'peer group' aspect of social interaction."[42] Newport's "Alive with Pleasure" campaign, which continues today, portrays smokers in fun, social environments in its advertisements.[43] In 2004, Brown & Williamson started an ad campaign for their Kool brand cigarettes clearly aimed at youth—and African-American youth, in particular. The Kool Mixx campaign featured images of young rappers, disc jockeys and dancers on cigarette packs and in advertising. The campaign also included radio giveaways with cigarette purchases and a Hip-Hop disc jockey competition in major cities around the country. The themes, images, radio giveaways and music involved in the campaign all clearly have tremendous appeal to youth, especially African-American youth. Attorneys General from several states promptly filed motions against Brown & Williamson for violating the Master Settlement Agreement.[44]

***Retail Promotions.*** For decades, tobacco companies have specifically targeted minority communities, particularly African Americans, with intense advertising and promotional efforts. Beginning in the 1970s, the major tobacco companies used mobile van programs, like the Newport Pleasure Van, to expand their reach in urban areas through product sampling and coupon distribution.[45] The tobacco companies also developed specific strategies and specially designed product displays to adapt their point-of-sale marketing to smaller retailers that were more common in urban areas. Phillip Morris implemented promotion programs and paid retailers to exhibit product displays and grow their inventory. Brown & Williamson launched its Kool Inner City Point of Purchase Program, later the Kool Inner City Family Program, with the explicit goal, "to reach the core of Kool's franchise (young, black, relatively low income and education),"[46] with both retailer and consumer promotions.[47] Today, menthol cigarettes continue to be heavily advertised, widely available, and priced cheaper in certain African-American communities, making them more appealing, particularly to price-sensitive youth. A wealth of research indicates that African-American neighborhoods have a disproportionate number of tobacco retailers, pervasive tobacco marketing, and in particular, more marketing of menthol products.[48]

- Like many minority and low-income neighborhoods, African-American neighborhoods tend to have more tobacco retailers. Nationwide, census tracts with a greater proportion of African American residents have higher tobacco retailer density.[49]

- A 2011 study of cigarette prices in retail stores across the U.S. found that Newport cigarettes are significantly less expensive in neighborhoods with higher proportions of African Americans.[50]

- The 2011 California Tobacco Advertising Survey reports that there were significantly more menthol advertisements at stores in neighborhoods with a higher proportion of African-American residents and in low-income neighborhoods.[51]

- Another 2011 California study found that as the proportion of African-American high school students in a neighborhood rose, the proportion of menthol advertising increased, the odds of a Newport promotion were higher, and the cost of Newport cigarettes was lower.[52]

- A 2013 study of tobacco retail outlets in St. Louis found more tobacco advertising, including more menthol advertising, in areas with a greater proportion of African-American residents.[53] Another 2013 study found similar patterns in Ramsey County, Minnesota.[54]

**FDA Action Needed to Prohibit Menthol Cigarettes**

Despite strong evidence from the FDA and TSPAC reports and continued research on the public health harms, the FDA has yet to take action to prohibit menthol cigarettes. In 2013, the FDA issued an Advanced Notice of Proposed Rulemaking (ANPRM), soliciting additional research and comments from the public on prohibiting menthol cigarettes. In 2018, the FDA issued another ANPRM, seeking additional evidence on the public health harms of menthol cigarettes, along with other flavored tobacco products. Neither of these ANPRMs have led to the issuance of a rule to prohibit menthol cigarettes; however, in November 2018, FDA Commissioner Scott Gottlieb announced the agency's intention to ban menthol in combustible tobacco products, including cigarettes and cigars.[55] This announcement received strong support from the public health and African American communities, including the National Association for the Advancement of Colored People (NAACP), the National Urban League, the National African American Tobacco Prevention Network and the African American Tobacco Control Leadership Council.[56]

**State and Local Action to Restrict the Sale of Menthol Tobacco Products**

States and localities can implement additional sales restrictions on menthol cigarettes and flavored non-cigarette tobacco products. Despite inevitable opposition from tobacco companies, states and localities have clear authority to restrict the sale of flavored tobacco products (or any tobacco product) to reduce tobacco use and its harms to its citizens. Over 200 localities around the country restrict sales of flavored tobacco products, and at least 50 of these include menthol cigarettes in their sales restriction.[57] For example:

- In 2017, the San Francisco Board of Supervisors unanimously passed an ordinance to prohibit the sale of all flavored tobacco products, including menthol cigarettes and e-cigarettes.[58] This law, originally slated to go into effect on April 1, 2018, is the strongest flavor restriction in the US. However, R.J. Reynolds, manufacturer of the top-selling menthol brand, quickly responded by gathering signatures for a referendum petition, allowing voters to decide on the June 2018 ballot whether the restriction should be implemented.[59] San Francisco residents overwhelmingly voted (68.4% to 31.6%)[60] to implement the flavored tobacco sales restriction, despite the industry spending nearly $12 million to try to defeat the initiative.[61] Many California municipalities, including Sacramento, have followed San Francisco's lead and passed comprehensive sales restrictions.

- Oakland, CA's ordinance, effective July 1, 2018, restricts the sale of all flavored tobacco products, including menthol cigarettes and e-cigarettes, except in adult-only tobacco retailers.[62]

- Minneapolis and St. Paul, MN originally passed restrictions that restricted the sale of all flavored tobacco products, excluding menthol cigarettes, in all stores except adult-only tobacco retailers (effective 1/1/2016 and 4/15/2016, respectively). However, in 2017, both cities voted to expand these laws to also restrict the sale of menthol flavored tobacco products in all stores except adult-only tobacco retailers and liquor stores (effective 8/1/2018 and 11/1/2018, respectively).[63]

The Canadian government banned menthol cigarettes in October 2017, although most provinces had banned menthol cigarettes prior to the nationwide law. Preliminary evaluation results from Ontario, which banned menthol cigarettes on January 1, 2017, suggest that menthol smokers had higher rates of quitting and quit attempts following implementation of the law than non-menthol smokers.[64] These results are promising, but it is important to note that menthol cigarettes comprised a much smaller proportion of the

Canadian cigarette marketplace (~5%) than the US marketplace (36%), and the demographics of menthol smokers are very different between the two countries.

***Campaign for Tobacco-Free Kids, June 20, 2019 / Laura Bach***

**More information on Tobacco and African Americans is available at https://www.tobaccofreekids.org/fact-sheets/tobaccos-toll-health-harms-and-cost/toll-of-tobacco-on-specific-populations-african-americans**

**More information on Flavored Tobacco Products is available at tfk.org/flavortrap and http://www.tobaccofreekids.org/research/factsheets/pdf/0383.pdf.**

[1] See U.S. Food and Drug Administration's (FDA) Flavored Tobacco webpage at http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/FlavoredTobacco/default.htm.
[2] Kuiper, NM, et al., "Trends in sales of flavored and menthol tobacco products in the United States during 2011-2015," *Nicotine & Tobacco Research*, published online June 1, 2017.
[3] U.S. Federal Trade Commission (FTC), *Cigarette Report for 2017*, 2019, https://www.ftc.gov/system/files/documents/reports/federal-trade-commission-cigarette-report-2017-federal-trade-commission-smokeless-tobacco-report/ftc_cigarette_report_2017.pdf [data for top 5 manufacturers only].
[4] FDA. *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes* (2013).
[5] Tobacco Products Scientific Advisory Committee (TPSAC), FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[6] Chaiton, MO, et al., "Ban on menthol-flavoured tobacco products predicts cigarette cessation at 1 year: a population cohort study," *Tobacco Control*, published online May 29, 2019. Chaiton, M, et al., "Association of Ontario's ban on menthol cigarettes with smoking behavior 1 month after implementation," *JAMA Internal Medicine*, published online March 5, 2018.
[7] HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, http://www.cdc.gov/Features/YouthTobaccoUse/.
[8] FDA. *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes* (2013).
[9] TPSAC, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[10] TPSAC, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[11] Courtemanche, CJ, et al., "Influence of the Flavored Cigarette Ban on Adolescent Tobacco Use," *American Journal of Preventive Medicine*, published online January 9, 2017.
[12] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[13] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[14] SAMHSA's public online data analysis system (PDAS), National Survey on Drug Use and Health, 2015. http://pdas.samhsa.gov/#/survey/NSDUH-2015-DS0001/crosstab/?row=CIG30BR2&column=CATAG3&control=NEWRACE2&weight=ANALWT_C&results_received=true and https://pdas.samhsa.gov/#/survey/NSDUH-2015-DS0001/crosstab/?column=CATAG3&results_received=true&row=CIG30BR2&weight=ANALWT_C.
[14] FDA. *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol versus Nonmenthol Cigarettes* (2013).
[15] Cohn, AM, et al., "Menthol Smoking Patterns and Smoking Perceptions Among Youth: Findings from the Population Assessment of Tobacco and Health Study," American Journal of Preventive Medicine, 56(4): e107-e116, 2019.
[16] D'Silva, J, et al., "Differences in Subjective Experiences to First Use of Menthol and Nonmenthol Cigarettes in a National Sample of Young Adult Cigarette Smokers," *Nicotine & Tobacco Research*, 20(9): 1062-1068, 2018.
[17] Anderson, SJ, et al., "Marketing of menthol cigarette sand consumer perceptions: a review of tobacco industry documents," *Tobacco Control*, 20(Suppl 2): ii20-ii28, 2011.
[18] FDA, "Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes," http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PeerReviewofScientificInformationandAssessments/UCM361598.pdf, 2013.
[19] TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf

[20] TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf
[21] Smith, SS, et al., "Smoking cessation in smokers who smoke menthol and non-menthol cigarettes," *Addiction*, 109: 2107-2117, 2014.
[22] Smith, PH, et al., "Use of Mentholated Cigarettes and Likelihood of Smoking Cessation in the United States: A Meta-Analysis," *Nicotine & Tobacco Research*, 2019, published online June 17, 2019.
[23] Estimate based on market share data from FTC, *Cigarette Report for 2014, 2016*. [Data for top 5 manufacturers only] and pack sales data from the Alcohol and Tobacco Tax and Trade Bureau (TTB), https://www.ttb.gov/tobacco/tobacco-stats.shtml.
[24] Giovino, GA, et al., "Differential trends in cigarette smoking in the USA: is menthol slowing progress?" *Tobacco Control*, 2013.
[25] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016.
[26] Hickman, NJ, et al., "Menthol use among smokers with psychological distress: findings from the 2008 and 2009 National Survey on Drug Use and Health," *Tobacco Control*, 23: 7-13, 2014.
[27] Villanti, A., et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014," *Tobacco Control*, published online October 20, 2016
[28] TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf
[29] FDA, "Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes," http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PeerReviewofScientificInformationandAssessments/UCM361598.pdf, 2013; Tobacco Products Scientific Advisory Committee, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697;pdf.; Alexander, LA, et al., "Why we must continue to investigate menthol's role in the African American smoking paradox," *Nicotine & Tobacco Research, 18(S1):* S91-S101, 2016;
[30] See e.g., CDC, "Quitting Smoking Among Adults—United States, 2000-2015," *MMWR*, 65(52): 1457-1464, January 6, 2017, https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6552a1.pdf. Royce, J, et al., "Smoking cessation factors among African Americans and Whites: COMMIT Research Group," *American Journal of Public Health* 83(2):220-6, February 1993.
https://www.fda.gov/advisoryCommittees/CommitteesMeetingMaterials/tobaccoproductsScientificAdvisoryCommittee/default.htm
[31] TPSAC, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[32] HHS, "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.
[33] American Cancer Society, "Cancer Facts & Figures for African Americans, 2016-2018," 2016, http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-047403.pdf.
[34] Alexander, LA, et al., "Why we must continue to investigate menthol's role in the African American smoking paradox," *Nicotine & Tobacco Research*, 18 (Suppl 1): S91-S101, 2016.
[35] TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, July 21, 2011 https://wayback.archive-it.org/7993/20170405201731/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[36] Hafez, N. & Ling, P.M. "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control 15:* 359-366, 2006. See also Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007. RJ Reynolds. Black Street Scenes: review and recommendations. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1983. Available at http://legacy.library.ucsf.edu/tid/onb19d00.
[37] Hafez, N, & Ling, P, "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control*, 15: 359-366, 2006.
[38] Alpert, H, Koh, HK, & Connolly, GN, "After the Master Settlement Agreement: Targeting and exposure of youth to magazine tobacco advertising," *Health Affairs* 27(6):w503-w512, 2008.
[39] King, C, et al., "The Master Settlement Agreement with the tobacco industry and cigarette advertising in magazines," *New England Journal of Medicine* 345(7):504-11, August 2001.
[40] Landrine, H, et al., "Cigarette advertising in Black, Latino and White magazines, 1998-2002: An exploratory investigation," *Ethnic Disparities* 15(1):63-7, 2005.
[41] Fernandez, S, et al., "Cigarette Advertising in Magazines for Latinas, White Women, and Men, 1998-2002: A Preliminary Investigation," *Journal of Community Health*, 30(2): 141-151, 2005.
[42] RJ Reynolds. Strategic Research Report: The 1981 Brand Family Segmentation Study. Mangini, 1982. https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/#id=zfbf0092.
[43] Anderson, SJ, et al., "Marketing of menthol cigarette sand consumer perceptions: a review of tobacco industry documents," *Tobacco Control*, 20(Suppl 2): ii20-ii28, 2011.
[44] Hafez, N, & Ling, P, "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control*, 15: 359-366, 2006.

45 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007. Hafez, N. & Ling, P.M. "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control 15:* 359-366, 2006.
46 Hudson RC. Brown & Williamson. Inner city POP Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1979 Oct 15. http://legacy.library.ucsf.edu/tid/icb91d00.
47 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.
48 Lee, JGL, et al., "A Systematic Review of Neighborhood Disparities in Point-of-Sale Tobacco Marketing," *American Journal of Public Health*, published online ahead of print July 16, 2015.
49 Rodriguez, D, et al., "Predictors of tobacco outlet density nationwide: a geographic analysis," *Tobacco Control,* published online first on April 4, 2012. See also Lee, JGL, et al., "Inequalities in tobacco outlet density by race, ethnicity and socioeconomic status, 2012, USA: results from the ASPIRE Study," *Journal of Epidemiology and Community Health*, published online March 1, 2017.
50 Resnick, EA, et al., *Cigarette Pricing Differs by U.S. Neighborhoods—A BTG Research Brief.* Chicago, IL: Bridging the Gap Program, Health Policy Center, Institute for Health Resarch and Policy, University of Illinois at Chicago, 2012, www.bridgingthegapresearch.org.
51 Schleicher, N, et al., "Tobacco Marketing in California's Retail Environment (2008-2011), Final report for the California Tobacco Advertising Survey. Stanford, CA: Stanford Prevention Research Center, July 2013.
52 Henriksen, L., et al., "Targeted Advertising, Promotion, and Price for Menthol Cigarettes in California High School Neighborhoods," Nicotine & Tobacco Research, June 24, 2011.
53 Moreland-Russell, S. "Disparities and Menthol Marketing: Additional Evidence in Support of Point of Sale Policies," *International Journal of Environmental Research and Public Health*, 10: 4571-4583, 2013.
54 Widome, R, et al., "The relationship of neighborhood demographic characteristics to point-of-sale tobacco advertising and marketing," *Ethnicity & Disease* 18(2): 136-151, 2013.
55 FDA, "Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new stesp to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes," November 15, 2018, https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625884.htm.
56 NAACP, "NAACP Statement on FDA Plan to Ban Sale of Menthol and E-Cigarettes," November 14, 2018, https://www.naacp.org/latest/naacp-statement-fba-plan-ban-sale-menthol-e-cigarettes/. National Urban League, "National Urban League: Proposed Menthol Cigarette Ban Would Benefit African Americans' Health," November 13, 2018, http://nul.iamempowered.com/content/national-urban-league-proposed-menthol-cigarette-ban-would-benefit-african-americans-health.
57 Campaign for Tobacco-Free Kids, "States & Localities That Have Restricted the Sale of Flavored Tobacco Products," https://www.tobaccofreekids.org/assets/factsheets/0398.pdf.
58 San Francisco Health Code 140-17, Banning the Sale of Flavored Tobacco Products, http://sfbos.org/sites/default/files/o0140-17.pdf
59 Swan, R., "SF's battle over flavored tobacco heats up," *San Francisco Chronicle*, September 4, 2017, http://www.sfchronicle.com/bayarea/article/SF-s-battle-over-flavored-tobacco-heats-up-12172353.php. Matier & Ross, "SF ban on flavored tobacco looks headed for the ballot," *San Francisco Chronicle*, July 26, 2017, http://www.sfchronicle.com/bayarea/article/SF-ban-on-flavored-tobacco-looks-headed-for-the-11408689.php.
60 City and County of San Francisco Department of Elections. June 5, 2018 Election Results – Summary. See Local Measure E - Prohibiting Tobacco Retailers from Selling Flavored Tobacco Products. https://sfelections.sfgov.org/june-5-2018-election-results-summary.
61 Hoffman, J. "San Francisco Voters Uphold Ban on Flavored Tobacco Products," *New York Times*, June 6, 2018, https://www.nytimes.com/2018/06/06/health/vaping-ban-san-francisco.html.
62 Oakland Municipal Code Chapter 5.91, Licensure of Tobacco Retailers, https://library.municode.com/ca/oakland/ordinances/code_of_ordinances?nodeId=854090.
63 Minneapolis, MN. Municipal Code, Tobacco Dealers: https://www.municode.com/library/mn/minneapolis/codes/code_of_ordinances?nodeId=COOR_TIT13LIBURE_CH281TODE_281.15DE. St. Paul, MN Legislative Code Chapter 324, https://stpaul.legistar.com/LegislationDetail.aspx?ID=3145418&GUID=42F0956E-EBB2-43E4-A74C-76FCC9A9E37C&Options=&Search= .
64 Chaiton, MO, et al., "Ban on menthol-flavoured tobacco products predicts cigarette cessation at 1 year: a population cohort study," *Tobacco Control*, published online May 29, 2019. Chaiton, M, et al., "Association of Ontario's ban on menthol cigarettes with smoking behavior 1 month after implementation," *JAMA Internal Medicine*, published online March 5, 2018.

*"Menthols in general do better among the very young, and among very young blacks, almost the entire market is accounted for by Kool, Salem and Newport."*
-1974 research report prepared for Philip Morris[1]

The tobacco industry has a long history of going to great lengths to target the African-American community. Decades of research and the tobacco industry's internal documents affirm that the industry employs multiple campaigns and strategies to aggressively target and reach African Americans. Dating back to the 1950s, the tobacco industry has targeted African Americans with marketing for menthol cigarettes through sponsorship of community and music events, targeted magazine advertising, youthful imagery, price discounting and marketing in the retail environment.

This aggressive targeted marketing has paid off. African-American smokers, both adults and youth, now overwhelmingly prefer menthol cigarettes. Overall, 85 percent of African-American smokers (ages 12+), including 71.3 percent of African American youth smokers smoke menthol cigarettes.[2] The popularity of menthol is also evident in the cigarette brand preferences of African American youth who smoke. According to data from the 2015 National Survey on Drug Use and Health, 69.1 percent of African-American youth ages 12-17 prefer Newport brand cigarettes.[3] This preference for menthol cigarettes is the direct result of a decades-long marketing campaign by the tobacco industry.

**The Early Days: Building a Market for Menthol[4]**

The marketing of menthol cigarettes to the African-American community dates back to at least the 1950s. Salem led the menthol market in the 1950s and 1960s and is credited with establishing a popular market for menthols (menthols were initially a specialty cigarette, marketed for reducing throat irritability), but Kool overtook Salem in popularity in 1972.[5] Brown & Williamson began targeting African-Americans with Kool cigarettes after a 1953 survey showed that five percent of African Americans preferred Kool compared to two percent of White Americans. Brown & Williamson[*] seized the opportunity to capitalize upon this small preference margin, recognizing the marketing advantage of appealing to a newly urbanized and more concentrated population.[6] The establishment of popular African American magazines like *Ebony* and *Jet* also provided marketing venues that had not previously existed for reaching African Americans.

Kool advertisement, 1966
Image courtesy of Stanford Research into the Impact of Advertising (SRITA)

Brown & Williamson took to the airwaves to market Kool, with an advertising budget exceeding that of the other tobacco companies in the 1960s. During this time, cigarette advertisements, many featuring famous black athletes, tripled in *Ebony*.[7] The aggressive marketing campaign had a huge impact - from just 1968 to 1976, the percentage of African Americans smoking Kool jumped from 14 percent to 38 percent, with even greater preference for Kool among young African American males.[8] An R.J. Reynolds analyst noted that, "Kool became 'cool' and, by the early 1970s, had a 56% share among younger adult Blacks—it was the Black Marlboro."[9] Salem's successful initial promotion of the menthol category and Kool's

[*] Brown & Williamson merged with R.J. Reynolds in 2004, acquiring Kool. However, R.J. Reynolds and Lorillard merged in 2015, at which time R.J. Reynolds divested the Salem and Kool brands to ITG, while acquiring the Newport brand.

monopolization of the African American market played a significant role in the exponential growth of the menthol market, which grew by nearly 50 percent from 1956 to 1971.[10]

**The "Menthol Wars"**

Tobacco companies used multiple strategies to attract new customers in predominantly African American neighborhoods. When other tobacco companies realized Kool's growth initiated from targeting African Americans, they began competing for this market share with targeted marketing for Kool, Newport, Salem and Benson & Hedges. The companies contracted with "ethnic marketing firms" to conduct at least eight distinct campaigns targeting primarily African American populations: the Brown & Williamson Kool Van Program, the Brown & Williamson Kool Inner City Family Program, the Lorillard Inner City Sales Program, the Lorillard Newport Van Program, the Philip Morris Inner City Task Force, the Philip Morris Inner City Marketing Program, the R.J. Reynolds Black Market Program, and the R.J. Reynolds Black Young Adult Smoker Initiative (some of these programs continued into the 1990s).[11]


Kool advertisement, 1984
Image courtesy of Stanford Research into the Impact of Advertising (SRITA)

***Sampling and Mobile Van Programs***

The tobacco companies considered sampling to be an important strategy for attracting new customers, and they employed mobile van programs in across the country to reach African Americans.

- Lorillard introduced the Newport Pleasure Van program in 1979 in New York, expanding to cities across the United States to distribute free samples and coupons. The Newport Pleasure Van program incorporated a plan to facilitate brand switching, by rewarding customers who provided the contact information of known competitive brand smokers. Newport continued the Pleasure Vans through 1994, by which time it had successfully gained dominance of the menthol market.[12]

- In the 1980s, as part of the Kool Market Development Program, vans (mimicking Lorillard's strategy) traveled through Houston to distribute free cigarette samples, a program which later expanded to 50 cities. [13]

> *"A total of 1.9MM samples will be distributed to targeted smokers in 1983. Sample distribution will be targeted to: housing projects, clubs, community organizations and events where Kool's black young adult target congregate."*
> – Kool Market Development Program[14]

- R.J. Reynolds launched a van sampling program in Chicago that targeted nightclubs and neighborhood events with the Salem brand.

***Retailer Programs***

The tobacco companies developed specific strategies and specially designed product displays to adapt their point-of-sale marketing to smaller retailers that were more common in cities. Philip Morris implemented promotional programs and paid retailers to exhibit product displays and grow their inventory. Brown & Williamson launched its Kool Inner City Point of Purchase Program, later the Kool Inner City Family Program, with the explicit goal, "to reach the core of Kool's franchise (young, black, relatively low income and education),"[15] with both retailer and consumer promotions.[16]

### *Music and Event Sponsorship*

The tobacco companies also recognized the value of associating their brand with popular community events.

- Brown & Williamson used music as a way to target African Americans beginning in 1975 with the Kool Jazz Festival, and later the Kool City Jam, a free two-day concert.[17]

- R.J. Reynolds sponsored the “Salem Summer Street Scenes” festivals, during which they estimated reaching at least half of African Americans in Memphis, Detroit, Chicago, New York, and Washington, D.C.[18]

- Philip Morris sponsored “Club Benson & Hedges” promotional bar nights throughout the 1990s, targeting clubs frequented by African-Americans.[19]

Despite Kool and Salem’s dramatic rise and market share in the 1960s and 1970s, Newport’s aggressive marketing in the “Menthol Wars” era successfully doubled its share of the menthol market between 1981 and 1987, and in 1993 it became—and has remained—the market leader in sales of menthol cigarettes.[20]

### Appealing to Younger African Americans

Newport also grew its African American market share by purposefully attracting a younger consumer base.[21] Industry documents show that the tobacco companies knew that while menthol cigarettes were attractive to younger smokers, novice smokers actually preferred cigarettes with a lower menthol content, whereas older smokers preferred more menthol content. With its lower menthol content, Newport had a market advantage with younger smokers, and the brand’s youthful advertising made it even more appealing.[22]

Newport capitalized on the youth appeal of its product by employing youth-friendly marketing materials. In describing their Newport marketing strategy, Lorillard noted that, “Newport smokers perceive other Newport smokers as they do themselves—younger, outgoing, active, happy, warm, friendly, modern, extroverted.”[23] To this day, Newport cigarettes are advertised in magazines with imagery of young people—of various races—engaged in activities that look fun and social.

### Recent Marketing Strategies

Menthol cigarettes continue to be heavily advertised to African-Americans in a variety of ways.

### *Point-of-Sale Targeting*

Tobacco companies have taken advantage of the greater density of convenience stores and gas stations in lower-income and minority neighborhoods to heavily market and promote tobacco products. Their marketing strategies have included price discounts, promotional giveaways, heavy product placement and culturally tailored ad content at retail locations, both indoors and out. A wealth of research indicates that African American neighborhoods have a disproportionate number of tobacco retailers, pervasive tobacco marketing, and in particular, more marketing of menthol products.[24] In addition to being heavily advertised and widely available, certain tobacco products have been found to be priced lower in African American communities, making them more appealing, particularly to price-sensitive youth:

- A 2017 nationwide study found that stores in neighborhoods with the highest proportion of African Americans have more than double the odds of advertising price promotions for tobacco products, compared to stores in neighborhoods with the lowest proportion of African Americans.[25]

- A 2011 study of cigarette prices in retail stores across the U.S. found that Newport cigarettes are significantly less expensive in neighborhoods with higher proportions of African Americans.[26]

- A 2006 study of California smokers found that those who smoke menthol cigarettes are more likely to use promotional offers than non-menthol smokers.[27]

The use of value-added or coupon promotions makes cigarettes more affordable to kids and those with less financial resources. In *U.S. v. Philip Morris* (the 2006 civil racketeering judgment against major cigarette manufacturers), the court specifically found that tobacco companies use strategic price reduction strategies such as coupons and multi-pack discounts to target young people.[28] According to the Surgeon General, "Because there is strong evidence that as the price of tobacco products increases, tobacco use decreases, especially among young people, then any actions that mitigate the impact of increased price and thus reduce the purchase price of tobacco can increase the initiation and level of use of tobacco products among young people."[29]


Price promotions for Camel cigarettes in Durham, NC. Photo courtesy CounterTobacco.Org

Disparities in advertising of tobacco products are particularly evident for menthol cigarette brands, which African Americans use more than any other racial or ethnic group:

- A 2013 study found that census tracts in St. Louis with a higher proportion of black residents had more menthol and total tobacco product marketing, and that census tracts with a higher proportion of black children had a higher proportion of menthol marketing near candy.[30]

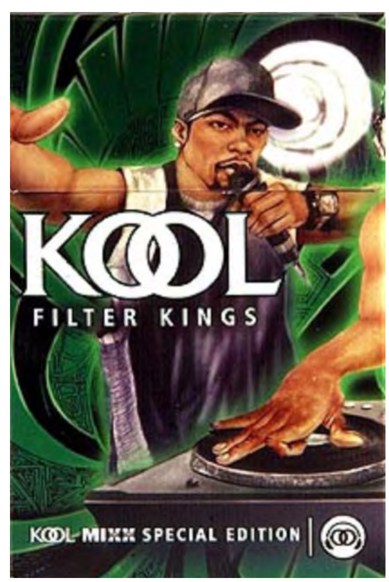
- The 2011 California Tobacco Advertising Survey reports that there were significantly more menthol advertisements at stores in neighborhoods with a higher proportion of African-American residents and in low-income neighborhoods.[31]

- Another 2011 California study found that as the proportion of African-American high school students in a neighborhood rose, the proportion of menthol advertising increased, the odds of a Newport promotion were higher, and the cost of Newport cigarettes was lower.[32]

- A 2010 study that compared characteristics of storefront tobacco advertisements in a low-income, community with a large African-American population and a high-income, nonminority community found that the African-American community had more tobacco retailers and advertisements were more likely to be larger and promote menthol products.[33]

### *Cultural Imagery*

There is compelling evidence that tobacco companies not only advertise disproportionately in communities with large African-American populations, they also create advertising specifically targeted to these communities. Cigarette ads highly prevalent in African-American communities and publications are often characterized by slogans, relevant and specific messages, or images that have a great appeal among those in the black community or depict African Americans in an appealing light.[34]

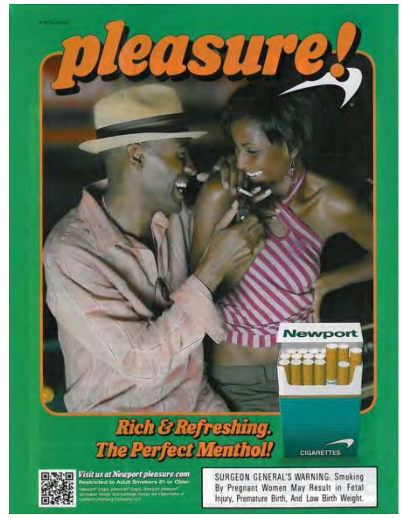



Kool Mixx cigarettes, 2004
Image courtesy of Stanford Research Into the Impact of Advertising

In 2004, Brown & Williamson started an ad campaign for their Kool brand cigarettes clearly aimed at youth—and African-American youth, in particular. The Kool Mixx campaign featured images of young rappers, disc jockeys and dancers on cigarette packs and in advertising. The campaign also included radio giveaways with cigarette purchases and a Hip-Hop disc jockey competition in major cities around the country. The themes, images, radio giveaways and music involved in the campaign all clearly have tremendous appeal to youth, especially African-American youth. Attorneys General from several states promptly filed motions against Brown & Williamson for violating the Master Settlement Agreement.[35] Simultaneously, Brown & Williamson promoted a new line of cigarette flavors like Caribbean Chill, Mocha Taboo, and Midnight Berry using images of African-Americans and themes attractive to African-American youth. These cigarettes were promoted through dance clubs and hip-hop music venues. In a similar vein, in the 1980s and 1990s, Uptown and "X" brand (emulating Malcolm X) cigarettes were also introduced, with the explicit aim of targeting African Americans, although these brand quickly failed due to community backlash.[36]

### *Magazine Advertising*

The tobacco industry's strategy of targeting magazines with high African American readership, which began in the 1960s, continues. Expenditures for magazine advertising of mentholated cigarettes increased from 13 percent of total ad expenditures in 1998 to 76 percent in 2006.[37] During the two years after the Master Settlement Agreement (MSA) in November 1998, the average annual expenditures for Newport in magazines with high youth readership increased 13.2 percent (from $5.3 to $6.0 million).[38] From 1998 to 2002, *Ebony,* a magazine tailored to the African American culture, was 9.8 times more likely than *People* to contain ads for menthol cigarettes.[39] An assessment of menthol cigarette ads run from June 2012 to February 2013 found that the tobacco industry spent an estimated $31 million on menthol cigarette direct mail, email, print and online advertisements in just a 9-month period. During this time, 61 percent of Newport print ads featured at least one African-American model. These ads ran in twenty publications including *Jet*, *Ebony*, and *Essence*, which have predominantly African-American readership.[40]




Newport advertisement in
*Essence Magazine*, February 2015
Image courtesy of TrinketsandTrash.Org

### Tobacco Industry Philanthropy in the African American Community

The tobacco company's decades long campaign to capture the African American market coincided with concerted efforts to forge ties with the African American community in an effort to build a positive brand identity. Since the 1950s, Philip Morris and Brown & Williamson have, at various times, been engaged with the National Urban League, the National Association for the Advancement of Colored People (NAACP), and the United Negro College Fund, and have provided funding and organizational support to a host of African American organizations.[41] In addition, the tobacco industry has supported historically African American colleges and universities as far back as the 1890s when R.J .Reynolds helped to finance the founding of Winston Salem State University.[42] However, industry documents reveal the companies' true intentions in forming these relationships:

*Brown & Williamson:* *"Clearly the sole reason for B&W's interest in the black and Hispanic communities is the actual and potential sales of B&W products within these communities and the profitability of these sales…this relatively small and often tightly knit [minority] community can work to B&W's marketing advantage, if exploited properly."*[43]

*Lorillard:* *"Tie-in with any company who help black[s] – 'we help them, they help us.' "*[44]

Tobacco companies continue to contribute to African American organizations and political leaders.

- Recently, R.J. Reynolds funded the National Action Network, a civil rights organization founded by Reverend Al Sharpton, to conduct community forums to build opposition to local action to prohibit menthol cigarettes. These forums attempted to frame the issue as criminalization of the African American community, ignoring the devastating impact of the tobacco industry's targeted marketing and the public health benefits of prohibiting menthol. In 2016 and 2017, these forums occurred in Oakland, Los Angeles and Minneapolis.[45] In early 2019, a representative from NAN testified against proposed legislation in New York City to restrict the sale of menthol cigarettes.[46]

- During the 2013-2014 election cycle, tobacco companies donated over $100,000 to African American lawmakers and affiliated political action committees.[47]

- As of 2017, Altria continues to contribute to the Congressional Black Caucus Foundation (CBCF), the California Black Chamber of Commerce Foundation, the California Legislative Black Caucus Policy Institute, and the National Black Farmers Association.[48] As of 2016, they also contributed to the National Black Caucus of State Legislators.[49] Both Reynolds and JUUL support the U.S. Black Chambers, Inc.[50] The President and Chief Executive Officer of CBCF from 2013-2018 was the former Vice President of Government Affairs Policy & Outreach for Altria Corporate Services, having worked for the tobacco industry for twenty years.[51] In its 2016 Annual Report, CBCF reported receiving between $100,000-$249,000 from Altria and $50,000-99,000 from R.J. Reynolds (RAI Services).[52]

- Since the 1960s, the tobacco industry has supported the National Newspaper Publishers Association (NNPA), a trade association representing more than 200 African American-owned community newspapers.[53] The most recently available financials show that Reynolds gave over $225,000 to the NNPA in 2017.[54] The President and CEO of NNPA has joined Rev. Al Sharpton of NAN in voicing opposition to local proposals to restrict the sale of menthol cigarettes.[55]

- The National Black Chamber of Commerce (NBCC), the Congress of Racial Equality (CORE), the National Organization of Black Law Enforcement Executives (NOBLE), the National Black Police Association (NBPA) and Law Enforcement Action Partnership (LEAP), all of which have received industry funding, have voiced active opposition to proposals to extend the federal ban on flavored cigarettes to menthol.[56] NBPA even launched a campaign to encourage submission of public comments to FDA in opposition of extending the prohibition on flavors to menthol, resulting in over 36,000 comments submitted in opposition to the ban.[57] Representatives from LEAP and NOBLE have also presented at NAN's forums opposing local restrictions on menthol cigarettes. [58]

- In 2014, Altria donated $1 million to the Smithsonian's National Museum of African American History and Culture.[59]

Other African American organizations have fought against the industry's targeted marketing. In 2016, the NAACP voted to adopt a resolution to support state and local restrictions on flavored tobacco products, including menthol (according to a spokesperson in 2016, the NAACP no longer receives tobacco industry funding).[60] Delta Sigma Theta, an African American sorority, approved a resolution in 2013 to urge FDA to prohibit menthol cigarettes.[61] In 2018, both the NAACP and the National Urban League issued statements in support of FDA action to prohibit menthol cigarettes.[62] In 2019, the NAACP testified in favor of proposed legislation in New York City to restrict the sale of menthol cigarettes.[63]

**Impact on the African American Community**

Menthol cigarettes have had a profound negative impact on public health, and have had a particularly destructive impact on the African American community. In 2013, the U.S. Food and Drug Administration (FDA) released a report finding that menthol cigarettes lead to increased smoking initiation among youth and young adults, greater addiction, and decreased success in quitting smoking. The FDA and FDA's Tobacco Product Scientific Advisory Committee (TPSAC) concluded that African Americans are disproportionately burdened by the health harms of menthol cigarettes.[64] TPSAC, in its 2011 report to the FDA, estimated that by 2020, 4,700 excess deaths in the African American community will be attributable to menthol cigarettes, and over 460,000 African Americans will have started smoking because of menthol cigarettes.[65]

African Americans suffer the greatest burden of tobacco-related mortality of any racial or ethnic group in the United States. [66] Each year, approximately 45,000 African Americans die from smoking-related disease.[67] Smoking-related illnesses are the number one cause of death in the African-American community, surpassing all other causes of death, including AIDS, homicide, diabetes, and accidents.[68] If current smoking rates persist, an estimated 1.6 million black Americans alive today under the age of 18 will become regular smokers, and about 500,000 will die prematurely from a tobacco-related disease.[69]

***Campaign for Tobacco-Free Kids, February 28, 2019 / Laura Bach***

**More information on Tobacco and African Americans is available at**
**http://www.tobaccofreekids.org/facts_issues/fact_sheets/toll/populations/african_americans/.**

1 The Roper Organization. *A Study of Smoking Habits Among Young Smokers*. 1974 July. Philip Morris Records. https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/#id=hjdv0130.

2 Villanti, AC, et al., "Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004-2014," *Tobacco Control*, published online October 20, 2016. See also, Corey, CG, et al., "Flavored Tobacco Product Use Among Middle and High School Students—United States, 2014," *Morbidity and Mortality Weekly Report,* 64(38): 1066-1070.

3 SAMHSA's public online data analysis system (PDAS), National Survey on Drug Use and Health, 2015. http://pdas.samhsa.gov/#/survey/NSDUH-2015-DS0001/crosstab/?row=CIG30BR2&column=CATAG3&control=NEWRACE2&weight=ANALWT_C&results_received=true.

4 Gardiner, PS, "The African Americanization of menthol cigarette use in the United States," *Nicotine & Tobacco Research*, 6(S1): S55-S65, 2004.

5 Brown & Williamson. The growth of menthols 330000-770000. Macon, GA: Brown & Williamson Tobacco Corporation, 1978. http://legacy.library.ucsf.edu/tid/ank50f00.

6 Gardiner, PS, "The African Americanization of menthol cigarette use in the United States," *Nicotine & Tobacco Research*, 6(S1): S55-S65, 2004.

7 Pollay, RW, et al., "Separate, but not Equal: Racial Segmentation in Cigarette Advertising," *Journal of* Advertising, 21(1): 45-57, 1992.

8 Gardiner, PS, "The African Americanization of menthol cigarette use in the United States," *Nicotine & Tobacco Research*, 6(S1): S55-S65, 2004.

9 Burrows, DS, *Strategic Research Report: Younger Adult Strategies and Opportunities.* R.J. Reynolds, 1984. http://legacy.library.ucsf.edu/tid/ene39d00.

10 Lorillard. The menthol cigarette market—a summary—Job number 9016. Greensboro, NC: Lorillard, 1972 Feb. Available at http://legacy.library.ucsf.edu/tid/ipc31e00.

11 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

12 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

13 Hafez, N. & Ling, P.M. "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control 15:* 359-366, 2006. See also Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

14 Kool Market Development Program. 1983. Brown & Williamson Records. https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/lqcy0025.

15 Hudson RC. Brown & Williamson. Inner city POP Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1979 Oct 15. http://legacy.library.ucsf.edu/tid/icb91d00.

16 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

17 Hafez, N. & Ling, P.M. "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control 15:* 359-366, 2006. See also Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

18 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007. See also RJ Reynolds. Black Street Scenes: review and recommendations. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1983. Available at http://legacy.library.ucsf.edu/tid/onb19d00.

19 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

20 Yerger, VB, et al., "Racialized geography, corporate activity, and health disparities: Tobacco industry targeting of inner cities," *Journal of Health Care for the Poor and Underserved*, 18: 10-38, 2007.

21 Klausner, K, "Menthol cigarettes and smoking initiation: a tobacco industry perspective," *Tobacco Control*, 20(S2): ii12-ii19, 2011.

22 Klausner, K, "Menthol cigarettes and smoking initiation: a tobacco industry perspective," *Tobacco Control*, 20(S2): ii12-ii19, 2011.

23 Lindsley, VD. [Re:] Newport Creative Exploratory. 1993 December 13. Marketing to Youth MSA Collection. https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/gzwj0045.

24 Lee, JGL, et al., "A Systematic Review of Neighborhood Disparities in Point-of-Sale Tobacco Marketing," *American Journal of Public Health*, published online ahead of print July 16, 2015.

25 Ribisl, KM, et al., "Disparities in tobacco marketing and product availability at the point of sale: results of a national study," *Preventive Medicine*, in press as of April 2017.

26 Resnick, EA, et al., *Cigarette Pricing Differs by U.S. Neighborhoods—A BTG Research Brief.* Chicago, IL: Bridging the Gap Program, Health Policy Center, Institute for Health Research and Policy, University of Illinois at Chicago, 2012, www.bridgingthegapresearch.org.

[27] White, VM, et al., "Cigarette Promotional Offers: Who Takes Advantage?" *American Journal of Preventive Medicine*, 30(3): 225-231, 2006.
[28] *U.S. v. Philip Morris*, 449 F. Supp. 2d at 639-40.
[29] HHS, *Prevention Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General,* 2012, http://www.cdc.gov/tobacco/data_statistics/sgr/2012/index.htm, at 530.
[30] Moreland-Russell, S, et al., "Disparities and Menthol Marketing: Additional Evidence in Support of Point of Sale Policies," *International Journal of Environmental Research and Public Health*, 10: 4571-4583, 2013.
[31] Schleicher, N, et al., "Tobacco Marketing in California's Retail Environment (2008-2011), Final report for the California Tobacco Advertising Survey. Stanford, CA: Stanford Prevention Research Center, July 2013.
[32] Henriksen, L., et al., "Targeted Advertising, Promotion, and Price for Menthol Cigarettes in California High School Neighborhoods," Nicotine & Tobacco Research, June 24, 2011.
[33] Seidenberg, AB, "Cigarette Advertising Differs by Community Demographic Profile," *American Journal of Health Promotion* 24(6):e26-e31, July/August 2010.

[34] Hutchinson, EO, "Joe Camel Dominants More Than Billboards in Black America," June 23, 1997, http://www.pacificnews.org/jinn/stories/3.13/970623-cigarettes.html
[35] Hafez, N, & Ling, P, "Finding the Kool Mixx: how Brown & Williamson used music marketing to sell cigarettes," *Tobacco Control*, 15: 359-366, 2006.
[36] US Department of Health and Human Services (HHS), "Tobacco Use Among US Racial/Ethnic Minority Groups – African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/index.htm.
[37] Alpert, H, Koh, HK, & Connolly, GN, "After the Master Settlement Agreement: Targeting and exposure of youth to magazine tobacco advertising," *Health Affairs* 27(6):w503-w512, 2008.
[38] King, C, et al., "The Master Settlement Agreement with the tobacco industry and cigarette advertising in magazines," *New England Journal of Medicine* 345(7):504-11, August 2001.
[39] Landrine, H, et al., "Cigarette advertising in Black, Latino and White magazines, 1998-2002: An exploratory investigation," *Ethnic Disparities* 15(1):63-7, 2005.
[40] Richardson, A, et al., "How the industry is marketing menthol cigarettes: the audience, the message, and the medium," *Tobacco Control*, 24: 594-600, 2015.
[41] Yerger, V.B. & Malone, R.E. "African American leadership groups: smoking with the enemy," *Tobacco Control,* 11: 335-345, 2002.
[42] Gardiner, P.S. "The African Americanization of menthol cigarette use in the United States," *Nicotine & Tobacco Research* 6(S1): S55-S65, 2004.
[43] Yerger, V.B. & Malone, R.E. "African American leadership groups: smoking with the enemy," *Tobacco Control,* 11: 335-345, 2002. Quote from Bateman, M. [Total Minority Marketing Plan]. Brown and Williamson. September 7, 1984. Bates No. 531000141-0144. http://legacy.library.ucsf.edu/tid/eph40f00.
[44] Davis, R, Black Marketing Research - Findings & Recommended Actions to Date, Lorillard, June 9, 1978, Bates No. 84274935/4944.
[45] Levin, M, "Battling Menthol Restrictions, R.J. Reynolds Reaches out to Sharpton, Other Black Leaders," *Fair Warning*, February 9, 2017, https://www.fairwarning.org/2017/02/rjreynoldssharptonmentholrestrictions/.
[46] West, MG, "New York City Council Weighs Ban on Flavored E-Cigarettes, Menthols," *Wall Street Journal*, January 30, 2019, https://www.wsj.com/articles/new-york-city-council-weighs-ban-on-flavored-e-cigarettes-menthols-11548895703.
[47] Levin, M, "The Troubling History of Big Tobacco's Cozy Ties with Black Leaders," *Mother Jones*, November 17, 2015, http://www.motherjones.com/politics/2015/11/tobacco-industry-lorillard-newport-menthol-black-smokers.
[48] 2017 Recipients of Charitable Contributions from the Altria Family of Companies, accessed July 25, 2018, http://www.altria.com/Responsibility/Investing-In-Communities/Documents/GranteesList.pdf.
[49] 2016 Recipients of Charitable Contributions from the Altria Family of Companies, accessed May 5, 2017, http://www.altria.com/Responsibility/Investing-In-Communities/Documents/GranteesList.pdf.
[50] U.S. Black Chambers, Inc. http://usblackchambers.org/, see Sponsors section. Accessed February 14, 2019.
[51] Congressional Black Caucus Foundation, "CBCF Announces New President/CEO and Chair of Board of Directors," February 1, 2013, https://www.cbcfinc.org/cbcf-announces-new-presidentceo-and-chair-of-board-of-directors/.
[52] Congressional Black Caucus Foundation, 2016 Annual Report, https://www.cbcfinc.org/wp-content/uploads/2019/01/CBCF_2016_Annual_Report_WEB.pdf.
[53] McCandless, PM, et al., "Quid Pro Quo: Tobacco Companies and the Black Press," *American Journal of Public Health*, 102(4): 739-750, 2012.
[54] Reynolds American, Inc., "2017 Corporate Contributions to 501(c)(4&6) Organizations & Inaugural Activities," http://s2.q4cdn.com/129460998/files/doc_downloads/corporate_poltical/2017-Corporate-Contributions-to-501-(c)-(4)-and-501-(c)-(6)-Organizations.pdf. Levinthal, D, "Tobacco giant gives $250,000 to group representing black-owned newspapers," The Center for Public Integrity, March 17, 2016, https://www.publicintegrity.org/2016/03/17/19436/tobacco-giant-gave-250000-group-representing-black-owned-newspapers. Loyd, R, "Rev. Al Sharpton's talk on banning menthols draws debate over policing tobacco companies," *Oakland North*, November 16, 2016, https://oaklandnorth.net/2016/11/16/rev-al-sharptons-talk-on-banning-menthols-draws-debate-over-policing-tobacco-companies/.
[55] See e.g., Sharpton, A., and Chavis, B., "Opinion: Prohibitions and Bans: Serious, Unintended Consequences," *Oakland Post*, June 11, 2017, http://www.oaklandpost.org/2017/06/11/opinion-prohibitions-and-bans-serious-unintended-consequences/. Brown, SM, "New York City Council Ignoring 'Unintended Consequences' in Discussing Menthol Ban," *blackpressUSA*, January 28, 2019, https://www.blackpressusa.com/new-york-city-council-ignoring-unintended-consequences-in-discussing-menthol-ban/.
[56] Levin, M, "The Troubling History of Big Tobacco's Cozy Ties with Black Leaders," *Mother Jones*, November 17, 2015, http://www.motherjones.com/politics/2015/11/tobacco-industry-lorillard-newport-menthol-black-smokers.

[57] Memorandum: Summary of Write-in Campaigns to Docket FDA-2013-N-0521, January 31, 2014, https://www.fairwarning.org/wp-content/uploads/2015/11/Memorandum_from_FDA_Center_for_Tobacco_Products_to_the_Division_of_Dockets_Management_re_Summary_of_Write_In_Campaigns7.pdf.
[58] Levin, M, "Battling Menthol Restrictions, R.J. Reynolds Reaches out to Sharpton, Other Black Leaders," *Fair Warning*, February 9, 2017, https://www.fairwarning.org/2017/02/rjreynoldssharptonmentholrestrictions/. See also Bond Graham, D, "Tobacco Industry Lobbyists Descent on Oakland to Oppose Ban of Flavored Blunt Wrappers and Cigars," *Easy Bay Express*, June 7, 2017, https://www.eastbayexpress.com/SevenDays/archives/2017/06/07/tobacco-industry-lobbyists-descend-on-oakland-to-oppose-ban-of-flavored-blunt-wrappers-and-cigars?mode=print. Phifer, I, "Sharpton straddles fence on menthol cigarette ban," *Minnesota Spokesman-Recorder*, February 1, 2017, https://spokesman-recorder.com/2017/02/01/sharpton-straddles-fence-menthol-cigarette-ban/.
[59] Smithsonian, "Altria Group Donates $1 Million to the Smithsonian's National Museum of African American History and Culture," July 31, 2014, http://newsdesk.si.edu/releases/altria-group-donates-1-million-smithsonian-s-national-museum-african-american-history-and-c.
[60] National Association for the Advancement of Colored People (NAACP), *Resolutions Ratified by the National Board of Directors Under Article IX, Section 1 of the Constitution of the NAACP*, 2016, http://www.naacp.org/wp-content/uploads/2016/03/Resolutions.2016.pdf. See also Tavernise, S, "Black Health Experts Renew Fight Against Menthol Cigarettes," *New York Times,* September 13, 2016, https://www.nytimes.com/2016/09/14/health/menthol-cigarettes-fda.html.
[61] Delta Sigma Theta, *Prohibiting the Use of Menthol as a Characterizing Flavor in Cigarettes*, 2013 National Convention Workbook, http://www.tobacco.ucsf.edu/sites/tobacco.ucsf.edu/files/u9/Attachment%205-Delta%20Resolution.pdf.
[62] NAACP, "NAACP Statement on FDA Plan to Ban Sale of Menthol and E-Cigarettes," November 14, 2018, https://www.naacp.org/latest/naacp-statement-fba-plan-ban-sale-menthol-e-cigarettes/. National Urban League, "National Urban League: Proposed Menthol Cigarette Ban Would Benefit African Americans' Health," November 13, 2018, http://nul.iamempowered.com/content/national-urban-league-proposed-menthol-cigarette-ban-would-benefit-african-americans-health.
[63] Calder, R and Campanile, C, "Al Sharpton raises concerns about ban on menthol-flavored cigarettes," *New York Post*, January 30, 2019, https://nypost.com/2019/01/30/al-sharpton-raises-concerns-about-ban-on-menthol-flavored-cigarettes/.
[64] TPSAC, FDA, *Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations*, July 21, 2011 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[65] Tobacco Products Scientific Advisory Committee, FDA, "Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.
[66] HHS, "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.
[67] US Department of Health and Human Services (HHS), "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.
[68] American Cancer Society, "Cancer Facts & Figures for African Americans, 2013–2014," 2013, http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-036921.pdf. American Heart Association, "*African Americans and Cardiovascular Diseases: Statistical Fact Sheet, 2012 Update,"* http://www.heart.org/idc/groups/heart-public/@wcm/@sop/@smd/documents/downloadable/ucm_319568.pdf.
[69] HHS, "Tobacco Use Among US Racial/Ethnic Minority Groups—African Americans, American Indians and Alaskan Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General," 1998, http://www.cdc.gov/tobacco/data_statistics/sgr/1998/complete_report/pdfs/complete_report.pdf.

# Communication from Public

**Name:** Campaign for Tobacco-Free Kids
**Date Submitted:** 07/11/2019 01:47 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

# PREFACE

This report was written by the Tobacco Products Scientific Advisory Committee (TPSAC) of the Center for Tobacco Products of the Food and Drug Administration (FDA). TPSAC was mandated by the Family Smoking Prevention and Tobacco Control Act to deliver a report to FDA on the public health impact of menthol in cigarettes within a year of the committee's formation establishment. The report was written within the requirements of the Federal Advisory Committee Act, which governs the committee's meetings. During 10 meetings, from March 30-31, 2010 through March 17-18, 2011 (see Appendix B for dates), TPSAC and Menthol Report Subcommittee developed its approach to the task of writing the report, wrote and reviewed draft chapters, and reached conclusions and drafted recommendations. Chapters were discussed in meetings by the full committee and there was opportunity for comment.

Over the course of the 10 meetings of the TPSAC or Menthol Report Subcommittee, TPSAC received valuable input from many public commenters, including researchers, tobacco industry, consultants to the tobacco industry, representatives of the public health sector, and others. The tobacco industry also responded to requests from TPSAC for specific materials. The voting members of TPSAC received useful comments from the non-voting members of the committee; TPSAC acknowledges their collegial input.

Many others provided materials that were considered by TPSAC in writing the report. TPSAC is grateful to contractors to FDA from the University of California, San Francisco, and RTI International who reviewed various sources and prepared reports for TPSAC on a very timely basis. David Mendez, PhD, from the University of Michigan School of Public Health, executed modeling to assist TPSAC in characterizing the public health impact of menthol cigarettes. Lisa Henriksen, PhD, from Stanford University, made a strong and timely contribution to the development of chapter 5. TPSAC appreciates the efforts of these two scientists, which were made on a very demanding schedule. TPSAC also thanks Denise Gellene, who edited this report and met the challenges posed by the deadline.

In submitting this report, TPSAC has met the requirement of the Family Smoking Prevention and Tobacco Control Act with regard to developing this report and making recommendations on the public health impact of menthol in cigarettes. Of course, TPSAC would be pleased to offer further guidance to FDA on this topic in the future, if needed.

# CHAPTER 1: OVERVIEW: WHAT THIS REPORT IS ABOUT

## INTRODUCTION

Menthol is an organic compound, either derived from natural sources or synthesized, that is widely used in consumer and medicinal products. It has cooling, analgesic, and irritative properties, reflecting its interactions with specific neuronal receptors that can modulate pain and communicate to areas of the brain concerned with taste and other sensations. It has long been used in cigarettes and for some cigarettes it is a flavor-characterizing additive. Menthol is also an active pharmaceutical ingredient in many products. In medical products, whether menthol is the sole pharmaceutical ingredient, as in throat lozenges or one among many such ingredients as in a cold or cough medicine, menthol is regulated as a drug with restrictions on allowable doses and uses, and requirements with respect to instructions for use and warnings. When used in cigarettes, menthol—like most other ingredients in tobacco products—is not regulated according to the safety standards applied to food and drugs.

The Family Smoking Prevention and Tobacco Control Act (the "Act") charges the Tobacco Products Scientific Advisory Committee (TPSAC) with developing a report and recommendations that address "the issue of the impact of the use of menthol in cigarettes on the public health including such use among children, African Americans, Hispanics, and other racial and ethnic minorities." The Act has the overall purpose of protecting "…the public health by providing the Food and Drug Administration with certain authority..." The issue of menthol in cigarettes was the first brought to TPSAC by the Food and Drug Administration (FDA); under section 907(e) TPSAC is to complete its report and recommendations on menthol in cigarettes within one year of its establishment, that is, by March 23, 2011.

This report addresses the use of menthol in cigarettes as called for by the Act. The goal is to cover the evidence related to the public health impact of the use of menthol in cigarettes and to offer evidence-based recommendations to FDA. As this is the first report prepared by TPSAC, it also describes the principles and practices by which TPSAC has developed this report, offering a precedent that will be followed, as appropriate, for future reports. This chapter and Chapter 2 introduce the methods that TPSAC has used and the basis for their selection.

## THE CHARGE TO TPSAC FROM THE FAMILY SMOKING PREVENTION AND TOBACCO CONTROL ACT

The Act gives TPSAC a specific but broad charge with regard to the use of menthol in cigarettes. The report is to address the public health impact and to make recommendations on menthol in cigarettes. Under section 907 (a)(3)(B)(i),TPSAC is requested to address the following with regard to menthol:

- The risks and benefits to the population as a whole, including users and nonusers of tobacco products;
- The increased or decreased likelihood that existing users of tobacco products will stop using such products; and
- The increased or decreased likelihood that those who do not use tobacco products will start using such products.

If a standard were to be implemented in regard to menthol, under section 907 (b), the Secretary needs to consider additional matters, including technical achievability of the standard and any countervailing effects on the health of adolescent and adult users and non-tobacco users. Such effects could include the creation of a significant demand for contraband.

**WHAT IS A MENTHOL CIGARETTE?**

Under the Act, menthol is an additive, as defined in Section 900 (1). Menthol is reported to be present in most cigarettes in the United States (Henningfield et al. 2003; Giovino et al. 2004). However, TPSAC did not identify any systematic and recent data on menthol content in cigarettes. Those cigarettes marketed as menthol have sufficient menthol content for menthol to become a "characterizing flavor." A submission to TPSAC from the Lorillard Tobacco Company identified menthol levels of around 1000 ppm (wt/wt) of cigarette tobacco or higher as providing a characterizing flavor (Lorillard 2010). R.J. Reynolds Tobacco Company "...typically characterizes a cigarette as a menthol cigarette when the cigarette's menthol level is 0.3 percent or greater" by weight (R. J. Reynolds Tobacco Company 2010, p.1). Heck (2010) in a literature review noted that the menthol content of some cigarette tobaccos reaches two percent by weight. Celebucki et al. (2005) analyzed 48 menthol brands, finding an average value of 2.64 mg per cigarette. For the purpose of this report, TPSAC has not adopted a quantitative definition for a menthol cigarette, but instead relies on the brand designation.

In the brands not marketed as menthol, the amount of menthol is much lower—about 0.03 percent of the tobacco weight (Giovino et al. 2004). In response to questions from TPSAC, the R.J. Reynolds Tobacco Company submitted written comments, which included the statements below (R.J. Reynolds Tobacco Co. 2010, p.3).

> "When menthol is found in non-menthol cigarettes, the levels are extremely low —usually at a level of 50 ppm (0.005 percent) or less."
>
> "Menthol might be detected at trace levels in a non-menthol cigarette as an incidental byproduct of various tobacco processes, such as the manufacture of reconstituted tobacco."
>
> "Non-menthol cigarettes sometimes use small amounts of commercial flavorings, and these flavorings as prepared by the suppliers may use incidental amounts of menthol as a flavor component."
>
> "Some non-menthol cigarettes are made with extremely small quantities of menthol added to provide a fresh taste without imparting a characterizing menthol taste, or to brighten the tobacco flavor."

In response to the same questions from TPSAC, Altria Client Services commented in its June 30, 2010 submission for Philip Morris USA Inc. that: "PM USA does not include menthol as part of the flavor recipes used in non-menthol cigarettes," (Altria Client Services 2010, p.14). While TPSAC has been given the charge of addressing menthol in cigarettes generally, it has focused this report on menthol cigarettes. This focus is consistent with the language of the Act which refers to menthol in Section 907 (a)(1)(A) in discussing constituents or additives that are "…a characterizing flavor of the tobacco product or tobacco smoke."

## THE TPSAC FRAMEWORK FOR ASSESSING THE IMPACT OF MENTHOL CIGARETTES ON PUBLIC HEALTH

In general, determining the public health impact or population harm of a tobacco product involves assessment of multiple factors. As described in the 2001 Institute of Medicine report, *Clearing the Smoke*, based on a harm reduction conceptual framework described by MacCoun and Reuter (2001), population harm is associated with the toxicity of the product (per use), the intensity of its use (per user) and the prevalence of use (Stratton et al. 2001). With regard to population impact, prevalence needs particular emphasis as it defines the size of the population at risk from a product. Menthol cigarettes could increase prevalence by increasing the rate of initiation and subsequent addiction and by more strongly maintaining addiction and reducing successful cessation.

TPSAC has formulated a framework that is specific to its charge related to the public health impact of menthol cigarettes. As TPSAC evaluates the available information on menthol cigarettes, it will do so within an overall conceptual framework or "model" for cigarette smoking that defines points at which the presence of menthol cigarettes could harm either the health of the individual smoker or of the public generally (Figure 1). TPSAC is charged with addressing "...the issue of the impact of the use of menthol in cigarettes on the public health..." and with further considerations related to population impact and users and non-users under section 907 (a)(3)(B)(i). The framework in Figure 1 is useful for both levels—individual and population. The model set out in Figure 1 begins with experimentation with cigarette smoking on the part of children, adolescents, and young adults and ends with the development of disease and death caused by smoking cigarettes. The model is not inclusive in showing all factors that contribute to this sequence from experimentation to disease incidence, but it does include those who might be affected by menthol cigarettes.

The model implies various potential indicators of the consequences of menthol cigarettes: (1) rates of experimentation and initiation; (2) the prevalence of nicotine addiction; (3) rates of quit attempts and successful cessation; (4) population smoking prevalence, the summative consequence of initiation and cessation; and (5) incidence and mortality rates of smoking-caused diseases. These same indicators are of interest within particular subpopulations, reflecting TPSAC's charge in the Act. It is important to note that disease is not the primary or sole outcome that determines the public health impact of menthol cigarettes. The availability of menthol cigarettes could have no significant effect on risk for disease outcomes, yet have a significant effect on increasing initiation or reducing the success of cessation. The resultant increase in the prevalence of smoking would represent a negative public health impact.

## QUESTIONS TO BE ADDRESSED WITH REGARD TO MENTHOL CIGARETTES

The framework (Figure 1) highlights issues for which focused reviews need to be carried out to address critical questions related to the charge to TPSAC. The following questions are addressed in the reviews included in this report and answered according to a standardized terminology for strength of evidence. Each is relevant to the assessment of public health impact and the recommendations to be made by TPSAC to FDA.

<u>Related to Individual Smokers</u>

1. Does availability of menthol cigarettes increase the likelihood of experimentation?
2. Does availability of menthol cigarettes increase the likelihood of becoming a regular smoker?
3. Does inclusion of menthol in cigarettes increase the likelihood of the smoker becoming addicted?

4. Does inclusion of menthol in cigarettes increase the degree of addiction of the smoker?
5. Are smokers of menthol cigarettes less likely to quit successfully than smokers of non-menthol cigarettes?
6. Do biomarker studies indicate that smokers of menthol cigarettes receive greater doses of harmful agents per cigarette smoked compared with smokers of non-menthol cigarettes?
7. Do smokers of menthol cigarettes have increased risk for diseases caused by smoking compared with smokers of non-menthol cigarettes?

Smoking at the Population Level

1. Does the availability of menthol cigarettes increase the prevalence of smoking in the population, beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?
2. Does tobacco company marketing of menthol cigarettes increase the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?

## ORGANIZATION OF THE TPSAC REPORT

This report contains seven additional chapters. They cover TPSAC's approach to identifying and weighing the scientific evidence; physiological responses to menthol and to menthol and nicotine; the prevalence and patterns of smoking among the population as a whole and in subpopulations such as by race/ethnicity and gender; marketing of menthol cigarettes; the effects of menthol cigarettes versus non-menthol cigarettes on initiation, dependence and cessation; and biomarkers of exposure and risks for health outcomes. The last chapter integrates the information from the preceding chapters. It offers TPSAC's answers to the questions above based on the weight of evidence. It also provides results of modeling that are informative as to public health impact. The report concludes with TPSAC's recommendations to FDA.

## REFERENCES


Altria Client Services. *Background information to Tobacco Products Scientific Advisory Committee menthol discussion.* TPSAC submission June 30, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218779.pdf].

Celebucki CC, Wayne GF, Connelly GN, Pankow JF, Chang EI. Characterization of measured menthol in 48 US cigarette sub-brands. *Nicotine & Tobacco Research* 2005 Aug;7(4):523–31.

Giovino GA, Sidney S, Gfroere JC, O'Malley PM, Allen JA, Richter PA, Cummings KM. Epidemiology of menthol cigarette use. *Nicotine & Tobacco Research* 2004 Feb;6 Suppl 1:S67–81.

Heck JD. A review and assessment of menthol employed as a cigarette flavoring ingredient*. Food and Chemical Toxicology* 2010;48(Supplement 1):S1–S38.

Henning field JE, Benowitz NL, Ahijevych K, Garrett BE, Connolly GN, Wayne GF. Does menthol enhance the addictiveness of cigarettes? An agenda for research. *Nicotine & Tobacco Research* 2003 Feb;5(1): 9–11.

Lorillard Tobacco Company. *Response to the FDA requests for information on menthol cigarettes*. TPSAC submission July 15-16, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218780.pdf].

MacCoun R, Reuter P. *Drug War Heresies: Learning From Other Vices, Times and Places*. Cambridge, England: Cambridge Press, 2001.

RJ Reynolds. *Topics on menthol cigarettes*. TPSAC submission June 30, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218782.pdf].

Stratton K, Shetty P, Wallace R, Bondurant S. (Eds.). *Clearing the smoke: assessing the science base for tobacco harm reduction*. Institute of Medicine, Washington, DC: National Academies Press, 2001.

## Chapter 2: TPSAC'S APPROACH TO ITS CHARGE

### INTRODUCTION

This report was developed by the Menthol Subcommittee of the TPSAC.The Menthol Subcommittee developed the chapter outline and general approach during open meetings. The initial draft chapters were written by subgroups of the subcommittee and then reviewed by all of its members. The completed report was then considered by the full TPSAC. The remainder of this chapter describes how TPSAC approached its charge.

### PRINCIPLES UNDERLYING TPSAC'S APPROACH

TPSAC is charged with reviewing and evaluating evidence, reaching conclusions based on the evidence and making recommendations to the FDA on the public health impact of menthol in cigarettes. In assuming this task, TPSAC adopted core principles to guide its approach and report, including being transparent and evidence-based, and reflecting consensus among TPSAC members.

First among these principles is that the fact finding, evidence gathering and synthesis, and deliberations about the evidence are conducted in a transparent manner. By transparency, TPSAC refers to using open and replicable processes that make the basis of its findings and recommendations completely accessible. In following the FDA's processes and meeting the requirements of the Federal Advisory Committee Act, TPSAC carried out its work in open meetings, unless a closed meeting was needed because of commercial, confidential information. Evidence evaluation and TPSAC deliberations were conducted in a transparent manner.

Second, the recommendations of the TPSAC are evidenced-based, meaning that TPSAC identified and relied on scientific and other information relevant to the topic of menthol cigarettes to develop its recommendations. The range of information considered by TPSAC was extremely broad, including survey data, the findings of laboratory studies of pharmacological activity and toxicity, epidemiological evidence, results of marketing research, and reviews of industry documents. Evidence gaps were anticipated and are identified in this report as specifically as possible. Where evidence was lacking or insufficient, TPSAC made its recommendations with acknowledgement of the gap. In cases where there was not enough evidence to make a recommendation, TPSAC identified the research to be done to address the gap. This strategy has been key to maintaining transparency.

While TPSAC made an effort to identify all relevant evidence on menthol in cigarettes, this was impracticable, given the timeframe for this report and the extent of the materials available. TPSAC has provided a clear statement and listing of what materials it did consider. Because there were too many tobacco industry documents to be systematically reviewed, these non-peer reviewed information sources were selectively reviewed and treated as evidence when appropriate. Reviews of these documents were carried out by FDA consultants and there are plans for publication of the summaries in the peer-reviewed literature. The internal documents were a source for understanding the menthol marketing practices of the tobacco industry targeting children, adolescents and ethnic minorities.

Third, the TPSAC used a consensus-based approach to develop this report. The draft report was developed by the Menthol Subcommittee of TPSAC for consideration and approval by the members of TPSAC. While individual TPSAC members and other Special Government Employees have authored various portions of the report, it is a product of the committee and its findings represent a consensus of TPSAC members. In complex and uncertain matters, such as the subject of this report, experts may not share precisely the same views of the scope and quality of the evidence and of its implications. This report captures a range of views, as appropriate, to characterize uncertainty in the evidence considered. After the evidence was collected and reviewed, TPSAC employed a consensus-based approach to develop the recommendations for this report.

**PROCESSES FOR EVIDENCE-BASED DECISION MAKING**
**Overview**

Processes for decision making in public health are grounded in an understanding of what is known and not known about the problem of concern. In making evidence-based decisions with regard to public health, there is a long history of using comprehensive reviews as the foundation for evaluating the state of evidence and for selecting among policy options. The reviews are generally systematic and often carried out by multidisciplinary expert panels, following protocols. Findings present the strength of evidence for a particular factor with regard to the outcome of interest, e.g., the strength of evidence for causation or for a beneficial effect of an intervention. The findings are followed by a decision-making process that might result in promulgation of a guideline, policy, or regulation.

The landmark 1964 Report of the US Surgeon General on tobacco and disease and the consequences of its findings are exemplary (US DHEW 1964). That report, which reached the momentous conclusion that smoking causes lung cancer in men, stands as one of the first comprehensive evidence-based reviews. It used a transparent methodology, involving a critical survey of all relevant literature by an expert panel whose members did not have committed viewpoints at the outset, and applied an explicit framework for assessing the strength of evidence for causation. The causal criteria applied, now often referred to as the "Surgeon General's criteria," are still in use today, and include: temporality, consistency, coherence, specificity, and strength (US DHHS 2004). The causal conclusions of the 1964 report triggered a wide range of individual and governmental actions, including the Federal Cigarette Labeling and Advertising Act of 1965 and a Congressional mandate that a health warning appear on all cigarette packages. In 1967, the Federal Communications Commission (FCC) ruled that the Fairness Doctrine in advertising applied to cigarette ads on television and radio and required broadcasters who aired cigarette commercials to provide air time for information about the health hazards of smoking. Policy actions have similarly followed findings of subsequent reports, e.g., the 1986 report on involuntary smoking (US DHHS 1986).

These same evidence-based approaches have become fundamental in many other areas in clinical medicine and public health. The current paradigm of "evidence-based medicine" involves the systematic review of evidence as the basis for formulating guidelines for clinical and public health practice. Standardized approaches have been developed for carrying out such reviews and the international Cochrane Collaboration engages thousands of researchers and clinicians throughout the world to carry out reviews. In the United States, the Agency for Health Care Research and Policy supports 14 Evidence-based Practice Centers to carry out reviews related to health care. There are also numerous reports from committees of the National Research Council and the Institute of Medicine that exemplify the use of systematic reviews in evaluating evidence as a guide to policy formulation.

Examples include reviews carried out on Agent Orange and the Gulf War, vaccines, asbestos and cancer, arsenic in drinking water, and secondhand smoke and cardiovascular disease risk. A 2008 report of the Institute of Medicine on presumptive disability decision making for veterans proposed a comprehensive scheme for evaluating evidence on whether an exposure sustained in military service had contributed to disease causation (IOM 2008).

Risk assessment is widely used within the government (including FDA) and by other entities in the management of risks from environmental and other factors (National Research Council 1983; 2009). It is an evidence-based decision-making tool that has four elements: (a) hazard identification (is there a risk?);( b) exposure assessment (what is the distribution of exposure to the agent?); (c) dose-response (how does risk vary with dose or exposure?); (d) risk characterization (what is the burden of risk associated with the agent of concern and how is that risk distributed?). The conduct of a risk assessment results in a clear documentation of what is known about a particular agent, and correspondingly what is not known, i.e., the sources of uncertainty. In applying risk assessment to environmental agents, there is also interest in whether particular groups are at higher risk to be exposed (vulnerability) or at heighted risk for the adverse effect(s) (susceptibility). These well worked-out concepts of risk assessment—uncertainty, vulnerability, and susceptibility—are applicable to TPSAC's consideration of menthol cigarettes.

This brief and necessarily selective examination of approaches to evidence review and evaluation documents that models are available for consideration by TPSAC that have proved successful in practice. They have several common elements: transparent and explicitly documented methods; consistent and critical evaluation of all relevant literature; application of a standardized approach for grading the strength of evidence; and clear and consistent phrasing of conclusions.

**Systematic reviews**

Systematic reviews have become the foundation for evidence-based policy in public health. A systematic review involves the identification of all relevant literature to a particular topic via a transparent and replicable search strategy; the culling of the identified publications for those meeting predetermined criteria for inclusion; a comprehensive and standardized assessment of the selected studies for strengths and weaknesses; the assembly of the findings into tables and figures; and the summarization of the findings and the statement of a conclusion on the strength of evidence. Protocols for carrying out such reviews are available.

A systematic review may also involve a quantitative analysis of the evidence, often referred to as a meta-analysis. Such meta-analyses are based on the summary findings of studies, generally as gleaned from papers, but sometimes from authors. The data from individual studies may be combined to yield a single point estimate for an association; by combining the findings of multiple studies, a more precise estimate can be made and the heterogeneity (variation) in the findings of studies formally assessed. If there is variation, the data might be explored for explanations of the variation, using stratification or meta-regression. Conducting a meta-analysis is beyond the scope of this report, but could be conducted for future consideration.

**Causal inference and classification of strength of evidence**

After gathering evidence through a defined process, e.g., a systematic review, the next step is the determination of what the evidence shows. In public health, a critical determination is whether there is sufficient evidence to show a causal association, i.e., whether some factor is either harming or benefiting human health. This process of assessing evidence and determining whether there is a causal relationship is referred to as causal inference.

There is an extensive literature on causal inference, both on its philosophical underpinnings and on the methodology for evaluating the strength of evidence for causation. These approaches have in common a systematic identification of all relevant evidence, i.e., a systematic review, criteria for evaluating the strength of evidence, and language for describing the strength of evidence for causation. The topic of causal inference and its role in decision-making has been recently covered in the 2004 report of the Surgeon General (US DHHS 2004) and in the 2008 report of the Institute of Medicine's Committee on Evaluation of the Presumptive Disability Decision-Making Process for Veterans (IOM 2008).

The 2004 Report of the US Surgeon General on smoking and health (US DHHS 2004) provides an updated review of the methods used in that series of reports, which began with the 1964 report (US DHEW 1964). The review approach embodies the common elements described in the preceding paragraph and uses evidence evaluation criteria that originated with the 1964 report and the writings of Sir Austin Bradford Hill (the "Hill criteria") (Hill 1965) (Table 1). The use of these criteria has now been refined through decades of application. These criteria are not rigid and are not applied in a "check list" manner. In fact, only one—temporality—is required for inferring a causal relationship, since exposure to the causal agent must precede the associated effect. Consistency refers to replication of the finding of an association between cause and effect in multiple studies carried out in different populations by different study types and by different investigators. Consistency of findings weighs against non-causal explanations for an association. Coherence refers to the meshing of different lines of evidence, including experimental findings and understanding of biological mechanisms. For many human diseases, other than the infectious diseases, specificity is not useful, since the non-communicable diseases, such as cancer and coronary heart disease, have multiple causes. In general, stronger associations and the presence of a dose-response relationship provide evidence against non-causal explanations for association. Stronger associations are less likely to be due to bias or confounding as is the presence of a dose-response relationship. The magnitude of an effect reflects underlying biological processes and, depending on these processes, might be appropriately small or large. An effect may not necessarily increase progressively with dose, depending on the underlying process.

The "bottom line" from causal inference is a clear statement on the strength of evidence for causation. Such statements should follow a standardized classification to avoid ambiguity and to assure comparability across different agents and outcomes.

TPSAC reviewed the above approach, which involves the systematic evaluation of evidence to reach a conclusion with regard to disease causation. TPSAC's charge for menthol cigarettes extends beyond disease causation, however, and TPSAC needs to reach conclusions on diverse issues, include, for example, the consequences of marketing. In reviewing evidence, TPSAC has adopted the general approach described in the causal inference literature. This involves the compilation and review of relevant information to reach a judgment as to the strength of the available evidence in a structured and transparent fashion.

**TPSAC'S APPROACH**

**Sources of evidence and identification of evidence to be reviewed**

In writing this report, TPSAC had multiple sources of evidence to consider, including:

- The peer-reviewed literature: In using this term, TPSAC refers to the studies published in journals or other formats that undergo a process of peer review and editorial evaluation prior to publication. Peer review provides a filter, albeit imperfect, to assure quality prior to publication. Such publications can generally be identified by searching major data bases, such as PubMed.

- Reports written and commissioned by the FDA: TPSAC was provided with multiple reviews of the literature and other reports that were developed by FDA staff or contractors to the FDA. These reports included overviews of the evidence on menthol that were presented at the March 30–31, 2010 meeting and compilations of industry documents from the Legacy data base that were presented at the October 7–8, 2010 meeting. These reports also included the secondary analysis of existing datasets which were made available to TPSAC members and public for the January 10-11, 2011 meeting. Some of these reports have been submitted to the peer-reviewed literature and will become available through that route as well. The reviews of the Legacy documents will be published in a supplement to the journal *Tobacco Control.* FDA also arranged for secondary analyses of various studies and data bases that provided relevant data.

- Tobacco company submissions: The tobacco companies made various submissions to TPSAC under Section 904, some classified as commercial/confidential. These submissions were made on multiple occasions during TPSAC meetings and were directed at the general topic of the meetings. During its initial meeting on March 30–31, TPSAC developed 17 questions for documents to be provided under Section 904 and asked the industry to develop responses, which were offered at the July 15–16, 2010 meeting.

- Public comments: TPSAC received comments from a wide range of public stakeholders. The scope of such presentations was broad.

In developing this report, TPSAC considered evidence from these diverse sources, recognizing the potential strengths and weaknesses of each type of information. The peer-reviewed literature can be systematically accessed through various search engines and TPSAC has attempted to identify all relevant literature, using searches carried out by FDA and its contract0rs, and also carrying out its own searches. TPSAC used the bibliography assembled by FDA as one resource to identify the most relevant literature. The members of the Menthol Subcommittee also reviewed submissions by the tobacco industry and the public generally to identify other, relevant articles. For other sources, TPSAC did not have resources or sufficient time to carry out its own searches of the Legacy data base nor did it independently review the industry documents that were submitted. Instead, it relied on the reviews of those documents by FDA contractors.

**Selection and evaluation of evidence**

The report approached diverse topics, each drawing on somewhat disparate lines of evidence. For example, in describing patterns of menthol cigarette use, TPSAC relied in part on updated analyses of recent survey data, even though it had not been reported in the peer-reviewed literature. For such analyses, the methods are well standardized and TPSAC could use the results with confidence based on its review of the approach. In contrast, the research on whether smokers of menthol cigarettes have risks for smoking-caused diseases different from those of smokers of non-menthol cigarettes is based on reports of epidemiological studies that have been published in the peer-reviewed literature. TPSAC did not consider abstracts or meeting presentations for which additional documentation was not available.

TPSAC evaluated all studies considered using evaluation criteria appropriate to the particular type of evidence. For example, assessments of survey findings considered response rate and representativeness, the potential for information bias, and sample size. In considering epidemiological studies, the chapter authors assessed population selection and the external validity of findings, bias and confounding, sample size, and appropriateness of data analysis methods. For surveys, response rates and the potential for misclassification were considered. In considering the literature on marketing, attention was directed at the rigor of study design, the limitations of the data collected, analytical methods, and generalizability (external validity) of findings. These reviews were conducted by the various chapter authors, with referral to the Menthol Subcommittee as needed. Particular attention was given to those studies with findings that were more critical in evidence classification. Given the constraint of time, TPSAC did not establish a formal review process with a review template and multiple reviewers per study.

**Classification of the strength of evidence**

In this report, TPSAC addresses nine questions, seven at the individual level and two at the population level. Its reviews are the basis for the answers to these questions, which cover a wide range of factors and outcomes (Figure 1). To assure consistency and transparency, TPSAC provides its summary statements on the strength of evidence in a uniform fashion, offering a classification intended to be useful for decision making.

TPSAC used the following hierarchical classification for the strength of evidence providing its summary judgments:

- The evidence is sufficient to conclude that a relationship is more likely than not.
- The evidence is sufficient to conclude that a relationship is at least as likely as not.
- The evidence is insufficient to conclude that a relationship is more likely than not.
- There is insufficient evidence to determine whether a relationship exists.

This classification was discussed extensively by TPSAC and its members were unanimous in accepting it for use in this report. This classification is based around the concept of "equipoise", i.e., the point of strength of evidence at which the "weight of evidence" is in balance, equally for or against the presence of a relationship. This point reflects an approximate matching of the strength of evidence for a relationship with the evidence against, constituting findings pointing away from or toward a relationship, taking uncertainty into account. In basing this classification around the point of equipoise, TPSAC plans to use an identifiable point, albeit via judgment, as the anchor for its four-level classification.  Additionally, strength of evidence above the point of equipoise might be interpreted as offering a basis for considering a policy action.

In classifying the weight of evidence, TPSAC relied on the judgment of its members as they evaluated the systematically assembled evidence.  In this regard, TPSAC followed standard professional practice in public health and regulatory decision making.  Strength of evidence was considered to increase with (1) the number of studies providing consistent findings, and (2) the general proportion of studies providing consistent findings. Greater emphasis was given to larger, better executed studies that had been published in the peer-reviewed literature. The coherence of the evidence was also given weight. Because of the variable nature of the evidence considered from chapter to chapter, TPSAC did not propose specific criteria that would be applied uniformly.

These assessments were carried out by the individual chapter authors and then further discussed by the writing subgroup for the chapter.  Conclusions were then reviewed and discussed by the Menthol Subcommittee and subsequently by all members of the TPSAC.  Consistent with the principles set out by TPSAC, the conclusions reflect a consensus of its members.

**USE OF MODELS TO ASSESS IMPACT**

The TPSAC has the overall charge of addressing the "...impact of the use of menthol in cigarettes on the public health, including such use among children, African Americans, and other racial and ethnic minorities."  The framework for considering the consequences of menthol cigarettes (Figure 1) identifies a series of indicators of impact under this charge:  rates of experimentation, initiation, and progression or regular use or addiction among youths and young adults; rate of successful cessation; and risk for cigarette-caused morbidity and premature mortality.   In approaching the assessment of the impact of menthol cigarettes, TPSAC intends to rely, in part, on models that are mathematical representations of the conceptual framework embodied in Figure 1.  A model is constructed to reflect understanding of the mechanistic pathways that determine outcome(s) and how causal factors act through these pathways to produce outcome(s) in the "real world." Models can be used to quantify the impact of menthol cigarettes on the various indicators, providing estimates of impact that reflect the potential consequences of menthol cigarettes at the various, linked points in the framework.

Models are an element of a "systems approach" to characterizing the factors that drive the tobacco epidemic and resultant disease burden, and to assessing the potential consequences of tobacco control measures.  Systems approaches based in "systems science" are an emerging paradigm for addressing public health problems (Best et al. 2007; Hammond 2009; Mabry et al. 2010).  Systems science approaches are valuable for tobacco control and other complex public health problems because they involve comprehensive consideration of the set of determining factors and of the relationships among these factors.  This broad-based understanding leads to the development of models that represent the actions of these factors in the "real world." While necessarily simplifying, models can be useful for exploring how different factors drive public health problems, and for exploring the utility of various control strategies.

Models have long been used to assess the impact of smoking on disease occurrence.  In 1953, shortly after the publication of the first major studies that showed the strong association of smoking with lung cancer, Levin published a paper setting out a still-used method for calculating the burden of lung cancer attributable to smoking (Levin 1953). He proposed a parameter, now often referred to as the population attributable risk or population attributable fraction (PAF). This parameter is estimated as:

$$PAF= P_E(RR - 1)/(1 + P_E(RR - 1))$$

where $P_E$ is the prevalence of exposure and RR is the relative risk of mortality associated with the risk factor. This parameter is estimated in the widely used Smoking Attributable Mortality, Morbidity and Economic Costs (SAMMEC) program developed by the Office on Smoking and Health of the Centers for Disease Control. One key concept embedded in this parameter is the comparison scenario for $P_E$, assumed to be a value of zero. This comparison state, which does not exist, is referred to as "the counterfactual," i.e., a scenario that is counter to the actual facts. For the purposes of the present report, TPSAC is concerned with counterfactual scenarios in which menthol cigarettes never existed.

This simple formula for estimating the PAF also indicates the two broad ways that menthol cigarettes could adversely impact public health: by increasing $P_E$ or by increasing RR. An increase in either parameter results in an increase in PAF. Thus, if menthol cigarettes increased $P_E$ but not RR, PAF would increase; if menthol cigarettes increased RR but not $P_E$, PAF would increase.

The utility of general models for tobacco control has gained increasing traction over the last decade, as the broad range of factors determining initiation and persistence of smoking and of disease risks within a population has been recognized (Best et al. 2007; Mendez 2010). The determinants range from the individual level, where genetics and education have a role, to the global level, where the actions of a small number of multinational companies affect the health of populations. A variety of models have been developed for use in the United States and other countries; they have been used to project consequences of various tobacco control approaches on smoking onset and prevalence and on disease burden (Levy et al. 2002; Best et al. 2007; Mabry et al. 2010).

For assessing the public health impact of menthol in cigarettes, a systems approach is warranted, given the diverse factors driving the smoking of menthol cigarettes. TPSAC cannot satisfactorily address its charge without taking a holistic approach that acknowledges the multiplicity of relevant factors and the potential for them to interact in complex ways. The relevant factors range from the biological impacts of tobacco and smoking on human cells to the influence of marketing on the population. There are well-defined interactions related to race and marketing. Evaluating menthol in isolation of social (ethnic, cultural and community), biologic (nicotine metabolism and receptor affinity), engineered (menthol-nicotine-tobacco matrix) and economic (price and marketing) influences may not easily be achieved and may lead to distorted conclusions about the major influences of menthol cigarettes on the public health. Consequently, TPSAC used models wherever appropriate to address its charge related to public health impact. The basic models might be extended to further explore specific issues, such as negative consequences of removing menthol from cigarettes in which it is a characterizing flavor.

**REFERENCES**

U.S. Department of Health Education and Welfare. *Smoking and health. Report of the Advisory Committee to the Surgeon General*. Washington, D.C.: U.S. Government Printing Office, 1964.

U.S. Department of Health and Human Services. *The health consequences of smoking. A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.

U.S. Department of Health and Human Services. *The health consequences of involuntary smoking. A report of the Surgeon General*. Washington, D.C.: U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, 1986.

Institute of Medicine. *Improving the presumptive disability decision-making process for veterans*. Washington, D.C.: National Academies Press, 2008.

National Research Council. *Risk assessment in the federal government: managing the process*. Washington, D.C.: National Academy Press, 1983.

National Research Council. *Science and decisions: advancing risk assessment*. Washington, D.C.: National Academies Press, 2009.

Hill AB. The environment and disease: association or causation? *Proceedings of the Royal Society of Medicine* 1965;58:295–300.

National Cancer Institute. *Greater than the sum: systems thinking in tobacco control. Tobacco Control Monograph No. 18*. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, 2007.

Hammond RA. Complex systems modeling for obesity research. *Preventing Chronic Disease* 2009;6(3):A97.

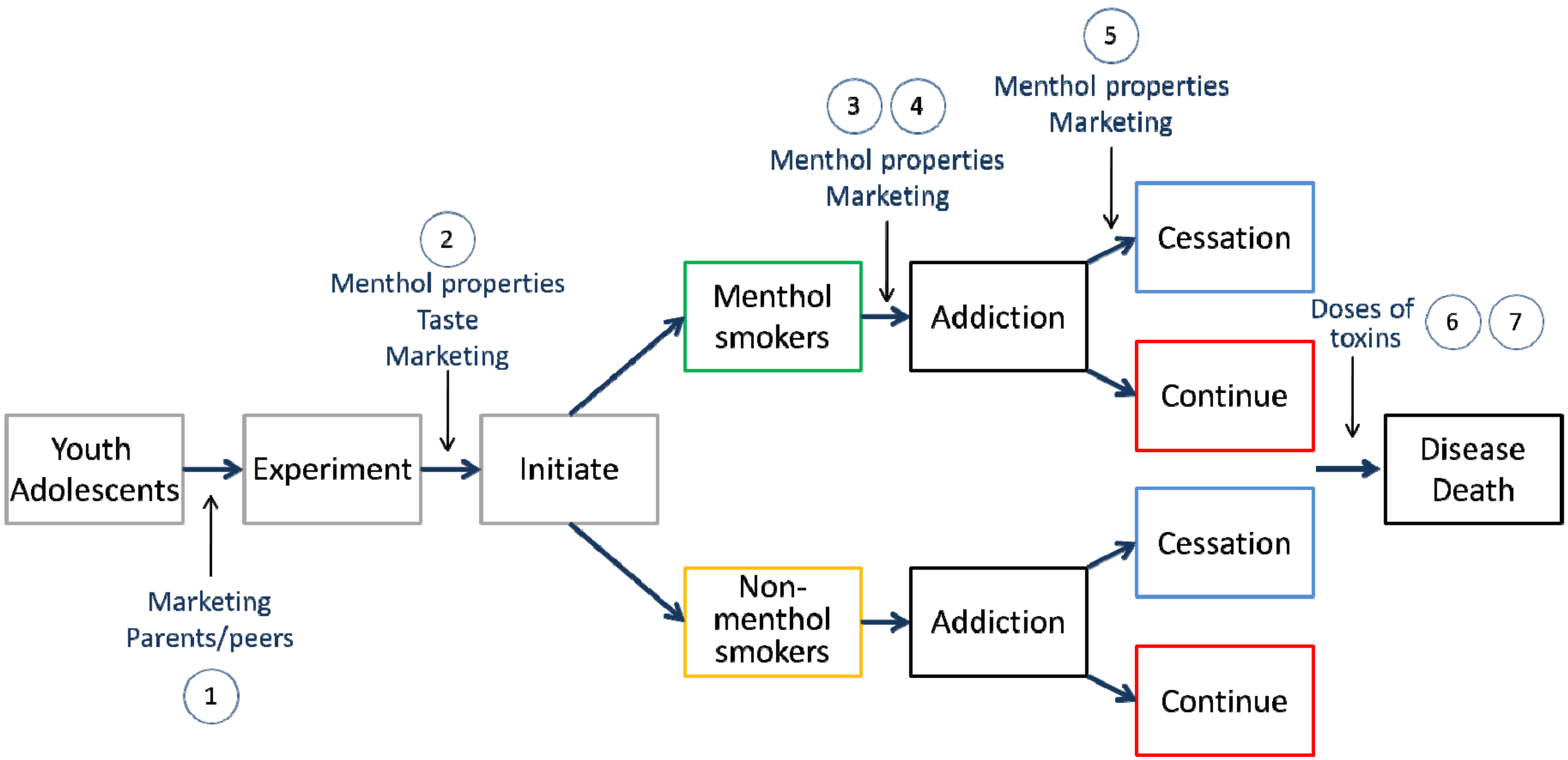
Mabry PL, Marcus SE, Clark PI, Leischow SJ, Méndez D. Systems science: a revolution in public health policy research. *American Journal of Public Health* 2010;100(7):1161-3.

Levin ML. The occurrence of lung cancer in man. *Acta - Unio Internationalis Contra Cancrum* 1953;9(3):531-41.

Méndez D. A systems approach to a complex problem. *American Journal of Public Health* 2010;100(7):1160.

Levy DT, Chaloupka F, Gitchell J, Mendez D, Warner KE. The use of simulation models for the surveillance, justification and understanding of tobacco control policies. *Health Care Management Science* 2002;5(2):113-20.

Figure 1. Model of Smoking and Health: From Experimentation to Disease




Footnote: Numbers refer to TPSAC questions related to individuals. Marketing refers to marketing of menthol cigarettes.

**<u>CHAPTER 3: THE PHYSIOLOGICAL EFFECTS OF MENTHOL CIGARETTES</u>**

## INTRODUCTION

Menthol is a flavor additive widely used in consumer and medicinal products. It can be natural or synthetic, has a minty taste and aroma, and may have cooling, analgesic or irritating properties. As noted in chapter 1, menthol is an active ingredient in certain medicinal products, such as cough drops, and when used in medicinal products, it is regulated as a drug. The use of menthol in tobacco products is not regulated. Menthol is present in varying concentrations in 90 percent of tobacco products, including cigarettes that are not marketed as menthol cigarettes.

The Family Smoking Prevention and Tobacco Control Act charges the Tobacco Products Scientific Advisory Committee (TPSAC) with developing a report and recommendations that address "the issue of the impact of the use of menthol in cigarettes on the public health including such use among children, African Americans, Hispanics, and other racial and ethnic minorities." Chapter 3 reviews the physiological effects of menthol in cigarettes. It reviews menthol's chemical structure, its mechanism of action, its interaction with key constituents of tobacco and tobacco smoke, and its affect on the sensory experience of smoking.

Specifically, chapter 3 will address the following questions:

- Does menthol have cooling and/or anesthetic properties that moderate the harshness of cigarette smoke?
- Does menthol make low-tar, low-nicotine cigarettes more acceptable to smokers?
- Does menthol have an effect on nicotine or nicotine-derived nitrosamine metabolism?
- Is it biologically plausible that menthol increases the addictiveness of cigarette smoking?

The answers will assist TPSAC in addressing the nine overarching questions listed and discussed in chapter 1 that are the subject of this report. While the information in chapter 3 is relevant to all nine questions, it is of particular importance to those examining the impact of menthol cigarettes on individual smokers.

## METHODS

Chapter 2 provided the general framework for this report and the Tobacco Products Scientific Advisory Committee's approach to gathering, reviewing and weighing the evidence. Using this framework, chapter 3 draws on sources that provide information about the physiological effects of menthol or necessary background information. The sources of information includes papers published in peer-reviewed literature, documents supplied to the committee by tobacco companies, FDA white papers and unpublished tobacco company documents. Chapter 3 relies in part on animal and human studies that biochemically and/or behaviorally assess the physiological effects of exposure to menthol.

## WHAT IS MENTHOL?

Chemically, menthol is a monocyclic terpene alcohol. It is a naturally occurring chemical chiefly derived from the peppermint plant (*Mentha piperita*) or the corn mint (*Mentha arvensis*), but it can also be synthetically produced. The chemical structure of menthol is shown in Figure 1. Menthol can exist as one of eight stereoisomers—molecules with identical formulas but different three-dimensional shapes. These isomers include menthol, isomenthol, neomenthol and neoisomenthol, each of which can exist as l, also called (-), or d, also called (+). Each of the stereoisomers has distinct pharmacologic characteristics. The l, or (-), isomer of menthol is the natural isomer and conveys the typical taste and sensory characteristics of menthol. The d, or (+), isomer is active but less so than l-menthol (Eccles 1994).

Tobacco companies use both natural and synthetic menthol in cigarettes. The natural menthol found in cigarettes (l isomer) is typically crystallized from steam-distilled oil of the corn mint plant (R.J. Reynolds 2010, p.6). Synthetic menthol (dl - menthol) is racemic, meaning it contains both the d and l isomers and has different taste characteristics from natural menthol (Lorillard Tobacco Company 2010, p.11, Heck 2010). Some cigarette manufacturers use natural menthol only; others use a mixture of natural and synthetic menthol. Natural menthol has been reported to impart greater cooling and mintness and less sharpness, perhaps due to trace chemicals in the natural extract (Wayne and Connolly 2004). Peppermint and spearmint oils may also be added along with menthol to some cigarettes to modify the taste and other sensory characteristics of the smoke (Wayne and Connolly 2004).

Menthol is volatile and has a relatively low boiling point (212 degrees C) (Heck 2010). Consequently, menthol readily vaporizes during cigarette smoking and easily transfers from the cigarette smoke to the smoker, with little pyrolysis, or decomposition. (Jenkins et al. 1970). In mainstream smoke, the vast majority of menthol is in the particulate phase (Jenkins et al. 1970).

Menthol is added to cigarettes in numerous ways: (1) spraying the cut tobacco during blending; (2) application to the pack foil; (3) injection into the tobacco stream in the cigarette maker; (4) injection into the filter on the filter maker; (5) insertion of crushable capsule in the filter; (6) placement of a menthol thread in the filter; and (7) a combination of the above (R.J. Reynolds 2010, p.7, Altria Client Services 2010). Over time, menthol diffuses throughout the cigarette irrespective of where it was applied. Menthol cigarettes are typically blended using more flue-cured and less burley tobacco (Wayne and Connolly 2004). This is because some of the chemicals in burley tobaccos create an incompatible taste character with menthol.

Menthol in cigarettes can be measured either by weight or yield. When measured by weight, menthol content is expressed either as the ratio of the weight of menthol to the weight of the tobacco in the cigarette (mg menthol/gm tobacco), or the weight of menthol in the entire cigarette (mg menthol/ cigarette). Ratios also can be expressed as parts per million (ppm), where 1000 ppm is equivalent to 0.1 percent. Yield per cigarette measures menthol in cigarette smoke and is expressed in mg. Though the menthol-in-smoke measurement is more biologically relevant, it is important to note that menthol yield is generated using standard smoking machine test methods and may not reflect how individual smokers consume menthol cigarettes. Smokers on average take in larger amount of smoke that the machine predicts, particularly when smoking lower yield cigarettes. Thus smokers of menthol cigarettes are likely to be exposed to more than the machine determined menthol yield per cigarette.

Menthol produces a minty taste and aroma and elicits cooling sensations. At low concentrations menthol has a soothing effect, but at high concentrations menthol is irritating. Menthol is reportedly added to cigarettes both as a characterizing flavor (higher levels) and for other taste reasons (lower levels). These other taste reasons include brightening the flavor of tobacco blends and/or smoothing or balancing the taste of the blend (R.J. Reynolds 2010, p.15). The lowest detectable concentration identified by smokers as menthol characterizing is about 0.12 percent (Lorillard Tobacco Company 2010, p.13). Most menthol cigarettes contain 0.30 percent or higher. Menthol concentrations in non-menthol cigarettes average about 0.01 to 0.03 percent (Wayne et al. 2004). (b) (4) [redacted]. In addition to taste, menthol also contributes to smoke impact and to modulation of the irritation from nicotine.

In a recent survey of 48 U.S. menthol cigarette brands and sub-brands, the average menthol content in cigarettes by weight was 2.64 mg/ cigarette, with a range from 1.61 to 4.38 mg (Celebucki et al. 2005). The average menthol content in tobacco by weight was 3.89 mg/ gm tobacco, with a range from 2.35 to 7.76. Menthol concentrations tended to be highest in cigarettes with the lowest machined-measured tar deliveries, for reasons discussed below. Thus ultralight cigarettes typically had the most menthol, followed by light cigarettes and full flavor cigarettes. Altria presented data on menthol concentration in tobacco and in smoke for U.S. menthol cigarettes marketed in 2008 and 2009 (Altria Client Services 2010, p.25). The median menthol in tobacco was about 0.6 percent (6 mg/gm tobacco) and the median menthol in smoke was about 0.6 mg/cigarette. The lowest menthol in smoke was 0.35 mg/cigarette and the highest 1.29 mg/cigarette. The latter was in Camel LT KS Men HP cigarettes in which a menthol capsule is crushed prior to machine smoking. Menthol is also present in many non-menthol cigarettes at lower concentrations.

Examples of the menthol contained in the cigarettes and delivered in the smoke (as tested by standard condition machine smoking) for common full flavor menthol cigarette sub-brands are as follows (units are mg): Marlboro FF DS Men HP – 4.1, 0.71; Camel Crush KS HP, breaking capsule – 5.3, 0.87; Camel FF KS Men HP – 3.6, 0.71; Kool FF 100 HP/SP – 4.4, 0.74; Salem FF KS HP Green Label – 3.3, 0.61; Newport FF LS Men HP – 2.3, 0.46 (Altria Client Services 2010).

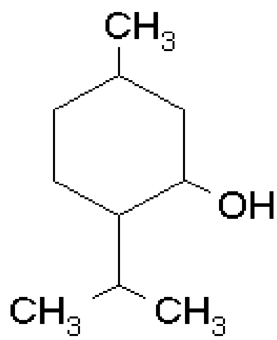
Low yield cigarettes – light and ultralight brands – are low yield primarily due to increased ventilation or air dilution. Compared to full flavor menthol cigarettes, light and ultralight menthol cigarettes have lower transfer efficiency—the percentage of menthol in the smoke compared to the menthol in the cigarette. The increased filtration and ventilation of lower tar delivery products decreases transfer efficiency. In full flavor menthol cigarettes, the transfer efficiency of menthol averages 10–20 percent, while the transfer efficiency in ultralight menthol cigarettes can be as low as 5 percent (Altria Client Services 2010, p.22–24; Cook et al. 1999). To cite a specific example, menthol transfer from the Newport cigarette is 20 percent, while transfer from Newport Light is 12 percent (Lorillard Tobacco Company 2010, p.6). The higher menthol content in light and ultralight cigarettes compensates for the lower transfer efficiency. The transfer efficiency can change with storage of cigarettes as menthol moves from the tobacco to the filter, from which it may be less available for elution (Altria Client Services 2010).

Tobacco companies have explored adding chemicals with menthol-like cooling effects to cigarettes. A number of cooling agents were developed by Wilkinson Sword Ltd in the 1970s and are identified as WS compounds (Leffingwell & Associates 2010). Several of these chemicals including WS-3, WS-5, WS-12, WS-14 and WS-23, act on the same receptors as menthol and have similar cooling effects, but lack menthol's minty taste and aroma (Ma et al. 2008). Other cooling chemicals have been developed by other companies. (b) (4) [redacted] but to TPSAC's knowledge, they were never added to mass marketed cigarettes. (b) (4) [redacted]

(b) (4)

. In any case, when considering regulation of menthol in cigarette, the presence of menthol analogs or alternative should also be considered.

Figure 1




**MENTHOL'S MECHANISMS OF ACTION**

Menthol acts on receptors expressed primarily on sensory nerves, including in the trigeminal nerves that innervate the nose, mouth and airways (Abe et al. 2005). Specifically, menthol acts on Transient Receptor Potential (TRP) channels that contribute to the detection of physical stimuli, including temperature and chemical irritation (Levine et al. 2007; Macpherson et al. 2006). Menthol has been reported to act on three of these receptors: the TRPM8 (transient receptor potential melastatin 8), TRPA1 (transient receptor potential ankyrin1) and TRPV3 (transient receptor potential, vanilloid family, member 3). (b) (4) The TRPM8 receptor, which is responsive to cold, and the TRPA1 receptor, which is a chemosensory receptor, are expressed in the sensory neurons of the trigeminal and dorsal root ganglia. The TRPV3 and TRPV1 receptors are responsive to heat and capsaicin. The TRPV3 receptors are expressed in skin cells, and TRPV1 in trigeminal nerve and dorsal root ganglia cells. All of these receptors have roles in mediating sensations of pain or irritation (Eid et al. 2009).

The TRPM8 receptor is activated by both cold and by menthol (Voets et al. 2004; Maccpherson et al. 2006; Bautista et al. 2007), explaining why menthol elicits sensations of cooling. Menthol decreases cold pain thresholds and enhances pain responses to noxious cold stimuli (Hatem et al. 2006; Wasner et al. 2004). TRPM8 receptors are located on sensory, or afferent, nerves. At low doses menthol produces cooling and analgesia and at high doses menthol can cause irritation and pain via effects on these receptors. With prolonged stimulation menthol desensitizes TRPM8 receptors (Kuhn et al. 2009).

The TRPA1 receptor chiefly mediates the pain response to irritant chemicals, including the unsaturated aldehydes in cigarettes smoke (Andre et al. 2008; Bessac and Jordt 2008). This receptor also transmits responses to noxious cold (Karashima et al. 2009), and inflammatory pain (Bautista et al. 2006). Chemicals interact with TRPA1 to produce cough and airway inflammation (Geppetti et al. 2010). Menthol activates and inhibits the TRPA1 receptor, through which menthol can produce or reduce the irritation from tobacco smoke (Bressac and Jordt 2008; Talavera et al. 2009; Xiao et al. 2008; Karashima et al. 2007). Nicotine, a known irritant, also activates TRPA1 receptors (Karashima et al. 2007; Xiao et al. 2008). Menthol activates TRPV3 receptors to induce cooling in skin (Macpherson et al. 2006).

TRPV1 receptors, found in airway sensory fibers as well as the nasal mucosa, respond to chemical stimuli including capsaicin and many other irritant chemicals (Bessac and Jordt 2008). Nicotine induces irritation by effects both on nicotinic cholinergic receptors and on TRPA1 and TRPV1 receptors (Talavera et al. 2009; Dussor at el. 2003; Simons et al. 2003; Lee et al. 2009).

Menthol acts on olfactory nerves to produce a minty aroma and pungency, effects that decrease as people age (Murphy 1983). When applied to skin, menthol has cooling and antipruritic effects (Bromm et al. 1995). These anti-itching effects have been attributed to menthol's interaction with cold receptors and possibly with kappa opioid receptors (Galeotti et al. 2002).

In addition to its ability to relieve itching, menthol is a topical analgesic. Menthol desensitizes nociceptive C receptors, which are responsible for sending pain signals to the brain; this activity may contribute to analgesia (Cliff and Green 1994). Given in high doses orally (10 mg/kg) or in smaller doses into the brain (10 mcg intracerebroventricularly) menthol has potent analgesic effects in rodents, effects that depend on activation of the endogeneous opioid system, acting on kappa opioid receptors (Galeotti et al. 2002). Thus in high concentrations, menthol acts on the brain. However, the concentration threshold for effects on the brain is not known. Menthol increases skin blood flow at the site of application, which may also contribute to local analgesia (Harris et al. 2006). Menthol's other attributes include antibacterial and antifungal properties and the ability to enhance of penetration of topical drugs and chemicals (Iscan et al. 2002).

**MENTHOL DESENSITIZATION AND INTERACTION WITH NICOTINE**

With repeated or prolonged administration, menthol is known to cause desensitization to its own cooling and irritant effects. Menthol is also reported to reduce sensitivity to noxious chemicals, including nicotine. The irritating effects of nicotine on the airway are mediated by activation of nicotinic cholinergic receptors and TRPA1. In cellular electrophysiology studies and in a rodent model of nicotine-induced airway constriction reflex response, menthol inhibits effects of nicotine (Talavera et al. 2009). Other in vitro studies have reported that menthol results in desensitization of nicotine-induced neuronal activation (Hans et al. 2006; Reeh et al. 2006). [redacted] (b) (4)

In an experimental study, people whose tongues were repetitively dosed with menthol in solution became less sensitive to menthol's irritating and cooling effects (Dessirier et al. 2001). Menthol also reduced irritation from nicotine when applied to the tongues of people (Dessirier et al. 2001). (b)(4) [redacted]. Menthol did however reduce burning pain both in baseline and nicotine conditions. Higher levels of nicotine reduced the subjects' ability to discriminate dose-related odor and cooling effects of menthol compared to lower nicotine levels. While both menthol and nicotine have the potential to desensitize responses with repeated exposure, a study comparing olfactory thresholds for menthol and nicotine in smokers and non-smokers found the smokers had a much higher olfactory threshold for nicotine but no difference in threshold for menthol (Rosenblatt et al. 1998). The same was seen in both menthol and non-menthol smokers. Thus the effects of menthol are persistent in smokers.

**MENTHOL KINETICS, METABOLISM AND METABOLIC INTERACTIONS WITH NICOTINE AND TOBACCO-SPECIFIC NITROSAMINES**

Menthol moves from cigarette smoke into the lungs and then into the bloodstream. Smokers systemically absorb an average of 5–20 percent of the menthol in a menthol cigarette, depending on the extent of ventilation (Altria Client Services 2010, Benowitz et al. 2004). For a cigarette containing 3 mg of menthol (0.3 percent), a smoker of 20 cigarettes per day is exposed to an average systemic dose of 12.5 mg menthol per day.

Once it enters the general circulation, menthol is rapidly metabolized, making it difficult to measure free menthol in the blood or urine. Menthol is metabolized primarily through glucuronidation, a process that takes place in the liver to detoxify substances, and through oxidation, which also takes place in the liver. Glururonidation primarily is driven by the liver enzyme UDP-glucuronosyl transferase 1A4 (Green and Tephly 1998). The result of this process is a compound called menthol glucuronide. Oxidation of menthol to hydroxylated metabolites has been observed in studies in rats (Yamaguchi et al. 1994; Madyastha and Srivatsan 1988). In humans, approximately 50 percent of an oral dose of menthol is excreted in the urine as menthol glucuronide (Gelal et al. 1999). The half-life of menthol glucuronide after oral menthol dosing is about 50 minutes in plasma and 74 minutes in urine, although there appears to be a longer terminal half-life, most likely due to the slow release of the highly lipid-soluble menthol from body tissues and/or due to enterohepatic recirculation (Gelal et al. 1999). It is difficult to do pharmacokinetic studies with inhaled menthol because the dose absorbed cannot be known with certainty. Urine menthol glucuronide concentrations have been measured in a cross-sectional study of smokers of menthol and non-menthol cigarettes (Benowitz et al. 2010). On average, menthol levels are higher in menthol smokers, but many non-menthol smokers also have high menthol levels due to consumption of menthol-containing foods.

While free menthol concentrations are quite low in blood, they are high in tobacco smoke. As a result, menthol concentrations will be high in the mouth, throat and lungs. Estimating concentrations in smoke is important to assess the plausibility that menthol has effects on sensory nerves and possible drug metabolism in the upper and lower airways in relation to concentrations that have effects in animals or cell preparations. Assuming that a menthol cigarette delivers 0.8 mg of menthol in smoke and that a smoker takes 8 puffs on a cigarette, the menthol per puff is 0.1 mg. Assuming that all of the menthol in a puff is absorbed and that the inhalation volume associated with one puff (puff volume plus air) is 800 ml, the concentration of menthol would be 1250 mcg/L, which would be 8.0 uM/L. There is uncertainty about the partition of menthol between smoke and lung tissue, but this gives some rough approximation about what levels might act in the lungs, where there are drug metabolizing enzymes. Concentrations could be considerably higher in the mouth and throat, before the inhaled smoke is fully diluted with the fresh air inhaled with the smoke. These high concentrations are in contrast with the low concentrations of free menthol in the blood stream and presumably in the liver, as discussed in more detail below.

**Interactions with nicotine**

Menthol may alter the metabolism of constituents of tobacco smoke, including nicotine. Menthol inhibits the metabolism of nicotine in liver microsomal test systems (MacDougall et al. 2003). (b) (4) [redacted]. The IC 50 (concentration that inhibits metabolism by 50%) was 70.5 uM for l menthol and 37.8 uM for d menthol in the MacDougall study. This concentration is higher than the concentrations typically detected in the blood of smokers, raising the question of whether circulating menthol levels in smokers would be adequate to inhibit liver metabolism of nicotine. However, nicotine is also metabolized in the lungs (Turner et al. 1975), where, as described previously, menthol levels in smoke are likely to be high enough to inhibit nicotine metabolism. In an experimental study of smokers, Benowitz et al. (2004) found that smoking menthol cigarettes inhibits nicotine metabolism in smokers. This was a two-week crossover study in which 14 smokers smoked menthol or non-menthol cigarettes on alternating weeks. After smoking a particular type of cigarette for several days, each subject was given an intravenous infusion of deuterium-labeled nicotine and cotinine to determine the effects of menthol cigarette smoking on the disposition kinetics of nicotine and cotinine. Nicotine clearance was on average 10 percent slower while smoking menthol cigarettes. Menthol inhibited both oxidative metabolism of nicotine to cotinine, and glucuronidation of nicotine. Menthol had no effect on cotinine metabolism. Potential limitations of this study include its small sample size, that its subjects were all heavy smokers and that its subjects were predominantly men.

Studies that used a different measure of nicotine oxidative metabolism found that menthol had no statistically significant effect on the breakdown of nicotine. These studies measured the ratio of the nicotine metabolites trans-3' hydroxycotinine to cotinine (Dempsey et al. 2004), which result from the activity of the enzyme CYP2A6, the major enzyme involved in the oxidation of nicotine. The ratio of trans-3' hydroxycotinine to cotinine, which can be measured in blood, saliva or urine, is highly correlated with the clearance of nicotine. Using this ratio, three studies found no difference in nicotine metabolism between menthol and non-menthol smokers. One was a cross-sectional multi-site study of 1044 menthol and 2297 non-menthol smokers conducted by Altria (Total Exposure Study, Wang et al. 2010). Another was a study of 755 African American smokers participating in a clinical trial of smoking cessation (Ho et al. 2009). The third was a study of 89 smokers with schizophrenia and 53 controls (Williams et al. 2007). The lack of a menthol effect is consistent with either no effect or a small effect of menthol on oxidative metabolism. The ratio would not be sensitive to an effect of menthol on nicotine conjugation. The Altria Total Exposure Study did look at urine ratios of nicotine glucuronide to nicotine, and found no effect of menthol cigarette smoking, arguing against an effect of menthol on nicotine conjugation (Altria Client Services 2010).

**Interaction with tobacco-specific nitrosamines**

Menthol may also inhibit the detoxification of the tobacco-specific carcinogen 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanol (NNAL). NNAL is formed as a major metabolite of the potent tobacco-specific nitrosamine and carcinogen 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone NNK (Hecht). NNK is present in cigarette tobacco, and is formed primarily by nitrosation of nicotine in the curing process. A major pathway of detoxification of NNAL is by glucuronidation, considered to be mediated by the isoenzymes UGT2B7 (Ren et al. 2000) UGT2B10 (Chen et al. 2007) and UGT2B17 (Lazarus et al. 2005). A substance that inhibits the detoxification of NNAL could potentially increase the risk of cancer. Richie et al. (1997) found in a study of 34 African American smokers and 27 Caucasian smokers that the ratio of NNAL glucuronide / NNAL in urine was significantly lower in African Americans. This finding suggested slower glucuronidation detoxification of NNAL in African American smokers. Since African Americans predominantly smoke menthol and Caucasians predominantly non-menthol cigarettes, Ritchie et al. hypothesized that menthol inhibits NNAL glucuronidation. Muscat (2009) specifically compared 67 menthol smokers to 80 non-menthol smokers, and found that the glucuronidation ratio was significantly lower in white menthol smokers and menthol smokers overall, with a non-significant trend in the same direction for African American smokers. Muscat et al. also found that menthol inhibited NNAL glucuronidation in vitro using human liver microsomes. In the latter study, the IC 50 values for inhibition of N-glucuronidation and O-glucuronidation of NNAL were 0.26 and 0.41 mM, respectively. These levels are higher than those found in the blood and presumably liver of menthol cigarette smokers. Whether such glucuronidation can occur in the lung is not clear. The Altria-sponsored Total Exposure Study, which included 1044 menthol and 2297 non-menthol cigarette smokers, mentioned previously, found no effect of menthol cigarette smoking within racial groups on the ratio (Altria Client Services 2010).

## MENTHOL AND SENSORY RESPONSE TO CIGARETTE SMOKING

### Effects on smoke smoothness and impact

Sensory attributes of tobacco smoke can be considered as a combination of taste, smell and chemesthesis (the latter referring to the feel, such as cooling, biting and burning) (Carpenter et al. 2007). These occur in the context of stimulation of physiological responses in olfactory and trigeminal nerves. These responses have been described by Philip Morris as tobacco smoke flavor, which includes attributes derived from aromatic volatile substances, tastes and feeling qualities such as dryness and cooling (Philip Morris 1999). Sensory attributes overall include resistance to draw, throat response (such as smooth, stinging, peppery, cool), mouth response, mouth fullness, dryness and harshness, tobacco taste, aftertaste strength and cooling effect.

As noted above, menthol produces a variety of sensory effects, including a minty taste and aroma, cooling/ soothing effects, anesthetic effects and irritant effects. Menthol contributes to many of the sensory effects of cigarette smoke, including strength, taste, harshness, smoothness, mildness, coolness taste, and aftertaste. (R.J. Reynolds 1984). The effects of menthol are related to concentration. Lower menthol concentrations produce cooling and anesthetic effects, while higher menthol concentrations produce burning and irritation.

At the very low menthol concentrations used in non-menthol cigarettes, menthol is likely to make smoke smoother and less harsh even though the distinctive minty tasted and aroma is not detectable (Wayne and Connolly 2004). At the concentrations found in menthol cigarettes, smokers report that menthol reduces irritation and that menthol cigarettes are less harsh and smoother than non-menthol cigarettes. Smokers of high menthol cigarettes appear to particularly like the taste and aroma of menthol.

Menthol also has irritant effects, as noted above. Throat irritation is an important contributor to smoke impact, which is a key component of the perceived strength and satisfaction of the cigarette. Both nicotine and menthol stimulate the trigeminal nerve in the mouth and throat to jointly produce the sensory effect of “bite,” or “throat grab.” Reviews of tobacco company documents and a submission from Altria describe the interaction between menthol, nicotine and tar in producing impact and other sensory effects (Wayne et al. 2004; Kreslake et al. 2008; Altria Client Services 2010; RJ Reynolds 1985). In cigarettes with low levels of tar and nicotine, the addition of menthol can enhance the “bite” or “throat grab” of the smoke, making such cigarettes more acceptable to consumers. Conversely, the addition of menthol to cigarettes high in tar and nicotine can reduce the irritating effect of nicotine, perhaps by cross desensitization, making these cigarettes more palatable. Among menthol cigarette smokers, perception of strength and impact correlate better with menthol delivery than with nicotine delivery (Perfetti 1982).

Thus menthol is not simply a flavoring agent but has drug-like characteristics that modulate the effects of nicotine on the smoker. The consequences of these effects for menthol cigarette smokers are twofold: the sensory stimulation from the “throat grab” of menthol could provide greater reinforcement of smoking behavior, and the reduced irritation provided by lower levels of menthol could lessen aversion to initial self-administration of nicotine among novice smokers, thereby facilitating continued smoking that leads to addiction. Additionally RJR documents (Carpenter et al. 2007) found a relationship between sensory preferences and smoking topography. Smokers who desired a strong cigarette took larger puffs compared to individuals who desired less strength. Since menthol is a determinant of perceived strength, this could be another reason for a relationship between menthol and greater intake of cigarette smoke.

(b) (4)

[redacted]

**Genetic interactions**

Individual differences in taste perception, such as the ability to taste bitter chemicals, are well known. These differences are at least in part genetically determined. There has been much research on genetic differences in response to the bitter chemicals phenylthiocarbamate (PTC) and 6-n-propylthiouracil (PROP). Some people can taste bitter taste (“tasters”) and some cannot (“non-tasters”). Tasters are less likely to become a smoker, suggesting that bitter taste makes smoking more aversive (Enoch et al. 2001; Cannon et al. 2005; Snedecor et al. 2006). The family of bitter receptors, TAS2R (taste receptor type 2) contribute substantially to the ability to taste bitter. One of the genes, TAS2R38, accounts for 85% of individual variability in response to bitter (Wooding 2004). The two most common genetic variants (haplotypes) of TAS2R38 are PAV and AVI. PAV homozygotes are most sensitive and AVI homozygotes are least sensitive to PTC/PROP. Among people of European descent, smokers with the AVI genotype rate higher taste/sensory and cue exposure-related motivations for smoking compared to smokers with the PAV genotype (Cannon et al. 2005). Thus the ability to perceive bitter taste seems to decrease taste-related motivations for smoking. This study found however that an intermediate taste sensitivity genotype, AAV, was protective against smoking, which seems inconsistent with earlier studies based on the taste sensitivity phenotype. Among African Americans the taster PAV genotype was inversely associated with smoking quantity, whereas the non taster AVI genotype was positively associated with smoking quantity (Mangold et al. 2008). Furthermore, in women, the non-taster genotype was associated with the level of nicotine dependence. Neither the Cannon nor the Mangold study examined interactions between genotype and menthol cigarette smoking. However, since menthol reduces bitterness for some cigarettes, and since reduced bitterness is associated with smoking more, the genetic data support the idea that menthol may affect smoking behavior and associated dependence. These studies also raise the possibility that menthol might interact with genetically determined taste sensitivity to facilitate smoking. That is, menthol could mask bitterness to allow smokers who are genetically more sensitive to bitterness to better tolerate tobacco smoke and therefore to become a smoker.

**Respiratory effects**

Menthol is used medicinally in decongestant products. Menthol produces a sensation of increased nasal patency, although nasal congestion is unaffected (Eccles 1990; Nishino et al. 1997; Kenia et al. 2008). Menthol inhibits ventilation (Harris 2006) and increases breath-hold time in humans (Sloan 1993). Menthol also acts as a cough suppressant (Laude et al. 1994; Morice et al. 1994). The respiratory effects of menthol—a sensation of cooling, increased breath-hold time and cough suppression—could promote deeper inhalation and/or longer retention of smoke in the lungs while smoking menthol cigarettes. In animal studies, menthol promotes bronchodilation (Wright et al. 1997) and the clearance of mucous from the lungs (Nishino 1997).

**Other effects**

Orally dosed menthol can cause vasodilation and relaxation of intestinal smooth muscle (Hawthorne et al. 1988). These effects, which are believed to be related to inhibition of calcium currents in smooth muscle (Hawthorne et al. 1988; Taylor et al. 1984), may explain the medical utility of menthol as a treatment for gastrointestinal disturbances. The relevance to the pharmacology of inhaled menthol is unclear. Oral menthol also has been found to increase heart rate, possibly a reflex response to menthol-induced vasodilation (Gelal et al. 1999). However, studies comparing menthol and non-menthol cigarettes have not found any cardiovascular effects of menthol (Pritchard et al. 1999; Pickworth et al. 2002). Studies of electroencephalographic responses to smoking found that response correlated with perceived impact and liking, which may be determined in part by menthol (Gullotta et al. 1989a, 1990, cited in Wayne, 2004). However menthol added to cigarettes had no direct effect on the electroencephalogram (Pritchard et al. 1999).

**EVIDENCE SYNTHESIS**

Chapter 3 set out to answer four questions relating to the physiological effects of menthol pursuant to TPSAC's charge. The responses to those questions are given below. TPSAC considered this information, along with other evidence gathered, reviewed and synthesized in this report, to assess the overall public health impact of menthol cigarettes and to make its recommendations to the FDA.

**Does menthol have cooling or anesthetic properties that moderate the harshness of cigarette smoke?**

The evidence is sufficient to conclude that menthol has cooling and anesthetic effects that reduce the harshness of cigarette smoke. Research indicates that menthol acts on both thermal and nociceptive receptors. This dual action results in both cooling and counter-irritant effects. Menthol desensitizes receptors by which nicotine produces irritant effects, thereby, reducing the irritation from nicotine in tobacco smoke.

The implications of these findings are that by reducing the harshness of tobacco smoke menthol could facilitate initiation or early persistence of smoking by youth. Also, by reducing the harshness of smoke, menthol could facilitate deeper and more prolonged inhalation of tobacco smoke, resulting in greater smoke intake per cigarette.

**Does menthol make low-tar, low-nicotine cigarettes more acceptable to smokers?**

The evidence is sufficient to conclude that menthol makes low-tar, low-nicotine cigarettes more acceptable to smokers. Like nicotine, menthol has irritant effects that contribute to the impact or "throat grab," of tobacco smoke. In light or ultralight cigarettes with lower nicotine delivery, menthol can be used to provide impact.

The implications of these findings are that menthol is likely to make low-yield cigarettes more satisfying, and smokers who switch to low-yield cigarettes for health concerns may be more likely to continue to smoke rather than quit.

**Does menthol have an effect on the metabolism of nicotine or tobacco-specific nitrosamines?**

The evidence is sufficient to conclude that it is at least as likely as not that menthol inhibits the metabolism of nicotine in smokers. The evidence in not sufficient to conclude that it is at least as likely as not that menthol inhibits the glucuronidation of NNAL in smokers. Studies using liver micosomes demonstrate that menthol can inhibit the metabolism of nicotine. One experimental within-subject human study, using a state-of-art method of measuring the rate of nicotine metabolism, indicates that menthol cigarette smoking inhibits the metabolism of nicotine by about 10 percent. Menthol could be affecting nicotine metabolism in the lungs, where some nicotine metabolism is known to occur and where menthol concentrations are likely quite high in menthol cigarette smokers. Several cross-sectional studies show menthol has no effect on the nicotine metabolite ratio, a biomarker of the rate of nicotine oxidation. However cross-sectional studies may not have adequate power to detect a 10 percent difference in the metabolite ratio. Given the small magnitude of the menthol effect on nicotine metabolism in the positive human experimental study, it is unlikely that such a metabolic difference would have much, if any, effect on smoking behavior.

Menthol in high concentrations has been shown to inhibit the metabolism of the tobacco-specific nitrosamine, NNAL, in isolated liver preparations. One cross-sectional study found lower ratios of NNAL glucuronide to NNAL in menthol cigarette smokers, but another larger study did not find such an effect. On balance the evidence to date is not sufficient to demonstrate a significant effect. However if menthol does inhibit NNAL metabolism, this could be a basis for higher cancer risk in menthol cigarette smokers.

Menthol is known to enhance the dermal penetration of a variety of drugs, and might in theory enhance the pulmonary absorption of nicotine and/or tobacco carcinogens. The data on menthol and exposure to tobacco toxins is reviewed in chapter 6.

**Is it biologically plausible that menthol enhances the addictiveness of cigarette smoking?**

The evidence is sufficient to conclude that it is biologically plausible that menthol makes cigarette smoking more addictive. The evidence reviewed suggests several mechanisms by which menthol could contribute to the initiation and persistence of cigarette smoking.

- Nicotine is required for the acquisition and maintenance of addiction to cigarette smoking. But as described previously, menthol can modulate nicotine effects and may act directly on nicotinic cholinergic receptors to alter nicotine response.

- While nicotine is required for nicotine addiction, the addictiveness of cigarettes is also influenced by sensory factors (Rose 2006; Henningfield et al. 2011 in press). Menthol provides an unmistakable

- Sensory experiences can contribute to conditioned aspects of smoking behavior. Once drug self-administration has been established, taste and other sensory factors can function as stimuli that can substantially enhance the strength and persistence of drug self-administration (Carroll and Meisch 2011; Panlilio et al. 2005).
- Stimuli associated with drug intake and/or withdrawal can come to evoke craving that promotes resumption of self-administration of the drug after a period of abstinence. Thus, menthol from food or toothpaste could serve as a sensory cue to prompt relapse to smoking. These mechanisms have been demonstrated in a variety of animal and human studies with a variety of addictive drugs (Wilson et al. 2004; Sayette and Griffin 2010).
- Another potentially relevant issue is the relationship between menthol and genetic differences in perception of taste. As noted above, various studies raise the possibility that menthol might interact with genetically determined taste sensitivity to facilitate smoking. Thus, there may be a genetically susceptible population for whom menthol cigarettes facilitate smoking.

# CHAPTER 4: PATTERNS OF MENTHOL CIGARETTE SMOKING

## INTRODUCTION

Chapter 4 summarizes recent national survey findings on patterns and trends of menthol cigarette use, providing a background for subsequent chapters on marketing (chapter 5) and initiation, dependence and cessation (chapter 6). In keeping with TPSAC's charge, this chapter gives particular attention to menthol cigarette use in special populations including adolescents, African Americans, Hispanics and other racial or ethnic minorities. This chapter also addresses the prevalence of menthol cigarette use in the generally population of smokers and provides some historical context to help understand the current demographics of menthol cigarette use. The trajectories of brands and use patterns over time are relevant to understanding current consumption patterns.

In order for the TPSAC to reach conclusions about the public health impact of menthol cigarettes and to make evidence-based recommendations to the FDA, TPSAC carefully considered the patterns and trends of menthol cigarette smoking. The first chapter of this report presented nine questions relevant to the TPSAC discussion of the public health impact of menthol cigarettes; seven questions are related to individual smokers and two are related to the population effects of smoking. The information and analysis presented in this chapter are particularly relevant to the following population-level questions:

- Does the availability of menthol cigarettes increase the prevalence of smoking in the population, beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?

## EARLY MENTHOL CIGARETTE USE

The invention of menthol cigarettes is generally credited to Lloyd "Spud" Hughes. In the 1920s, the Ohio smoker stored his tobacco in a tin with the menthol crystals he used to treat a persistent cold. He discovered that the tobacco absorbed the menthol flavor, which made the cigarettes easier to smoke. He started a menthol cigarette company, and his product spurred imitators. In the decades since, menthol cigarettes have grown to become an important product in the U.S. cigarette market. Today, approximately 25 percent of cigarette smokers use menthol cigarettes.

The development and use of menthol cigarettes in the U.S. is well-documented in scholarly articles and books, such as "Ashes to Ashes: America's Hundred-Year Cigarette War, the Public Health, and the Unabashed Triumph of Philip Morris" (Alfred A. Knopf 1997) by Richard Kluger and "The Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product That Defined America" (Basic Books 2007) by Allan M. Brandt. In preparing this chapter, TPSAC relied on "The Growth of Menthols 1933–1977," a 1978 report produced for Brown & Williamson by Market Science Associates (MSA), and "Menthol Review and Product Implications" (bates # 2044123054), which covers the period 1985–89. These two tobacco industry documents provide information on menthol cigarette use before 2000, a period not covered by the data sets and surveys discussed in the methods section of this chapter.

The "Growth of Menthols" report describes the salient trends in menthol cigarette development and use during four distinct time periods from 1933–1977. A summary of each period follows, based on this report.

The first period, from 1933–1955, begins with Hughes' accidental invention of menthol cigarettes. The company he founded started selling Spud brand cigarettes. By 1932, Spud, which no longer exists, was the fifth best-selling cigarette brand in the country, behind non-menthol brands Lucky Strike, Camels, Chesterfield and Old Gold. In 1933, Brown & Williamson introduced Kool, and by 1935, the brand captured 2.2 percent of the U.S. cigarette market. From the beginning, Kool had a therapeutic image. The brand was promoted as an alternative to the heavy, harsh-tasting experience of some non-menthol cigarettes, or for use during the winter months when lower indoor humidity was thought to contribute to dry throats. Kool marketing campaigns included, "For occasional use—Kool for a change," "In between the others, rest your throat with Kools," and "Switch to Kools from Hots."

In 1942, the Federal Trade Commission filed a suit and won a judgment against Brown & Williamson for false advertising related to the purported "health benefits" of Kool. By 1943, the brand's market share had fallen to 1.55 percent. To address this decline, Brown & Williamson brought out Willie the Penguin in 1947 as a "spokesanimal" for the ice-cool nature of the brand and by 1949 Kool's market share had climbed to 2.2 percent. In June, 1950, the landmark Reader's Digest article, "How Harmful Are Cigarettes?" reported on the potential health hazards of cigarettes. Nonetheless, Kool's market share rose to 2.6 percent. By 1952, Kool claimed approximately a 3 percent market share. With introduction of a king-size version in 1954, Kool's share edged up to 3.4 percent. The MSA report summarized Kool's early history as follows:

> "This quasi-medical appeal, and the increased advertising, while effective in increasing its market share, also retained and reinforced the Kools' image as a specialty product appealing to that special segment that wished to avoid "throat dryness" or wished to "rest their throat "from "hot" cigarettes." (MSA).

The second period, from 1956–1962, is described as "The Rise of Salem." R.J. Reynolds Tobacco Co. introduced Salem, the first menthol cigarette with a filter, in 1956. Salem had less menthol taste but more tobacco taste and tar delivery than Kool. According to the MSA report, reaction was phenomenal and within the year, Salem's share of market had caught up to Kool's. Salem's advertising positioned the brand as "a new idea in smoking," with a rich tobacco taste and menthol-fresh comfort. Salem had more burley tobacco but was only slightly flavored with menthol so the tobacco taste would not be masked. Its advertising was keyed to light, refreshing springtime smoking— "*refreshing as all outdoors*" was the slogan. Newport cigarettes also were introduced during this period but did not garner a noticeable market share. A 1956 product comparison found that Newport was a "very light" product. It lacked tobacco taste and had much less tar and nicotine compared to Salem and Kool.

In four years, annual sales of Salem rose to $35 billion in 1960 from $4 billion in 1956, giving the brand 7.5 percent of the cigarette market, far exceeding the market share of Kool. Thanks largely to Salem, menthol cigarette sales grew to account for 11 percent of the total U.S. cigarette market. With the success of Salem, menthol cigarettes evolved from a specialty product into a large, successful category.

During third period covered by the MSA report, from 1963–1974, Kool overtook Salem to re-establish itself as the menthol market leader, in part by capitalizing on its existing popularity with young adults and African Americans. In 1963, Kool already was the preferred cigarette of young smokers. Brown & Williamson saw the increasing number of marijuana users aged 12–17 (who seemed to prefer menthol cigarettes) as a potential market, according to the report. At the same time, Kool, already popular with African Americans, rapidly became the most popular cigarette within that racial group, in part due to advertising and promotions aimed at them. Data on African American smokers age 16 and over in 10 metropolitan areas showed that menthol cigarette use went from 14 percent in 1968 to 38 percent in 1975 before dropping slightly to 33 percent in 1977. Kool accounted for 60 percent of the menthol cigarette market among African Americans under age 35. The report estimates that 70 percent of the Kool's total 4-point share gain between 1968 and 1974 came from the gains among African Americans. Other surveys cited in the report indicated that Kool was making inroads with younger smokers. Kool's share of 16–25 year old smokers advanced from 3 percent in 1966 to about 16 percent in 1974. The report stated:

> "Kool is facing new risks at both ends of the age spectrum. It is attempting to stem the outflow to low tars (among older users) by offering lower tar line extensions. Simultaneously, programs capable of strengthening Kool's image among the new generation of starters, particularly blacks, are critical to maintaining Kool's overall market position."

Between 1964 and 1971, the number of menthol brands and sub-brands more than doubled from nine to 23. Newport's growth trend got underway in 1973, driven by its "Alive With Pleasure" campaign, which continued into the 1980s. The final period covered in the MSA report marks the growth of low-tar menthol cigarettes from 1975-1977.

By 1976 and through 1988, menthol cigarettes accounted for 28–29 percent of the overall cigarette market, according to Federal Trade Commission reports. Newport emerged as the best-selling menthol cigarette brand in 1993. Although Marlboro Menthols were introduced in 1965, they did not become popular until the mid-1990s. In 2003, Marlboro Menthols were the second-leading menthol brand behind Newport, with 5.4 percent of the total cigarette market.

"Menthol Review and New Product Implications," a Feb. 6, 1990 report produced for Philip Morris by the Leo Burnett Company (bates # 2044123055), examined menthol cigarette use patterns from 1985 to 1989. The report documents that menthol smoking among certain populations was well-established. It provided this description of menthol cigarette smokers in 1989: "Compared to non-menthol smokers, menthol smokers are likely to be female, black, younger and city dwellers." Reviewing the five-year trend from 1985 to 1989, the report noted that menthol cigarette smokers had become more African American, Spanish-speaking, older, wealthier, and more rural. The following chart summarized menthol smoking among different populations using the industry method of "indexing" menthol use to a standard of 100. A number under 90 indicates less menthol use among the identified group while a number over 120 means signals more menthol cigarette use among the identified group.

**Table 1: Index of Menthol Smokers 1988-89**

| Demographic | Index Menthol Vs. Non-Menthol 12 Months Ending 6/89 |
|---|---|
| Male | 77 |
| Female | 126 |
| White | 82 |
| Black | 633 |
| Spanish - speaking | 150 |
| 18-34 | 115 |
| 35+ | 90 |
| Under $30 | 102 |
| $30+ | 100 |
| No College | 95 |
| Any College | 88 |

**Source: Menthol Review and New Product Implications, 1990**

In 1989, the three top menthols have strikingly different profiles. Salem smokers were more female, older, educated and rural; Kool smokers were more male, and Newport smokers were black, young, urban, and less affluent and less educated than smokers of competing brands

**METHODS**

TPSAC searched PubMed for studies that quantitatively assessed patterns of menthol cigarette use within and among U.S. demographic groups. The search terms were "menthol cigarettes" [MeSH Terms] OR "cigarettes"[All Fields] OR "menthol" [All Fields] and "patterns "[All Fields]. The search yielded 11 potentially relevant references. TPSAC reviewed key information from each report, including the year of data collection, study methods, population sampled, the geographic region studied, smoking behavior, demographic variables and a summary of the methods. Reports were selected for inclusion if they directly compared patterns of menthol cigarette smoking among U.S. demographic groups. Manuscripts were excluded if they did not include patterns of menthol cigarettes in the U.S. population. Articles were also excluded if they were opinion pieces, policy statements, or review articles. Only articles from peer-reviewed journals were considered.

**Evidence evaluation**

***Primary sources***

TPSAC selected reports based on one or more of three primary data sources: the National Survey on Drug Use and Health (NSDUH), the Tobacco Use Supplements to the Current Population Survey (TUS-CPS), and the National Youth Tobacco Survey (NYTS). These three primary sources are described below.

NSDUH is a household survey which collects information on the U.S. civilian, non-institutionalized population aged 12 years and older. NSDUH had more than 68,000 respondents in 2008. NSDUH includes two questions that are relevant to cigarette use. The two questions read: *On the one day you smoked cigarettes during the past 30 days, how many cigarettes did you smoke? Were the cigarettes you smoked during the past 30 days menthol*? Prior to 2004, this question was worded differently. Thus TPSAC reviewed NSDUH data from 2004 to 2008 only. The NSDUH survey also asked about the specific brand that respondents smoked in the past 30 days. However, the responses to that question cannot be used to accurately track menthol cigarette use; many brands have menthol and non-menthol sub-brands but details about sub-brands are not collected in the survey. A description of menthol definitions for NSDUH and other surveys are described in table 2 below.

<u>TUS CPS</u> is cross-sectional data from 2003 and 2006/07. The data includes adult smokers (at least 18 years old) (*n* = 69,193). The CPS, administered by the U.S .Census Bureau, uses a multistage probability design to collect data from about 50,000 families monthly. This data, obtained in person or through computer-assisted telephone interviews, are used to produce reliable national and state estimates on labor force characteristics among the civilian, non-institutionalized U.S. population. The TUS is a supplement conducted with the CPS every two to three years to collect data on tobacco use, quitting behaviors, nicotine addiction and related attitudes and practices. The 2003 and 2006/2007 TUS CPS included one question that is relevant to cigarette use. The question reads*, Is your usual cigarette brand menthol or non-menthol?*

<u>NYTS</u> is an anonymous school-based survey that used a three-stage cluster sample design that oversampled African-American, Hispanic, and Asian students. NYTS was administered to 27,038 students Grades 6–12 in spring 2006. This survey was conducted among youth who had smoked in the past 30 days, had a usual cigarette brand, and could identify their usual brand as menthol or non-menthol. TPSAC's analysis was conducted among likely menthol smokers—those who said they smoked menthol cigarettes and identified a menthol brand (e.g., Kool) as their usual product.

| **Table 2: Measurement of menthol cigarette smoking** | | | |
|---|---|---|---|
| **Study** | **Survey** | **Definition of menthol cigarette smoking** | **Related survey question(s)** |
| Lawrence et al. 2010 | TUS CPS | Respondents reported the status of their usual cigarette smoked as menthol or nonmenthol | Is your usual cigarette brand menthol or non-menthol? |
| Rock et al. 2010 | NSDUH | Respondents reported smoking part or all of a menthol cigarette in the past 30 days | Were the cigarettes you smoked during the past 30 days menthol? |
| FDA presentation (Ralph S. Caraballo) | NSDUH | Cigarettes smoked in the past 30 days were menthol | Were the cigarettes you smoked during the past 30 days menthol? |

| | | | |
|---|---|---|---|
| Hersey et al. 2010 | NYTS | Based on consistency between smokers' report of the brand and the menthol status of the cigarettes they usually smoked. | Is the brand of cigarettes that you usually smoked during the past 30 days, menthol or non-menthol? |

***Selected reports***

Based on the above criteria, TPSAC selected four data sets and the associated reports for inclusion in this chapter. They are NSDUH itself; Hersey et al. 2010; Lawrence et al. 2010; and Giovino et al. 2004; 2009. TPSAC also drew from a presentation given by Ralph S. Caraballo (Office of Smoking and Health, CDC) at the FDA Tobacco Products Scientific Advisory Committee meeting on March 30, 2010. This presentation included an in-depth analysis of NSDUH. All journal articles and the presentation selected for review included nationally representative data**.** These publications provide a national picture of demographic patterns of menthol cigarette use Table 4 provides more detail on the selected reports.

**Limitations of the data**

One methodological concern is the possibility that both youth and adult smokers may misreport menthol cigarette use. This issue has been discussed in the scientific literature; the Giovino et al. (2004), for example, found that 7.9 percent of smokers age 12 and older who said they mostly smoked Kool, Newport or another menthol brand also reported they did not smoke menthol cigarettes. Conversely, Giovino et al. found that 4.2 percent of those who smoked brands that are only available in non-menthol form (e.g., Winston) said they smoked menthol cigarettes. According to Giovino et al., discrepancies in self-reported menthol cigarette use were higher for adolescent smokers aged 12 to 17 years than for adult smokers, although the 2004 paper does not provide specific data on this issue. TPSAC concludes that these discrepancies, over the time span considered, do not affect its trend analysis.

A second limitation is that TPSAC's primary sources—NSDUH, TUS CPS and NYTS—are cross-sectional annual surveys, i.e., data are collected at only a single point in time from the respondents. We have limited longitudinal data that track how smoking changes in specific individuals over time. Thus, our analyses of trends are at the population level.

Curtin et al. (submission to the FDA, June 2010) from R.J. Reynolds criticized the NSDUH data. They said the NSDUH question— *Were the cigarettes you smoked during the past 30 days menthol*?—was not specific enough to identify smokers whose usual cigarette was menthol (i.e., the question could capture non-menthol cigarette smokers who smoked one menthol cigarette). To address this, Curtain et al. reanalyzed data from a number of different surveys: National Health and Nutrition Surveys (NHANES; 2005/06, 2007/08), National Health Interview Survey (NHIS; 2005); NSDUH (2007); National Youth Tobacco Survey (NYTS, 2006). These surveys defined current smokers as those who had smoked on 10 or more of the last 30 days. Menthol use among current smokers was defined as usual cigarettes, usual brand, or usual brand smoked during the last 30 days for NHANES, NHIS, NYTS respectively. Based on these definitions, no differences were found in the rate of menthol cigarette use across the different age spectrum for the NHANES and NHIS surveys. The NYTS and NSDUH surveys showed a trend toward decreasing menthol cigarette use with increasing age.

Giovino (unpublished FDA submission 2010) presented data as a public comment that provided clarification on the NSDUH question regarding whether menthol cigarettes were smoked during the past 30 days. He noted that the question that eventually assessed menthol vs. non-menthol cigarette use status was preceded by a question regarding the brand of cigarettes that was smoked most often in the last 30 days. Once this inquiry was made, then subjects were asked if the brand of cigarettes smoked during the past 30 days was menthol. Using cross-sectional NSDUH data from 2004 to 2008 and based on the definition of use of menthol in the past 30 days, and making corrections for misclassifications (e.g., reporting Newport cigarettes as non-menthol cigarettes), he observed a statistically significant age gradient across smokers 12–17 years old (49.3 percent), 18–25 years old (37.5 percent) and 26–34 years old (29.9 percent), replicating the main findings from Rock et al. (2010). (See tables 2 and 4; also chapter 6).

## PREVALENCE OF MENTHOL CIGARETTE SMOKING

There are approximately 19.2 million menthol cigarette smokers in the U.S. (Caraballo 2010). Of this group, 18.1 million are adults ages 18 years or older. The remaining 1.3 million menthol smokers—nearly 6 percent of the total—are adolescents ages 12 to 17 (see Figures 1 & 2).

As a group, menthol smokers account for between 28 percent and 34 percent of all U.S. cigarette smokers, depending on the data used (Lawrence et al. 2010; NSDUH 2009). Detailed demographic information about menthol cigarette smokers is presented below. In keeping with TPSAC's charge, this information focuses on children, adolescents, African Americans, Hispanics and other racial and/or ethnic minorities.

### Adolescents

Adolescents 12 to 17 years of age smoke menthol cigarettes at a higher rate than any other age group (NSDUH 2009). Among adolescent smokers, 49.9 percent of those in middle school and 44.9 percent of those in high school report that they usually smoke a menthol cigarette brand (Caraballo and Asman, white paper).

Rates of menthol cigarette smoking are higher among established middle school smokers—those who have smoked cigarettes for at least one year—than among novice middle school smokers. According to Hersey et al., where they analyzed the NYTS 54.7 percent of established middle school smokers and 42.2 percent of novice middle school smokers usually smoke menthol cigarettes.

With regard to high school smokers, experienced and novice smokers use menthol cigarettes in roughly the same proportion; 43.1 percent of established high school smokers and 42.8 percent of new high school smokers say they usually smoke menthol cigarettes (Hersey et al. 2010).

Data from the TUS CPS, which does not survey people under 18, show that menthol smoking prevalence is highest among 18–24 year olds—an additional indication that menthol cigarettes are particularly popular among younger smokers (Lawrence et al. 2010).

### Race and ethnicity

The prevalence of menthol cigarette smoking is highest among African Americans across all socio-demographic and smoking-related categories, whether stratified by income, age, gender, marital status, region, education, age of initiation, and length of time smoking (NSDUH 2009; Lawrence et al. 2010).

Menthol cigarette use is particularly high among minority youth ages 12 to 17, according to an analysis of NYTS data by Hersey et al. The NYTS classifies smokers as "likely menthol cigarette smokers" based on their answers to questions that ask them to identify their brand and to state whether they usually smoke menthol.

**Figure 1: Percent of menthol cigarette use among past month cigarette smokers: 2004-2008, NSDUH**

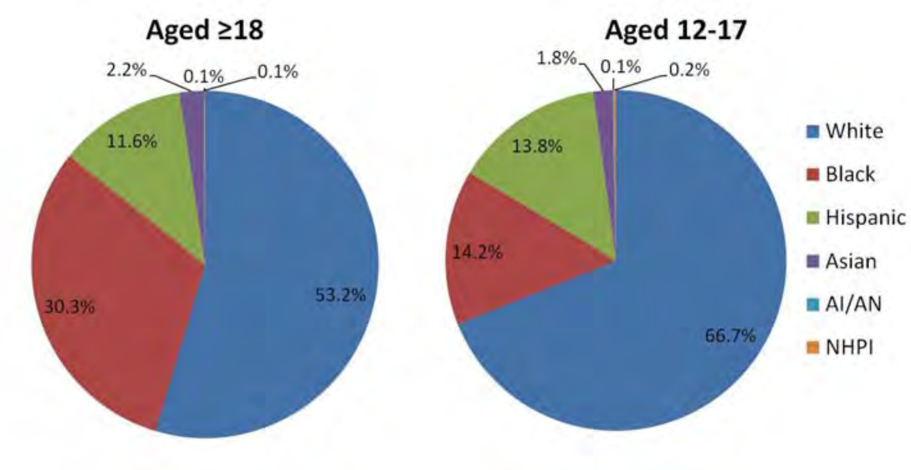
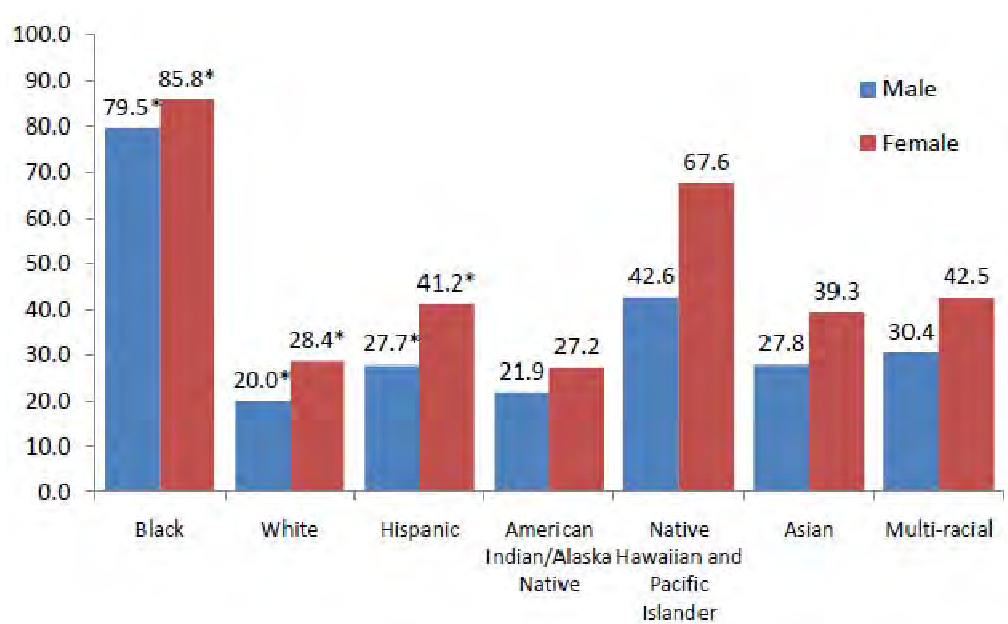



**Figure 2: Percent menthol cigarette use among past month cigarette smokers aged 12 and older by race/ethnicity: 2004-2008, NSDUH**




The respondents in this survey are identified as menthol smokers if they report that they smoke menthol cigarettes and they also report using a specific menthol brand (e.g., Newport). The answers to these two questions must be consistent in order for respondents to be classified correctly with certainty.

According to this definition, 80.6 percent of African American middle school smokers and 84.8 percent of African American high school smokers regularly smoke menthol cigarettes. Among Hispanics, 57.9 percent of middle school smokers and 56.4 percent of high school smokers reported smoking menthol cigarettes. In Asian Americans a menthol brand is used by 57.4 percent of middle school smokers and 43.6 percent of high school smokers (Hersey et al. 2010; see table 3). Menthol cigarettes were used less among non-Hispanic white youths; in this demographic, 43.1 percent of middle school smokers and 37.6 percent of high school smokers said they regularly smoked menthol cigarettes (Hersey et al. 2010).

The prevalence of menthol cigarette smoking varied for each racial/ethnic group by region (Lawrence et al. 2010). Rates of menthol cigarette use among white, Hispanic and American Indian/Alaska Native smokers are highest in the Northeast. For African American smokers, the rate of menthol smoking is highest in the Midwest. For Asian and Pacific Islander smokers, the prevalence of menthol cigarette smoking is highest in the West. Menthol cigarette smoking is significantly higher in metropolitan areas for all racial and ethnic groups except American Indians/Alaska Natives and Asian and Pacific Islanders.

**Table 3. Percentage of Youth Smokers Who Used a Menthol Brand of Cigarettes in Middle School and High School**

| **Subgroup** | **All current smokers** | |
|---|---|---|
| | **Middle school (*n* = 771)** | **High school (*n* = 2,510)** |
| All youth smokers | 51.7 (45.8–57.5) | 43.1 (37.0–49.1) |
| Male | 55.1 (43.9–54.7) | 39.4 (33.6–45.2) |
| Female | 48.1 (28.1–51.6) | 46.9 (38.9–54.9) |
| Less than 1 year | 42.2 (29.8–54.7) | 42.8 (34.5–51.2) |
| 1 year or more | 54.7 (48.2–61.3) | 43.1 (36.6–49.6) |
| African-American | 80.6 (72.0–89.3) | 84.8 (77.3–92.3) |
| Asian American | 57.4 (27.7–87.1) | 43.6 (24.3–63.0) |
| Hispanic | 57.9 (48.8–67.0) | 56.4 (48.7–64.2) |
| White (non-Hispanic) | 43.1 (36.2–50.0) | 37.6 (31.0–44.3) |
| Youth who are current smokers with either a menthol or a non-menthol brands | 6.3 (5.1–7.5) | 19.7 (18.1–21.4) |

**Source: NYTS 2006**

## Gender

Women are more likely to smoke menthol cigarettes than men (NSDUH 2009). This pattern is seen across all racial/ethnic groups except among American Indians/Alaskan Natives; in that group, men are more likely to smoke menthol cigarettes (NSDUH 2009; Lawrence et al. 2010).

## People with mental illness

While smoking prevalence is high among people with mental illness (Lasser et al. 2000), there are no peer-reviewed journal articles on menthol cigarette in this vulnerable group.

# TRENDS IN MENTHOL CIGARETTE USE

## Trends by age

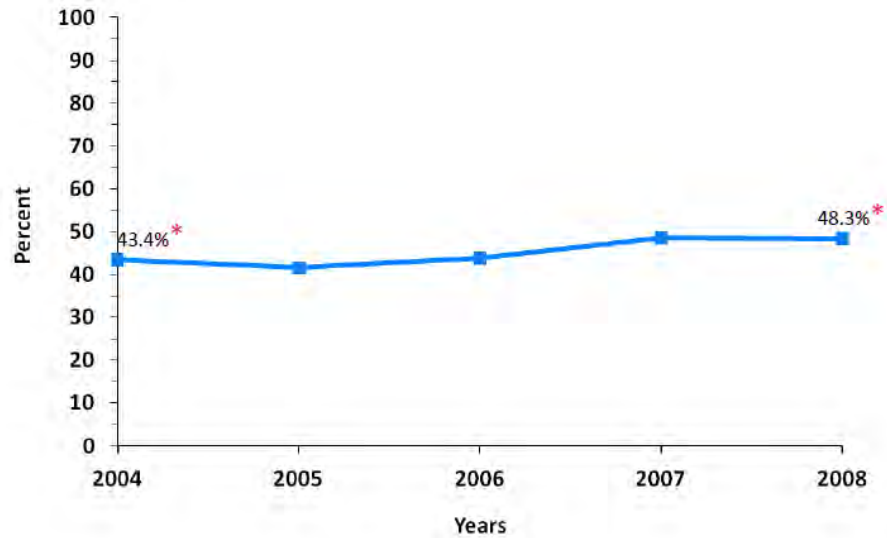
### *Adolescent smokers*

According to the NSDUH data, among all past month smokers 12 to 17 years of age, the proportion of menthol cigarette smokers rose to 48.3 percent in 2008 from 43.4 percent in 2004—a statistically significant 11 percent increase over four years (see Figure. 3). Driving this increase was a jump in menthol cigarette use among white adolescent smokers, the only racial/ethnic group to show a statistically significant increase over this period.

### *Adult smokers*

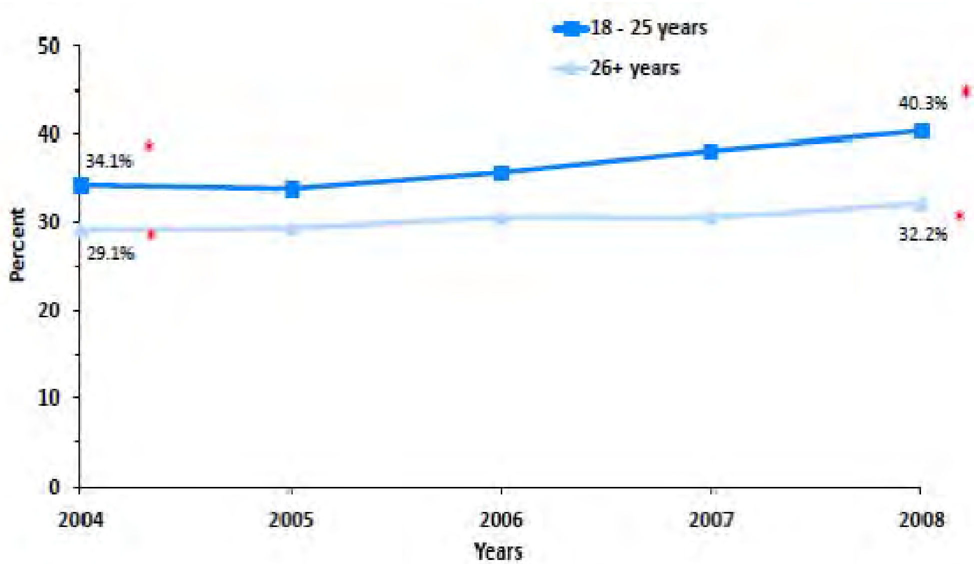
Among all past month adult smokers, the proportion of menthol cigarette smokers rose to 33.8 percent in 2008 from 30.2 percent in 2004—a 13 percent increase over four years (NSDUH 2009; see Figure 4). The increase was particularly sharp among young adults. The proportion of smokers aged 18 to 25 years who smoked menthol cigarettes rose to 40.3 percent in 2008 from 34.1 percent in 2004—a statistically significant 17 percent jump. Among smokers aged 26 years and older, the proportion who smoked menthol cigarettes rose to 32.2 percent in 2008 from 29.1 percent in 2004—an increase of 10 percent.

**Figure 3: Trends in menthol cigarette use among past month smokers aged 12-17 years: 2004-2008**




Source: National Surveys on Drug Use & Health, 2004-2008
*Statistically significant

**Figure 4: Trends in menthol cigarette use among past month adult smokers, by age group: 2004-2008**



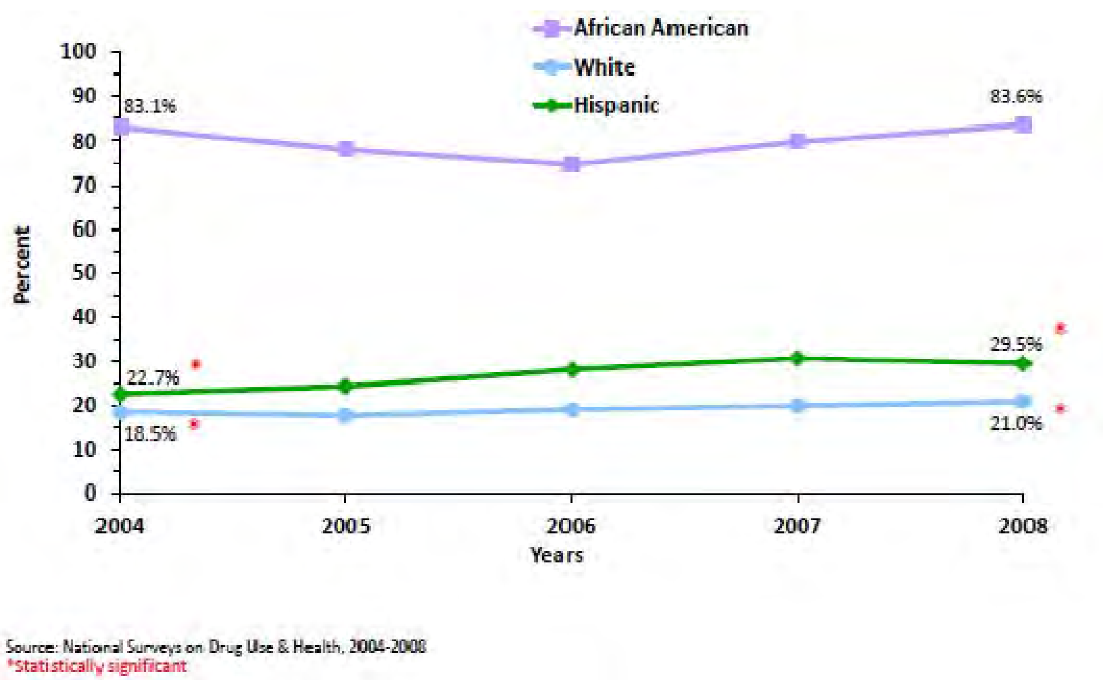

Source: National Surveys on Drug Use & Health, 2004-2008
*Statistically significant

**Trends by gender**

***Men***

The proportion of male cigarette smokers aged 12 years or older who smoked menthol cigarettes increased to 30.8 percent in 2008 from 26.9 percent in 2004, a statistically significant gain (NSDUH 2009). Statistically significant increases in past-month menthol cigarette use were observed among white and Hispanic male smokers aged 18 and older, according to NSDUH data. The proportion of white adult male past-month cigarette smokers who smoked menthol cigarettes increased to 21 percent in 2008 from 18.5 percent in 2004. The proportion of Hispanic adult male past-month cigarette smokers who smoked menthol cigarettes increased to 29.5 percent in 2008 from 22.7 percent in 2004.The proportion of African American adult male past-month cigarette smokers who smoked menthol cigarettes did not change, standing at 83 percent in both 2004 and 2008 (see Figure 5).

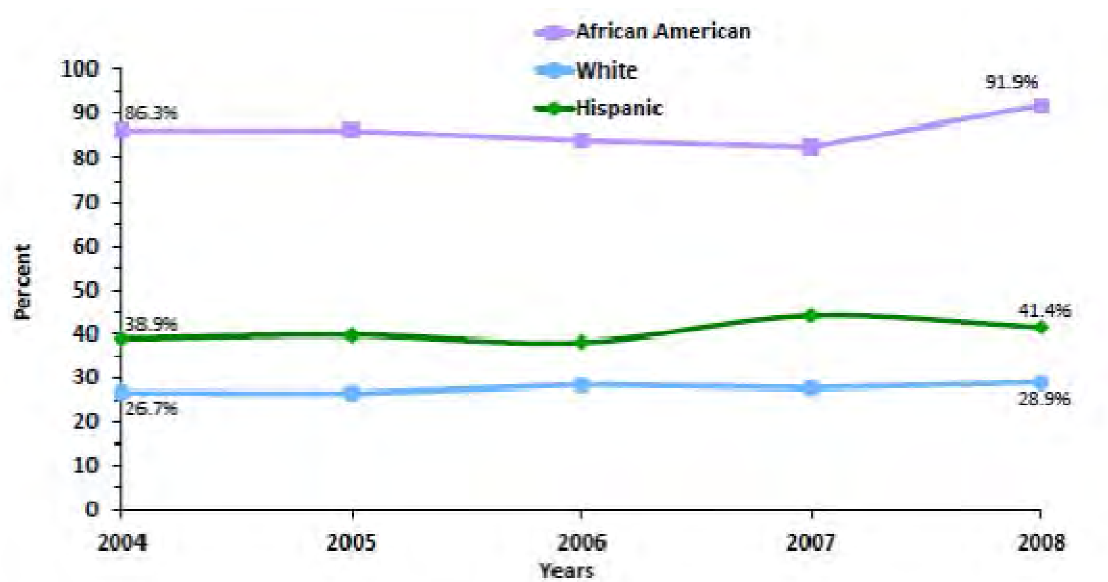
**Figure 5: Trends in menthol cigarette use among African American, White, and Hispanic men aged ≥ 18 years: 2004-2008**




***Women***

Although the proportion of adolescent and adult female smokers who smoked menthol cigarettes increased between 2004 and 2008, the changes were not statistically significant in any age or racial/ethnic category examined (NSDUH 2009; Caraballo 2010). The proportion of female cigarette smokers age 12 and older who smoked menthol cigarettes rose to 37.5 percent in 2008 from 35.9 percent in 2004. Among adult female African American smokers, the proportion of menthol smokers rose to 91.9 percent in 2008 from 86.3 percent in 2004. Among adult female white and Hispanic smokers, the proportion who smoked menthol cigarettes rose to 28.9 percent from 26.7 percent and to 41.4 percent from 38.9 percent, respectively, over the same period (Figure 6).

**Figure 6: Trends in menthol cigarette use among African American, White, and Hispanic women aged ≥ 18 years: 2004-2008**

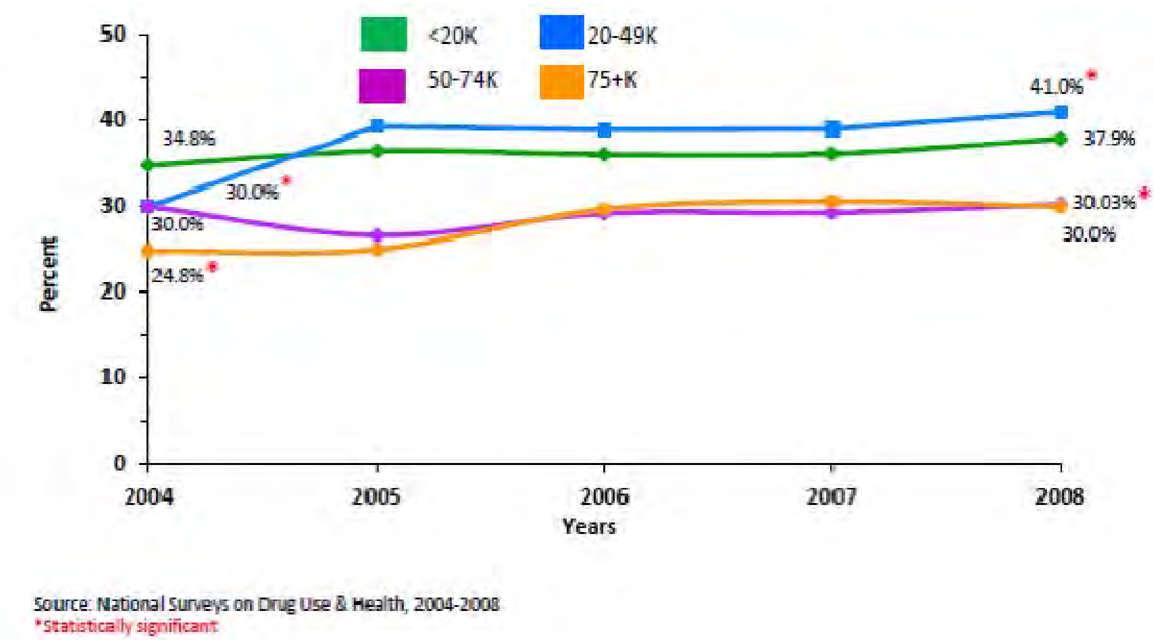



Source: National Surveys on Drug Use & Health, 2004-2008

**Trends by income**

Between 2004 and 2008, there were increases in the proportion of adult smokers who smoked menthol cigarettes among families with smokers and incomes between \$20,000 and \$49,999 and of \$75,000 or more (see Figure 7).

**Figure 7: Trends in menthol cigarette use among past month smokers aged ≥ 18 years, by family income: 2004-2008**




**SUMMARY**

Based primarily on three national data sets on smoking, the review in this chapter demonstrates that menthol cigarette use is high among women and the special populations relevant to TPSAC's charge—ethnic/racial minorities, including African-Americans and Hispanics, and adolescents. Specifically, TPSAC finds:

- Menthol cigarette use is very high among minority youth. More than 80 percent of adolescent African American smokers and more than half of adolescent Hispanic smokers use menthol cigarettes. Menthol cigarettes are used by more than half of Asian American middle-school smokers.

- Use of menthol cigarettes is rising among adolescents, driven by a significant increase in the number of white youth ages 12–17 who are smoking menthol cigarettes. Trend data also shows a significant increase in menthol cigarette use among young adult smokers and white and Hispanic men.

- The review of these national data sets also shows that menthol use is prevalent among the unemployed, people with an annual family income of less than \$10,000 and people who never married.

| Table 4: Studies of Patterns of Menthol Cigarette Smoking | | | | |
|---|---|---|---|---|
| | **Study Periods** | **Population** | **Key Results** | **Limitations** |
| Lawrence et al. 2010 | 2003 and 2006/07 TUS CPS | Adult current smokers ($n$ = 63,193) | African-American smokers were 10–11 times more likely to smoke mentholated cigarettes than white smokers men: odds ratio (OR): 11.59, 99% confidence interval (CI): 9.79–13.72; women: OR: 10.12, 99% CI: 8.45–12.11).<br><br>With the exception of American Indian / Aleut/ Eskimo smokers, non-white smokers were significantly more likely to smoke mentholated cigarettes than were white smokers.<br><br>Additional significant factors associated with mentholated cigarette smoking included being unmarried (never married: OR: 1.21, 99% CI: 1.09–1.34; divorced/separated: OR: 1.13, 99% CI: 1.03–1.23), being born in a US territory (OR: 2.01, 99% CI: 1.35–3.01), living in a non-metropolitan area (OR: 0.87, 99% CI: 0.80–0.96), being unemployed (OR: 1.24, 99% CI: 1.06–1.44) and lower levels of education.<br><br>Race/ethnicity-stratified analyses showed that women were more likely than men to smoke mentholated cigarettes.<br>Among African-American smokers, young adults (aged 18–24 years) were four times more likely to smoke mentholated cigarettes compared with individuals aged 65+ | Cross-sectional study<br>Small sample sizes for the AI/AN and API |
| National Survey on Drug Use and Health | 2004 to 2008 | Persons aged 12 or older (n =68,736) | Among past month smokers, the rate of smoking menthol cigarettes increased from 31.0 percent in 2004 to 33.9 percent in 2008; increases were most pronounced for adolescents aged 12 to 17 (43.5 percent in 2004 vs. 47.7 percent in 2008), young adults aged 18 to 25 (34.1 vs. 40.8 percent), and males (26.9 vs. 30.8 percent).<br><br>Past month smoking of menthol cigarettes was more likely among those who were recent smoking initiates (i.e., began smoking in the past year) than among those who were longer term smokers (i.e., initiated use more than a year ago) (44.6 vs. 1.8 percent, respectively); this pattern was consistent for persons aged 12 to 17 and those aged 18 to 25, for both genders, and for whites and Hispanics.<br>For African-Americans, past month use of menthol cigarettes was less likely among past month smokers who were recent smoking initiates than among their counterparts who were longer term smokers (73.9 vs. 82.8 percent). | Cross-sectional study |

**Table 4: Studies of Patterns of Menthol Cigarette Smoking**

| Study | Study Periods | Population | Key Results | Limitations |
|---|---|---|---|---|
| Giovino et al. 2003 | 1999 National Household Survey (NHS)<br><br>1998,99, 2000 Monitoring the Future (MtF)<br><br>2000 National Youth Tobacco Survey (NYTS)<br><br>2002 International Tobacco Control Policy Evaluation Survey (ITCPES) | 12 and older<br>(n= 71,764)<br><br>8th, 10th, and 12th graders<br>(n= 136,000)<br><br>middle and high school students (n= 35,838)<br><br>18 and older ever smokers (n=2500) | NHS and NYTS both confirm that Newport is the far leading brand among African-American adolescents.<br><br>Among African-American smokers more than three-fourths of the adolescents ages (12-17 yrs) and young adults (18-25 yrs old) used Newport<br><br>Baseline data from the ITCPES indicated that among adult smokers, females were more likely than males to use mentholated brands in the US (31.8% vs 22.1%) | Misclassification of self reported menthol status<br><br>Cross-sectional study |
| FDA Presentation (Ralph S. Caraballo) | 2004-2008 NSDUH Survey | 12 years old and older (n=68,000) | Total of 19.2 million menthol cigarette smokers<br><br>Among smokers aged 12-17 years, 1.1 million menthol smokers<br><br>Among smokers aged 18 and older. 18.1 million menthol smokers<br><br>African-American smokers are far more likely to smoke menthol cigarettes than smokers of other US racial and ethnic groups<br><br>7 of 10 African-American adolescent smokers reported smoking menthol cigarettes followed by about half of multirace and Asian smokers.<br><br>8 of 10 African-American adult smokers reported smoking menthol cigarettes followed by about half Native Hawaiian and other Pacific Islander adult smokers.<br>Female smokers more likely to smoke menthol cigarettes than male smokers. | Cross-sectional study<br>Accuracy for self-reporting smoking methanol cigarettes |
| Hersey et al. 2010 | 2006 National Youth Tobacco Survey | Grades 6th- 12th<br>N= 27,038 | 51.7% (95% *CI*: 45.8–57.5) of middle school smokers and 43.1% (95% C.I.: 37.0, 49.1) of high school smokers reported that they usually smoked a menthol brand of cigarettes, | Misclassification of self reported menthol status<br>Cross-sectional study |

DRAFT

**REFERENCES**


Substance Absuse and Mental Health Services Administration. *The NSDUH report: Use of menthol cigarettes*. Rockville, MD:Office of Applied Studies, Substance Abuse and Mental Health Services Administration,2009.

Giovino GA, Sidney S, Gfroere JC, O'Malley PM, Allen JA, Richter PA, Cummings KM. Epidemiology of menthol cigarette use. *Nicotine & Tobacco Research* 2004 Feb;6 Suppl 1:S67–81.

Hersey JC, Nonnemaker JM, Homsi G. Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. *Nicotine & Tobacco Research* 2010 Dec;12 Suppl 2: S136-46.

Lawrence D, Rose A, Fagan P, Moolchan ET, Gibson JT, Backinger CL. National patterns and correlates of mentholated cigarette use in the United States. *Addiction* 2010 Dec;105 Suppl 1: 13-31.

Caraballo, R. *Menthol and Demographics*. Food and Drug Administration Tobacco Products Scientific Advisory Committee, March 30, 2010. Washington, DC.

Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *Journal of the American Medical Association*. 2000;284:2606-2610.

# CHAPTER 5: MARKETING AND CONSUMER PERCEPTION

## INTRODUCTION

This chapter is concerned with addressing the question as to whether tobacco company marketing of menthol cigarettes increases the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available, and if this is the case in subgroups within the population. Accordingly, chapter 5 reviews menthol cigarette marketing strategies, against the background of broader tobacco marketing strategies and with reference to general marketing principles. In addition, this chapter examines consumer beliefs relevant to menthol cigarettes.

Specifically, Chapter 5 will address the following questions:

- How is menthol marketing different from and similar to non-menthol marketing, in terms of product, place, price, promotion and packaging?
- What health reassurance messages were/are used in menthol marketing messages?
- What other messages were/are conveyed to potential consumers by menthol marketing messages?
- Who are the target populations for menthol marketing? Is there evidence to show that youth, women, and specific racial/ethnic groups were targeted?
- Does menthol marketing influence the perceived taste and/or sensory experience of menthol cigarettes?
- Do consumers perceive menthol cigarettes as safer or less harmful than non-menthol cigarettes?

Chapter 4 contains additional information on the history of menthol cigarette marketing.

## METHODS

Chapter 2 provided the general framework for the report and the Tobacco Products Scientific Advisory Committee's (TPSAC) approach to gathering, reviewing and weighing evidence. Using this approach, chapter 5 drew on peer-reviewed papers and government reports; white papers and analyses either written or commissioned by the FDA; tobacco company presentations and written submissions; and public presentations and comments to TPSAC that provided data relevant to the topic at hand.

**HOW IS MENTHOL MARKETING DIFFERENT FROM AND SIMILAR TO NON-MENTHOL MARKETING, IN TERMS OF PRODUCT, PLACE, PRICE, PROMOTION AND PACKAGING?**

This section addresses similarities and differences between menthol and non-menthol marketing. The studies and reports were organized according to the elements that make up the tobacco marketing mix. Like the marketing of other products, cigarette marketing strategy typically involves specifying a target audience and establishing an appropriate marketing mix known as the "4P's," involving product, place, price, and promotion (NCI 2008). *Product* refers to brand name and variety, as well as more tangible physical aspects of functionality. *Place* refers to where tobacco products are sold and their availability to consumers. *Price* includes wholesale and retail pricing, and other discount strategies. *Promotion* includes advertising in traditional and non-traditional media, as well as sponsorship, sampling, direct marketing and other strategies. A fifth "P" – packaging – is sometimes added in more recent formulations of the 4P's model, although packaging can also be included either as part of Product or Promotion.

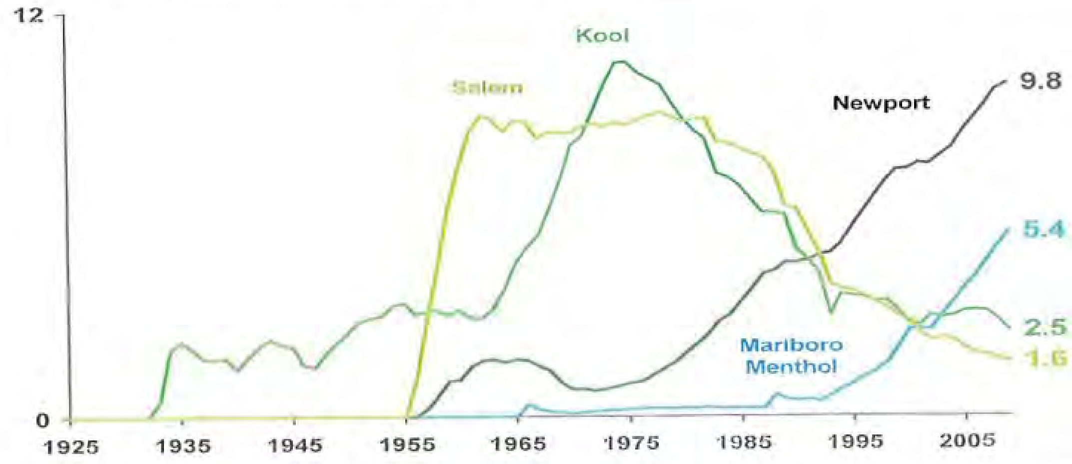
**Product**

Menthol cigarettes accounted for 27 percent of all cigarettes sold in the U.S. in 2009 (Altria Client Services, July, 2010; Graves/R.J. Reynolds Tobacco Co. , July, 2010). According to the Federal Trade Commission's Cigarette Report for 2006 (the most recent available), menthol market share increased from 16 percent in 1963 to 27 percent in 2005 of all cigarette sales, then decreased to 20 percent in 2006 (Federal Trade Commission 2009). However, this drop in market share was not reflected in the data that tobacco companies provided to FDA. Menthol market share has been increasing since 2005, and the current share is as high as it has been since the 1980s. These patterns were reported in submissions from the three major tobacco companies, Altria (manufacturer of Marlboro), R.J. Reynolds Tobacco Company (manufacturer of Kool, Salem, and Camel), and Lorillard (manufacturer of Newport). The prevalence surveys reviewed in chapter 4 also reflect increasing preference for menthol cigarettes among smokers.

Loomis (Oct 2010) described sales trends using AC Nielsen scanner data that were collected between August 2008 and July 2010 from convenience stores and a combination of food retailers, drug stores, and mass merchandisers. Consistent with the industry's reports, the percent of total sales for menthol cigarettes increased slightly, to 27.0 percent from 25.1 percent in convenience stores and to 25.7 percent from 24.5 percent in the combined channel. Approximately 80 percent of 195 different brand families featured at least one menthol variety. Menthol varieties accounted for 36.5 percent of the 1,401 varieties of cigarettes sold.

There are more than 350 different varieties of menthol cigarettes (R.J. Reynolds Tobacco Company, July, 2010), but five brand families accounted for 20.6 percent of total market share in 2009 (Altria Client Services, July 2010, Figure 2.2). As shown in Altria's figure, market share was 9.8 percent for Newport, 5.4 percent for Marlboro Menthol, 2.5 percent for Kool, and 1.6 percent for Salem. In addition, a 1.3 percent market share for Camel Menthol was reported separately by Altria. The pattern for market share is reflected in the brand preferences of adult smokers aged 20 or older: 11.6 percent smoked Newport; 5.9 percent, Marlboro Menthol; 2.7 percent, Kool; 1.2 percent, Salem; and 8.9 percent smoked other menthol brands (NHANES 2007-08, see Caraballo & Asman 2010). Additional comparisons of brand preference by race/ethnicity, gender, and age group are summarized in chapter 6.

**Figure 2.2. Key menthol brand share history**




SOURCE: Maxwell Reports 1925-1973; Management Science Associates, Inc. Shipment History 1974-2008; 72 Month Shipment Database 2009

Newport has been the most popular menthol brand since 1993 (Lorillard July, 2010). It is the most popular cigarette brand among African American smokers, preferred by 49.5 percent of African American smokers aged 12 or older (NSDUH 2005, see NSDUH Report 2007). Newport is distinctly more popular with younger smokers: 23.2 percent of adolescent smokers (ages 12–17) and 17.8 percent of young adult smokers (ages 18–25) smoked Newport, but only 8.7 percent of older smokers preferred the brand (NSDUH 2005, see NSDUH Report 2007). The brand's popularity with younger smokers is evident in all three racial/ethnic subgroups that were examined in the analysis of the NSDUH 2000 data by Giovino et al. (2004). Among African Americans, Newport was the most frequently used brand. Of African Americans who smoked in the past 30 days, 79.2 percent of 12–17 year olds, 76.7 percent of 18–25 year olds, and 31.5 percent of adults aged 26 or older smoked Newport. Among Hispanic smokers, Newport was the second most popular cigarette brand, preferred by 31.4 percent of 12–17 year olds, 16.7 percent of 18–25 year olds, and 7.1 percent of adults aged 26 or older. Newport was less popular among non-Hispanic white smokers, but preferred by 18.0 percent of 12–17 year olds, 9.3 percent of 18–25 year olds, and 2.9 percent of adults aged 26 or older. From its introduction in 1957, Newport was an exclusively menthol brand, but non-menthol varieties were test marketed in the 1980s (Stein 1982) and Newport Red, a non-menthol variety, was introduced in 2010.

Kool and Salem (both manufactured by R.J. Reynolds Tobacco Company) have been exclusively menthol brands since their introduction and gained the largest market share in the 1960s. Kool is the second most popular cigarette brand among African American smokers, preferred by 11.4 percent of African American smokers aged 12 or older (NSDUH 2005, see NSDUH Report 2007). The brand is more popular with older smokers: Among African Americans, Kool was the cigarette brand used most often by 14.1 percent of adults aged 26 or older, 4.6 percent of 18-25 year olds, and 2.1 percent of 12-17 year olds who smoked during the past 30 days (NSDUH 2000, see Giovino et al. 2004). Salem is also preferred by older smokers and is the fourth most popular cigarette brand among African American smokers: 6.9 percent of adults aged 26 or older, and 1.9 percent of 18–25 year olds and of 12–17 year olds used Salem most often (NSDUH 2000, see Giovino et al. 2004). Among Hispanic smokers aged 26 or older, 3.6 percent smoked Kool and 3.4 percent smoked Salem. Salem was slightly more popular than Kool among non-Hispanic white smokers aged 26 or older (3.0 percent vs. 1.8 percent). Among Hispanics and non-Hispanic whites, less than 1 percent of younger smokers reported smoking these brands. Salem is also favored primarily by female smokers (Giovino et al. 2004).

Introduced in 1965, Marlboro Menthol (manufactured by Altria/Philip Morris USA) is now the second leading brand of menthol cigarettes in the U.S.; it surpassed Kool and Salem in popularity after the introduction of Marlboro Milds in 2000 (Altria July, 2010). Its increase in market share is reflected in the Caraballo (2010) analysis of the NSDUH data: The proportion of smokers aged 20 or older for whom Marlboro Menthol was the brand used most often increased from 3.9 percent in 2003–2004, to 4.2 percent in 2005–2006, and to 5.9 percent in 2007–2008 (table 5 in Caraballo & Asman 2010).

Tobacco companies manipulate the concentration of menthol to achieve a desired taste, aroma, and cooling sensation based on anticipated consumer preference and demand. As discussed in chapter 3, many cigarettes contain menthol in quantities insufficient to be considered a characterizing flavor. Lorillard described this use of menthol as analogous "to the use of a few grains of salt in a sweet dish" (Lorillard, July, 2010, p. 19). Lower concentrations of menthol are known to appeal to younger smokers and women (Kreslake et al. 2008 NTR; Lee & Glantz, in press). A survey of products purchased and tested in 2003 observed lower concentrations of menthol in cigarettes labeled "light" and "ultralight" (Celebucki, Wayne, Connolly, et al. 2005). In the full flavor, 100 mm varieties, menthol concentration (measured in milligrams per gram of tobacco weight) was 2.44 mg/g for Newport, 2.64 mg/g for Marlboro Menthol, 2.78 mg/g for Salem, and 3.56 mg/g for Kool (Celebucki et al. 2005). A different rank order of brands was observed in Altria's summary of products that were tested in 2008–2009: 2.9 mg/g for Newport, 3.3 mg/g for Salem, 4.4 mg/g for Kool, and 4.5 mg/g for Marlboro Menthol (also full-flavor,100mm varieties) (July, 2010, Table 1.3). Kreslake et al. (2008, AJPH) compared menthol concentration for eight products tested in 2007 with values reported in tobacco industry documents for the same brands. The authors observed that the concentration of menthol had decreased in Newport, Kool, and Salem brands between 2000 and 2007, and increased by 25 percent in Marlboro Menthol. They concluded that increasing menthol content was intended to reposition Marlboro Menthol for older smokers and to distinguish it from Marlboro Milds, a variety with a lower menthol content that appealed to younger smokers. Lorillard presented data indicating that the menthol concentration of its Newport brand did not decrease during this time period (July 2010, Fig 1). Additional research about consumer perceptions of menthol content is addressed later in this chapter and in chapter 6.

**Place**

Menthol and non-menthol cigarettes are distributed in identical channels. The primary venues are retail outlets: convenience stores, small grocery or "corner" stores, gas stations, liquor stores, supermarkets, mass merchants, pharmacies, and tobacco stores. The total number of U.S. stores that sell cigarettes is unknown. The 2007 Economic Census identified at least 100 different types of businesses that sell tobacco and estimated sales for approximately 235,000 retailers in the U.S. (http://www.census.gov/econ/census07/). However, that figure likely underestimates the total number of retailers because the survey is limited to payroll establishments. A larger estimate of 543,000 retailers was obtained by extrapolating from the subset of states that maintained licensing records (DiFranza, Peck et al. 2001).

The retail channel is ideally positioned to target the lower income and racial/ethnic minority populations who smoke menthol cigarettes. Indeed, inequities in the concentration of tobacco retailers by neighborhood demographics are well documented. For example, the tobacco retailer density (outlets per roadway kilometer) was almost four times greater in Erie County census tracts with the lowest income residents than in tracts with the highest income residents; tobacco retailer density was two times greater in tracts with the highest proportions of African American residents than in tracts with the lowest proportions (Hyland, Travers, et al. 2003). Similar disparities in tobacco outlet density by income, race/ethnicity or both were observed in census tracts in New Jersey (Yu, Peterson, Sheffer et al. 2010), Iowa (Schneider, Reid, Peterson, et al. 2005), and Chicago (Novak, Reardon et al. 2006). In addition, more tobacco retailers were located near California high schools with larger proportions of low-income and Hispanic students (Henriksen, Feighery et al. 2008). Such disparities in tobacco retailer density contribute to the greater availability of cigarettes, both menthol and non-menthol, in areas of social and economic disadvantage.

**Price**

Price is a critical feature of tobacco marketing and influences myriad aspects of smoking behavior. Higher prices discourage initiation, reduce consumption, promote quitting, prevent relapse, and may lead smokers to substitute cheaper brands (Chaloupka et al. 2010). According to the Federal Trade Commission's Cigarette Report, the tobacco industry spends the largest share of its annual marketing budget—74 percent of $12.5 billion in 2006—on price discounts (Federal Trade Commission 2009). This section uses the term "price promotions" to refer to discounts and other strategies that reduce the price of cigarettes at the point of sale, such as retailer promotional allowances, multi-pack offers and gifts with purchase. Additional data about expenditures for sales promotions in relation to other marketing activities is provided in the section on Promotion.

Information about price and price promotions was obtained from multiple sources, including submissions to FDA by tobacco companies and other presentations to TPSAC, as well as peer-reviewed articles that analyzed data from retail scanners, or receipts from single-pack purchases, or audits of advertised prices at point of sale, or purchase prices reported by smokers themselves. Most studies examined reported data from nationally representative samples of stores or smokers. The studies below are grouped by data source.

***Industry submissions***

In its submission to FDA, R.J. Reynolds Tobacco Co. reported that the average price paid per carton of cigarettes was slightly higher for menthol than for non-menthol cigarettes for each year from 2000 to 2009, with more discrepant prices observed in more recent years (e.g., an average $49 for menthol and $46 for non-menthol in 2009) (presentation by Graves/RJ Reynolds, July, 2010). Data on the average price paid per pack (which constitutes the way that the majority of smokers buy their cigarettes) was not provided, but in response to a question, Monica Graves from R.J. Reynolds indicated the same trends held for pack prices. These data were presented in an aggregated form for the entire industry, and no data were presented by company or by individual brand, precluding determination of the use of different pricing approaches for individual brands. In addition, the data did not address whether there was a differential price paid for menthol and non-menthol cigarettes in geographic areas with different proportional representations of race/ethnicity, or during focal time periods (e.g., when tobacco taxes were increased).

From 2000 to 2009, the proportion of sales volume with a price promotion nearly doubled for non-menthol cigarettes (to 71 percent from 36 percent) and it more than doubled for menthol cigarettes (to 67 percent from 26 percent). However, these data were similarly aggregated over brands and companies, and by geographic location, and were not provided for more fine-grained time periods in relation to tobacco tax increases. In addition, these particular data only indicate whether or not some kind of price promotion was applied to menthol and non-menthol, and not the relative value of the price promotion. R.J. Reynolds drew attention to the menthol share of shipments being flat from 2000 to 2004 during a period when the percentage of volume promoted for menthol increased, and also that the menthol share of shipments grew from 2005 to 2009 when menthol promotional levels were relatively stable. This interpretation overlooks the alternative that the percentage of volume promoted may have reached a critical threshold by 2005, which acted to increase the share of menthol shipments thereafter.

***Retail scanner data***

Cigarette pack prices and sales volume derived from ACNielsen scanner data are designed to represent national markets for different types of retail outlets (Loomis Oct 2010). Loomis (2010) compared price and promotions for menthol and non-menthol sales in two retail channels: convenience stores and food retailers (supermarkets, drug stores and mass merchants combined) from 2008 to 2010. The average pack price was higher for menthol than non-menthol cigarettes in both retail channels, and 13 cents more (3 percent higher) in convenience stores, which is the retail channel that sells the largest volume of cigarettes. Over time, the use of multi-pack discounts was replaced by the use of "cents off" discounts for both menthol and non-menthol sales. In both retail channels, promoted sales accounted for a greater proportion of total sales for menthol than for non-menthol cigarettes. In convenience stores, 8.31 percent of menthol sales involved a promotion, compared with 5.11 percent of non-menthol sales. These figures cannot be compared with those reported by R.J. Reynolds because the two describe different types of promotions (retail vs. what appears to be wholesale) and different denominators (total pack sales in convenience stores vs. volume of shipments).

Using ACNielsen scanner data from supermarkets for the period 1994–2004, Farrelly et al. (2007) compared estimated change in pack price as well as tar and nicotine per cigarette for menthol and non-menthol brands (Farrelly, Loomis, & Mann 2007). Slightly higher average prices were observed for menthol than for non-menthol packs, and the discrepancy increased after the 1998 Master Settlement Agreement (MSA), in which tobacco companies agreed to restrict certain advertising practices. Over time, price increases were associated with increases in sales of cigarettes that contained more tar and nicotine, but this trend was more pronounced for menthol than for non-menthol cigarette sales. The authors concluded that menthol smokers are more likely than non-menthol smokers to compensate for price increases by smoking cigarettes with higher levels of tar and nicotine.

One limitation of studying retail scanner data is the potential for under-reporting of promoted sales due to missing information for some transactions. In addition, the scanner data are derived from a proprietary method of projecting to the population and are not a representative sample of stores. This proprietary sampling method also precludes researchers from determining whether promoted sales were higher in regions or neighborhoods with different race and ethnic group distributions.

***Store audits***

Store audits typically used trained coders to record advertised prices and sales promotions for particular cigarette brands or flavor categories in a random sample of tobacco retailers. For example, Ruel et al. (2004) conducted annual observations (1999–2002) in a geographically stratified sample of 11,703 stores in the U.S. (Ruel, Mani, Sandoval et al. 2004). They recorded the lowest advertised pack price for the leading menthol (Newport) and leading non-menthol (Marlboro) brand. Over the three years, the average price for Newport increased 78 cents (25 percent change) compared to 85 cents (29 percent change) for Marlboro. Increases in Newport prices were observed for all regions (West, Midwest, South, Northeast) and locales (urban, suburban, town, rural). The proportion of stores that advertised a price promotion for Newport increased by 19 percentage points, but the proportion of stores with a promotion for Marlboro increased by only 7 percentage points. In urban areas, a linear increase was observed for Newport promotions but not for Marlboro promotions. One shortcoming of these comparisons is that the two brands represent different corporate marketing strategies. According to Lorillard, Newport maintains the highest average price of major U.S. cigarette brands (Lorillard July 2010).

Toomey et al. (2009) observed the same pattern of differential pricing for menthol and non-menthol varieties of the same brand family. In a random sample of 214 Minneapolis convenience stores, the average difference between the single-pack price for the menthol and non-menthol varieties of the same (unidentified) brand was 37 cents (11 percent more for menthol). Menthol price was not correlated with the proportion of non-white residents or youth in the census tracts where the stores were located; non-menthol price was positively correlated with the proportion of non-white residents and negatively correlated with the proportion of youth. However, the study did not examine the availability of discounts or other price promotions.

***Population surveys***

Three surveys illustrated differences between menthol and non-menthol smokers in response to pricing. A 2002 survey of 4,618 California smokers found relatively more of those who smoked menthol brands reported taking advantage of price promotions than those who smoked non-menthol brands: percentages were 57.1 percent for those who smoked menthol-only brands (Newport or Kool), compared to 49.1 percent for Camel and 34.8 percent for Marlboro (given menthol variants were a small percentage of the market for both these brands) (White et al., 2006). This finding is consistent with the results of the scanner data showing that a larger proportion of menthol compared to non-menthol cigarette sales involved price promotions (Loomis, 2010). Among African American smokers in the California survey, 65.4percent of menthol smokers compared to 28.7percent of non-menthol smokers reported using promotional offers. Young adults, women, and daily smokers were also more likely to use promotional offers, but the difference between menthol and non-menthol smokers in these subgroups was not reported.

Fernander et al. (2010) undertook an analysis of the data from the 2003 and 2006-2007 Tobacco Use Supplement to the Current Population Survey (TUS-CPS) in order to compare the demographic traits and purchase behaviors of menthol and non-menthol smokers (Fernander et al. 2010). A larger proportion of menthol smokers (68.8 percent) than non-menthol smokers (59.2 percent) reported buying cigarettes by the pack. Adjusting for other factors, such as gender, race/ethnicity, age group, education level, income, smoking frequency and age of initiation, the odds of being a menthol smoker were significantly lower for smokers who reported buying cigarettes by the carton exclusively. The authors concluded that the finding is consistent with other studies suggesting that menthol smokers smoke fewer cigarettes.

In a separate analysis of the TUS-CPS, Tauras et al. (2010) examined questions about the type of cigarette smoked and the price that smokers last paid for either a pack or carton. Using data aggregated over multiple survey waves (2003 and 2006-2007), Tauras et al. (2010) estimated state-specific prices for menthol and non-menthol packs. Adjusted to 2010 dollars, the average menthol price was $3.88, which was 9 cents more than the average non-menthol price.

Tauras et al. (2010) also estimated the probability of being a menthol smoker, based on different state-specific prices for menthol and non-menthol cigarettes and adjusting for other characteristics of smokers. Holding these variables constant, a 10 percent increase in the price of menthol cigarettes was associated with a 2.3 percent decrease in the probability of being a menthol smoker. A 10 percent increase in the price of non-menthol cigarettes was associated with a 4.7 percent increase in the probability of being a menthol smoker. These different price elasticities suggest that menthol and non-menthol cigarettes are not close substitutes for each other. The authors concluded that, holding other factors constant, menthol smokers would be much less likely to switch to non-menthol cigarettes than non-menthol smokers would be likely to switch to menthol cigarettes. The pattern of results did not differ by gender or income. However, younger smokers (aged 18–24) and African American smokers were even less likely to substitute non-menthol cigarettes for menthol cigarettes, indicating stronger preference to menthol cigarettes among the population subgroups with a higher prevalence of smoking menthol. A limitation of this cross-sectional study is that it could not model change in smoker behavior (switching or quitting) over time. In addition, the analysis excluded smokers who indicated no preference for menthol or non-menthol cigarettes. However, this comprised only 2.3 percent of the sample, indicating that the vast majority of adult smokers had a definite preference.

*Summary.* Prices for both menthol and non-menthol cigarettes are increasing and the average price for menthol cigarettes is slightly higher than for non-menthol cigarettes. These patterns emerged regardless of the different data sources used to study price. There was limited information available on menthol pricing and price promotion by neighborhood race/ethnicity characteristics, in relation to tobacco tax increases, and in relation to brand. The retail scanner data indicates that a larger proportion of menthol than non-menthol sales is promoted. More menthol smokers take advantage of price promotions than non-menthol smokers, and this is particularly true for African Americans. Menthol smokers have stronger loyalty to their cigarette preference and are less sensitive to price fluctuations than non-menthol smokers.

**Promotion**

The main goals of the *Promotion* part of the marketing mix are to inform, persuade and remind (NCI 2008). Informing is generally considered important for newly developed products in order to tell consumers something about the product. Promotions aimed at reminding are typically aimed at consumers who already have positive attitudes towards the brand. Promotions that persuade tend to focus on the advantages of one brand over another. Branding is the use of a name, term, symbol or design to identify a product and the creation of a 'brand image,' is key to a successful promotional strategy. As explained further in a later section on menthol marketing messages, cigarette advertising is short on factual information and rich in imagery designed to establish and reinforce branding.

The aim of branding is to create a set of associations or perceptions about a brand in the mind of consumers, so that they will want to buy try the product and keep buying it (NCI 2008). Branding is a key aspect of marketing, whereby marketers create an image for the brand they promote, a brand image that promises the target market something they value. Persuasion-based promotions often link products with desirable images (such as lifestyle or healthful imagery) and identities (such as slogans or brand symbols), in order that consumers associate the brand with positive emotions or reduced negative emotions (NCI 2008). In a comprehensive review of the evidence, the NCI review concluded that "*tobacco advertising has been dominated by three broad themes: providing satisfaction (taste, freshness, mildness etc.), assuaging anxieties about the dangers of smoking, and creating associations between smoking and desirable outcomes (independence, social success, sexual attraction, thinness etc.)*" (NCI 2008, p170).

Later sections about messaging and targeting describe the message themes that distinguish menthol from non-menthol marketing. This section describes similar types of marketing activities used to promote both menthol and non-menthol cigarettes, noting some differences in practice. Price promotions that were discussed in the price section are included here because these are reflected in various marketing activities, such as retail advertising and direct mail, and are essential to understand the context of tobacco marketing practices.

As reported to the Federal Trade Commission, current promotional activities for cigarettes include advertising (print media and point-of-sale), direct marketing (direct mail, coupons, distribution of free cigarettes and specialty items, company website, other internet and telephone), sponsorship, public entertainment, promotional allowances for wholesalers and retailers, and retail price promotions (as described in the section on price). After the MSA eliminated billboard and transit advertising and curtailed sponsored events by tobacco companies, their annual spending on retail marketing more than doubled to $10.7 billion in 2006 from $4.7 billion in 1998 (Federal Trade

Commission 2009). Over the same period, retail marketing expenditures increased to 86 percent from 70 percent of the industry's total annual marketing dollars. These figures include retail advertising, promotional allowances, and price promotions (discounts, bonus cigarettes, and gifts with purchase). While total marketing expenditures decreased every year since 2003, proportional expenditures on point-of-sale advertising nearly doubled to 1.9 percent in 2006 from 1.1 percent in 2003. Proportional expenditures on price promotions increased to 80.4 percent in 2006 from 76.0 percent in 2003.

Tobacco companies exercise strict control over the retail outlet, using contractual obligations with store merchants to maximize the visibility of products and advertising for selected brands (Pollay 2007; Feighery, Ribisl, Clark et al. 2003; John, Cheney, & Azad 2009). The shift toward retail marketing is apparent to consumers; the average number of cigarette marketing materials per store and the proportion of stores with price promotions have increased since the MSA (Celebucki & Diskin 2002; Feighery, Schleicher, Cruz & Unger 2008; Wakefield et al. 2000). As described in the previous section about price, a larger increase was observed in the proportion of stores that promoted Newport than in the proportion of stores that promoted Marlboro (Ruel et al. 2004).

Lorillard (July, 2010) described its marketing plan in terms of four components: retail price promotions, retail advertising, print advertising, and direct marketing. The latter category includes a direct mail list for distributing coupons and its "P.S. Pleasure Scene" magazine that was started in 2003. The company reported that coupons represented the largest proportion of its direct mailing expenditures, but did not disclose the amounts. In 2008, Lorillard spent $19.7 million on magazine advertising, a category that represented less than 1 percent of its annual marketing budget in 2009. Retail price promotions comprise more than 90 percent of the company's annual marketing expenditures. In 2006, magazine advertising represented 0.4 percent of annual tobacco industry marketing expenditures and price promotions (discounts and retail value-added) represented 80.4 percent of total expenditures (Federal Trade Commission 2009).

R.J. Reynolds Tobacco Co. (July, 2010) reported using price promotion, direct mail, email, website promotion, event promotion, and direct sales in bars and clubs to promote both menthol and non-menthol brands, but did not disclose expenditures or compare them by brand type. The company proposed that a recent shift in preferences toward menthol could not be attributed to marketing activities because these were substantially constrained and because "menthol advertising has changed little in message and medium during this time frame" (Graves/RJ Reynolds, July 2010). In spite of a restricted environment, the industry's total expenditures for cigarette marketing increased every year after the MSA until 2003 (Federal Trade Commission 2009). In addition, even if message and medium remained constant for menthol brands, proportional expenditures to advertise and promote menthol brands could have increased.

The FTC does not publish expenditures separately by manufacturer, brand, or variety of cigarette (menthol vs. non-menthol). However, expenditure data for some marketing channels can be purchased from commercial sources. Using such data for cigarette advertising in magazines, one study found that spending for non-menthol brands decreased to $39.8 million in 2005 from $309.3 million in 1998, but spending for menthol brands increased to $43.8 million from $36.5 million in the same time period (Kreslake, Wayne, Alpert, et al. 2008). The proportion of expenditures for menthol brands increased to 52.4 percent from 10.6 percent of the total expenditures over this time period, and the spending for menthol exceeded spending for non-menthol brands in 2005. This pattern suggests greater effort to advertise menthol than non-menthol brands in magazines during a period of increased advertising restrictions.

(b) (4)

(b) (4) [redacted]

*Summary*. In a restricted environment, retail has become the dominant channel for tobacco marketing. Tobacco companies use similar marketing activities to promote menthol and non-menthol brands, but expenditure data suggest some differences in practice. In recent years, the tobacco industry spent as much or more on magazine advertising for menthol as for non-menthol brands, even though menthol brands represent a much smaller share of the market (b) (4) [redacted] (b) (4) [redacted]. Further evidence that speaks to differences in promotional practices for menthol—that the mix of marketing strategies used to promote these brands are determined by neighborhood demographics—is addressed in a later section on targeting.

**Packaging**

Cigarette packaging plays a key role in the creation and reinforcement of brand imagery (NCI 2008) and tobacco companies conduct considerable consumer research on all elements of packaging (Wakefield et al. 2002; DiFranza et al. 2002). Unlike many other products where the packaging is discarded after opening, smokers generally keep their cigarette pack with them until all the cigarettes in it are smoked. This means that the pack is frequently being taken out and put on display. This high degree of social visibility leads cigarettes to be described by marketers as "badge products." The use of a badge product associates the user with the brand image, giving the smoker some of the identity of the brand image. As one cigarette package designer, John Digianni, stated: "*A cigarette package is unique because the consumer carries it around with him all day . . .it's a part of a smoker's clothing, and when he saunters into a bar and plunks it down, he makes a statement about himself*." (Koten, cited in Wakefield et al. 2002).

Cigarette packaging becomes more important for overall marketing strategy, as traditional avenues for cigarette advertising are restricted. In a restricted advertising environment, aside from its key role in communicating brand image, cigarette packaging is used to create greater salience for brand families at the retail display (NCI 2008). Reviews of internal tobacco industry documents on cigarette packaging show that that variants within one brand family are designed to be sufficiently similar to indicate membership of the overall parent brand, and different enough for consumers to be able to distinguish between the variants. In this way, the arrangement of packs from the same brand family achieve greater “stand out” from the clutter of competing brands at the point of sale (Wakefield et al. 2002; DiFranza et al. 2002).

For both menthol and non-menthol cigarettes, different shades of the same color and the proportion of white space are commonly used to distinguish between variants of the same brand family. Lighter colors on packs are used to signify ‘lower tar’ cigarettes (Wakefield et al, 2002; DiFranza et al. 2002) and consumers interpret lighter shades on cigarette packaging to infer that the cigarettes are less harmful (Hammond & Parkinson 2009). In the presence of a ban on terms such as ‘light’, ‘low tar’ and ‘mild’ which connote reduced harm, tobacco companies use alternative brand descriptors such as ‘smooth,’ color descriptors such as ‘silver,’ and ‘tar’ numbers that are incorporated into brand names, and that consumers also interpret to mean reduced harm (Hammond & Parkinson 2009). The relationship between branding and consumer perceptions of harm and related sensory experience is discussed further in a later section.

Given the central role of packaging in cigarette branding and marketing (NCI 2008), it is somewhat surprising that no study has attempted to quantify and describe changes in cigarette packing over time or differences between packaging for menthol and non-menthol brands. However, historical examples of cigarette packs are available on the internet *http://www.cigarettespedia.com/index.php/Main_Page* (click on brand name) and more recently *http://www.tobaccolabels.ca/cigarettepackagepictures/unitedstates*. In a submission to FDA, R.J. Reynolds (June 30, 2010) reported using cool and fresh imagery for menthol products and blue and green colors in package labeling. According to consumer perception studies conducted by Lorillard, smokers generally associate and prefer green packaging with menthol cigarettes (Lorillard July, 2010). However, these studies were not described in the company’s report. Color theories suggest that green is commonly associated with “health” and “healing,” in addition to “nature,” “renewal,” “new beginnings,” and “harmony” (Frazer & Banks, 2004 in NCI, 2008). Green also connotes positive affective states, such as “calming,” “gentle,” and “peaceful” (cite in Anderson, Ling, & Glantz 2007). The following section describes the use of imagery and other messages in menthol marketing in more detail in connoting health reassurance.

**WHAT HEALTH REASSURANCE MESSAGES WERE/ARE USED IN MENTHOL MARKETING MESSAGES?**

In this section, we distinguish between two main types of messages that may provide health reassurance to consumers. First, messages may be explicit in nature, in that they make an obvious and direct connection between use of the product and a consequent expected health benefit or reduction of health risk. An example of an explicit health claim might be “*a cigarette to soothe a sore throat.”* This claim overtly promises that the product confers a medicinal benefit in relieving the symptoms of a specific health condition. Second, messages may be implicit, in that they connote some kind of benefit related to health or well-being, without expressly saying so. These implicit messages tend to be more indirect and make use of imagery, associations and/or descriptive language. An example of an implicit health claim might be “*a cigarette as fresh as a mountain stream.*” By associating its product with a fresh mountain stream, this phrase invokes imagery of nature and cleanliness and thereby infers healthiness. Implicit messages can be highly effective as communication tools, in covertly shaping consumers expectations about a product. In addition, their ambiguity makes them difficult for consumers to discount.

During the 1950s, growing concern among consumers about the health harms of cigarettes created considerable dissonance within smokers, who were anxious about the fact that they were incurring a health risk, but found themselves unable to quit. This cognitive dissonance made smokers open to messages that might reassure their health concerns (Pollay & Dewhirst 2002). From a marketing point of view, since the health harms of tobacco became widely known, explicit claims that one cigarette brand was healthier, safer or less harmful than another risked being rejected by consumers as not being believable. Furthermore, explicit claims had the undesirable consequence for the tobacco industry of reminding smokers that they were engaging in a behavior that was inherently harmful to their health. Instead, the tobacco industry turned to implicit marketing messages through the use of brand descriptors, slogans, and rich advertising imagery, to offer health reassurance (Pollay & Dewhirst 2002). These implicit messages promoted attributes such as taste, flavor, sensory experience, satisfaction and enjoyment.

In a review of tobacco industry documents and advertising, Sutton and Robinson (2004) identified extensive use of four types of messages in menthol marketing: healthy/medicinal claims, taste sensation (e.g., fresh, refreshing, cool, clean, crisp), youthfulness, and ethnic awareness. The first two categories are the focus of one section because these themes are inextricably linked in marketing messages and in the minds of consumers (see later sections on consumer perceptions).

**Healthy/medicinal claims and taste sensation**

Until the mid 1950's, marketing messages positioned menthol cigarettes for occasional use as a remedy for myriad ailments (Gardiner, 2004; Sutton & Robinson, 2004). For example, Samji and Jackler (2008) archived and reviewed several thousands of cigarette ads that were sampled from popular magazines and scholarly journals between 1920 and 1954. Only ads that depicted the throat or a throat doctor were selected for further description and their analysis was not specific to menthol advertising. Brand slogans for Spud, the first menthol cigarette (Ashton-Fisher Tobacco Co.), and for Kool, promoted these products as remedies for nose and throat irritation and for congestion. A 1937 ad featured a prescription from Dr. Kool, a cartoon penguin: "*Tell him to switch to Kools and he'll be all right. Doctors…agree that Kools are soothing to your throat*." The researchers remarked that the introduction of menthol played a central role in positioning tobacco products as a treatment rather than an irritant.

In their overview of research reviews of qualitative tobacco industry documents that were prepared for FDA, Lee and Glantz (in press) also noted that explicit health claims characterized menthol cigarettes as a healthier, less harsh alternative for smokers who required temporary relief from symptoms. To illustrate the extent to which health claims were widely accepted, the authors cited an example of a 1951 case report from the Journal of American Medical Association that referred to menthol cigarettes as "medicated cigarettes" with an "anesthetic and cooling effect" (Highstein & Zeligman 1951, cited in Lee & Glantz in press).

A brief history of tobacco marketing from the Institute of Medicine (2003) noted that explicit health claims persisted in spite of a 1942 agreement between the Federal Trade Commission and Brown & Williamson to end such advertising. The IOM report cited two slogans from 1946 and 1949: "*HEAD STOPPED UP? GOT THE SNEEZES? SWITCH TO KOOLS. . . THE FLAVOR PLEASES!*" and "*Got a COLD? Smoke KOOLS as your steady smoke for that clean, KOOL taste"* (table 3-1 in IOM, 2003). These and other examples serve to illustrate that early marketing messages linked claims about the perceived health benefits of menthol with its taste sensation. After the Federal Trade Commission codified the cigarette advertising guidelines in 1955, marketing messages about taste, flavor, aroma, and enjoyment replaced explicit health claims. The IOM report highlighted the industry's use of taste and sensory descriptors such as "mild," "light" and "smooth" to suggest the concept of product safety.

In a review of tobacco industry documents about marketing for "light" and "low-tar" cigarettes, Pollay and Dewhirst (2002) described how the industry repositioned menthol cigarettes from a health remedy for occasional use to a positive smoking experience for regular use. In response to growing public concern about the health impacts of smoking, motivation researchers and trade analysts advised the industry to adopt subtler tactics, using visual imagery and ad copy that implied healthfulness (Pollay 1989, cited in Pollay & Dewhirst 2000). A Brown & Williamson document highlighted the important role of menthol in assuaging smokers' concerns about health: "*Menthol in the filter form in the Salem advertising was a 'refreshing' taste experience. It can be very 'reassuring' in a personal concern climate. Undoubtedly, the medicinal menthol connotation carried forward in a therapeutic fashion as positive taste benefit*." (Cunningham & Walsh, 1980, cited in Pollay & Dewhirst 2002). The authors concluded the use of menthol was a critical element of the tobacco industry's efforts to convince consumers that particular cigarette brands are relatively healthy. As described by Pollay & Dewhirst, "*cigarette advertising is notoriously uninformative, with characteristic forms using veiled health implications and pictures of health along with vague promises of taste and satisfaction*" (2002, p.i28).

Sutton and Robinson (2004) observed that general market magazine and newspaper advertising of the 1950s and 1960s promoted menthol brands with outdoor scenes, such as woodlands, rain forests, rock gardens, and country streams. These images were paired with sensory descriptors, such as "cool," "clean," "fresh"—terms that connote health benefits. For example, advertising for Salem mentioned "perpetual springtime" and "a wonderful world of freshness" (MSA Inc. 1978, cited in Gardiner 2004) and Newport's introduction in 1957 featured the slogan: "*Rich taste – with a touch of refreshing mint*" (Anderson, in press).

Anderson (in press) examined 953 tobacco industry internal documents gleaned from a string of search terms about menthol marketing and consumer perception. Consistent with other accounts, she reported that menthol cigarettes were first popularized as a remedy to the burn, dryness and throat irritation that accompany smoking. The industry documents included examples of early advertising slogans for menthol cigarettes that promised healthful outcomes, such as "*Breathe easy, smoke clean*," (Brown & Williamson 1978 cited in Anderson, in press) and "*The beneficial head-clearing qualities of menthol*" (Brown & Williamson undated, cited in Anderson in press). When overtly health-oriented messages were forbidden, marketing messages exploited consumer perception of the characterizing flavor as both a taste and a sensation. In addition, the messages capitalized on the perception of a cooling sensation as healthful: "*What a wonderful difference when you switch to snow fresh Kools. Your mouth feels clean and cool, your throat feels soothed and fresh. Enjoy the most refreshing experience smoking*" (Brown & Williamson,1968, cited in Anderson, in press). Indeed, tobacco companies sought to preserve the connotations of menthol with health. For example, a 1978 Brown & Williamson document described its objective to "*provide product safety reassurance while enhanc[ing] the satisfaction and refreshment perception of the appropriate Kool styles…*" (Brown & Williamson,1978, cited in Anderson 2010). Anderson concluded that marketing messages served to reassure smokers that menthol cigarettes were healthier than non-menthol cigarettes and that this reassurance continues in contemporary marketing messages that feature more oblique references to health.

A study by Paek et al. (2010) highlighted the contributions of product labeling and visual imagery to communicate implicit health-related claims. Their content analysis examined the prevalence of implicit health-promotion messages for cigarettes in 1,300 magazine ads from 1954 to 2003. Equal numbers of ads for 10 brands were sampled from five time periods. The sample included ads for 10 brands, including Newport and Kool, but the analysis did not compare menthol and non-menthol advertising. The presence of an implicit health claim was coded whenever verbal cues used either factual terms (e.g., low tar, no additives, filter) or impressionistic terms (e.g., mild, natural, gentle calm, soft, smooth) to characterize cigarettes. The presence of an implicit health claim was coded whenever visual cues associated cigarettes with healthful places or objects, such as mountains, fields, an ocean, or a glass of water. Verbal health claims appeared in advertising copy for 49 percent of the ads from the post-MSA era (1999-2003) compared to 45 percent of the ads overall. Visual health claims were found in 50 percent of the post-MSA era ads, compared to 42 percent overall. The researchers concluded that implicit claims about health are as prevalent in contemporary cigarette advertising as they have been previously.

Throughout TPSAC meetings, tobacco industry representatives consistently pointed to taste as being the main driver of preference for menthol cigarettes among menthol cigarette smokers, with cooling sensation being considered to be part of the overall consumer taste experience (July 2010). Lorillard indicated in its submission that terms such as 'smooth,' 'fresh,' 'refreshing' and 'mild' are only intended to communicate taste, flavor and satisfaction (Lorillard, July 2010), and not to implicitly communicate that menthol cigarettes are less hazardous than non-menthol cigarettes.

_Summary_. Analyses of tobacco industry internal documents and the marketing messages the industry produced provide corroborating evidence of explicit and unwarranted claims that smoking menthol cigarettes would improve smokers' health. Over time, marketing messages increasingly relied on sensory descriptors and imagery to imply that menthol cigarettes are safer than non-menthol cigarettes.

**WHAT OTHER MESSAGES WERE/ARE CONVEYED TO POTENTIAL CONSUMERS BY MENTHOL MARKETING MESSAGES?**

Marketing messages about health claims and sensory appeals derive from direct references to menthol, but other marketing messages convey the product's appeal without reference to its characterizing flavor. In a 1982 marketing report, R.J. Reynolds characterized menthol smokers (the "Coolness Segment") as the youngest, the most economically disadvantaged, and the most likely to be in minority and ethnic groups, who "*tend, more than average, to desire their brand of cigarettes to symbolize personal qualities such as youth; modern womanhood; romance; career orientation; and success*" (cited in Anderson, in press). Previous research describes two dominant themes used to appeal to these target audiences and their aspirations. One theme is the exuberance of youth, which Sutton and Robinson (2005) labeled as "youthful, silliness, fun" and Anderson (in press) characterized as "fun-loving, sociable, and youthful." Menthol advertising also associates product use with images of an idealized self and social identity—a theme that Sutton and Robinson (2005) labeled as "ethnic awareness," and Anderson (in press) characterized more broadly as "identity or in-group belonging." These themes are not mutually exclusive; the same advertisement may serve to communicate both types of messages (see for example, Figure 3 in Anderson in press).

**Youthfulness and sociability**

Newport introduced its "Alive with Pleasure!" campaign in 1972 with advertising that portrayed young people having fun, but engaged in activities that seemed childish or juvenile (Sutton and Robinson, 2005). According to Klausner's (in press) review of tobacco industry documents, the Newport campaign was based on the assumption that peer influence is critical to smoking uptake and the advertising imagery sought to recreate and reinforce that influence. After the first four years, Newport was still lagging behind Kool and Salem, but its market share increased among youth. "*Newport's SOM [share of market] among smokers 14–17 years old is significantly higher than brand's Total SOM, reflecting strong appeal to young/new smokers*" (Esty 1976, cited in Klausner, in press). Newport's "Pleasure" campaign (the "Alive with…" part of the slogan was later dropped) continues to this day. Newport has been the leading menthol cigarette brand and the second leading cigarette brand among youth since the early 1990s.

Anderson (in press) acknowledged that images of youthfulness and sociability were not unique to marketing messages for menthol. Indeed, a 1981 R.J. Reynolds report observed, *"…The benefit of smoking which has most frequently and most successfully been exploited by brand families appears to* *be Social Interaction*." After this approach proved effective for Lorillard's Newport brand, R.J. Reynolds launched a similar campaign for Salem. "*Advertising must convince younger adult smokers that Salem is smoked by natural, unpretentious but interesting people who are social leaders/catalysts (make things happen) whose sense of humor and wit makes them fun and exciting to be with*" (RJ Reynolds 1981, cited in Anderson in press). Anderson concluded that it was menthol's younger profile relative to other cigarettes that made the themes of youthfulness and sociability particularly appealing and persuasive.

Two empirical studies addressed consumer perceptions of youthfulness in cigarette marketing messages. In one study, 561 adults viewed and rated the perceived age and level of attractiveness of models in magazine ads for menthol and regular cigarettes (Mazis et al. 1992). Advertisements for menthol brands were judged to have significantly younger models (average 25.7 years) than advertisements for regular cigarette brands (average 31.9 years). Irrespective of their own age group, people rated younger models in the advertisements as being more attractive than older models.

Barbeau et al. (1998) asked 913 sixth- to eighth-grade students from Massachusetts to rate magazine ads for four cigarette brands (Newport, Camel, Marlboro and Virginia Slims) and four non-cigarette products. All the ads were from 1994 and featured human figures or anthropomorphic characters. The majority of students judged each of the four cigarette ads to say that smoking will make people look cool (72 percent to 84 percent), attractive (53 percent to 81 percent), popular (50 percent to 80 percent) and healthy (51 percent to 71 percent). Students' responses indicated that the advertisements communicate ideas that were in violation of the Tobacco Institute Voluntary Advertising and Promotion Code. Like the adults in the previous study (Mazis et al. 1992), the students rated Newport models as looking younger than the models appearing in ads for other cigarette brands. Weaknesses of both studies are that they surveyed convenience samples and could not control for objective differences between models that appeared in ads. Nonetheless, the results suggest that the message that Newport is a brand for younger consumers was apparent to both adults and adolescents.

**Identity/In-group belonging**

Establishing a sense of belonging is a central task of identity development in adolescence, particularly for racial/ethnic minorities (Castro 2004). Images of the self as a smoker or non-smoker contribute to this identity. As concluded in chapter 7 of NCI's Monograph 19 (2008), much tobacco advertising creates the perception that smoking will satisfy adolescent psychological needs relating to popularity, peer acceptance and positive self-image. Furthermore, adolescents who believe that smoking can satisfy their psychological needs or whose desired image of themselves is similar to their image of smokers are more likely to experiment with cigarettes (NCI 2008, p280).

Several histories of menthol marketing commented on appeals to racial identity, which coincided with increased market share among African Americans in the 1960s and 1970s (Gardiner 2004; Sutton & Robinson 2005). For example, commenting on Kool brand advertising of this period, Sutton and Robinson (2005) observed a departure from the standard fare of waterfalls, country streams and romantic couples found in white-oriented media to darker-skinned models, slang terms, and more masculine imagery in African American-oriented media. Increasingly, marketing messages for menthol cigarettes appropriated images of athletes, entertainers, hairstyles, clothing, music and other elements of African American popular culture (Gardiner 2004; Giovino et al. 2004; Hafez & Ling 2005; Sutton & Robinson 2004). Several researchers observed that the word "cool," and its significance to the African American community, played a central role in the appeal of the Kool brand as well as the product category (Gardiner 2004; Castro 2004).

Balbach et al. (2003) examined ads for R.J. Reynolds' brands from three magazines aimed at an African American audience. Nearly all of the ads were for menthol brands. Between 1989 and 1990, every ad depicted an escapist or fantasy theme when a setting was visible, most of the ads (74 percent) featured expensive objects when objects were visible, and approximately half of the ads (58 percent) portrayed nightlife whenever social life was shown. All three themes remained evident in ads that were sampled from the same magazines a decade later, although fewer of the ads featured expensive objects. In combination with evidence gleaned from their review of R.J. Reynolds' internal documents (discussed in the section on targeting), the authors concluded that marketing messages associated menthol cigarettes with luxury objects, a glamorous nightlife, and a fantasy world in order to appeal to the aspirations of young adult African Americans.

Nightlife settings were observed in menthol marketing aimed at a broader audience of young adults. Belstock et al. (2008) examined all cigarette and alcohol advertising that appeared in Maxim, FHM, Cosmopolitan and Ebony in 2003 and 2004. These magazines were selected because of their popularity with young adult readers (ages 18–24). Although none of the 317 alcohol ads referred to cigarettes, 32 of the 114 cigarette ads (28 percent) included text or imagery related to alcohol. Cigarette and alcohol advertisements were equally likely to portray a bar or club setting that implied a nighttime or after-hours social gathering. Newport and Kool were two of the four cigarette brands that featured alcohol-related content in their advertising. However, the proportion of total ads for menthol and the proportion of menthol ads with alcohol content were not reported.

Anderson's review of industry documents (in press) noted that menthol marketing appeals to multiple group identities, especially, but not exclusively, to African Americans. She observed that menthol marketing conveys varied images of menthol smokers because the three largest, exclusively menthol brands developed such different identities. Several examples from industry documents characterized Kool as having a more masculine image than other brands, Salem a more feminine image, and Newport as the brand with the youngest demographics in the industry. Anderson concluded that no single unified image of a menthol smoker emerges from marketing messages about the product.

Two empirical studies examined consumer perceptions of menthol smokers, and commented on the degree to which perceptions fit the messages conveyed in menthol marketing. Allen and Unger (2007) examined selected socio-cultural factors associated with menthol smoking in a convenience sample of African Americans from Los Angeles. They interviewed 432 smokers of at least five cigarettes per day (296 menthol and 136 non-menthol) recruited from a campus medical center, shopping malls and other community sites. Differences between groups of smokers were presented as odds ratios (adjusted for age and employment status) and without response frequencies. The results suggested that for both males and females, a significant correlate of menthol use was the belief that most African Americans smoke menthols. Among females (but not males), an additional correlate was a lack of belief that menthol smoking "*is a Black thing*."

Segerstrom et al. (1994) randomly assigned 100 white and 94 African American community college and university students with a short written description of a target smoker that varied by race (African American or white) and cigarette type (menthol or regular). Students then rated the smoker on 15 attributes using semantic differential scales (e.g., rich/poor, unpopular/popular, weak/strong). Overall, the pattern of ratings according to the subject's own race and smoking status was inconsistent and no single unified image of a menthol smoker emerged. Although the small sample size limits conclusions about differences in perceptions between groups, the study finding is consistent with the conclusion of Anderson's document review (in press). However, the study did not examine perceptions of those who smoked different brands of menthol cigarettes, which would likely differ.

_Summary_. Menthol marketing features youthful imagery and consumers perceive differences between menthol and non-menthol marketing in terms of the relative age of the models. Menthol marketing also uses socially and culturally relevant messages about in-group identity to appeal to different market segments. Different group identities are emphasized in marketing for different brand families, which may explain why consumers do not share a singular impression of a menthol smoker.

The next section considers the role of youthful imagery and other messages about in-group identity in cultivating target markets for menthol brands.

**WHO ARE THE TARGET POPULATIONS FOR MENTHOL MARKETING? IS THERE EVIDENCE TO SHOW THAT YOUTH, WOMEN, AND SPECIFIC RACIAL/ETHNIC GROUPS WERE TARGETED?**

Few products are promoted to the entire population in an undifferentiated manner. The planning of promotional strategy requires the definition of a clear target market, whereby the population is segmented into defined subgroups. This target market can include people who are potential buyers, current users, those who make the buying decision, or those who influence it. Extensive qualitative and quantitative research is undertaken to identify the salient beliefs, values and preferences of the planned target market, which might be defined on the basis of age, gender, ethnicity, income, and lifestyle, among other attributes (NCI 2008). Promotional strategies are then designed for and directed to this well-defined consumer group (or segment). Typically, many consumer tests are undertaken to pre-test and refine branding elements. The message in a segmented campaign may have broad appeal, but will be most salient to and resonate with the specific targeted segment. The NCI review concluded that "*the tobacco industry has become increasingly sophisticated in applying market research to population segments in order to design products, messages, communication channels and promotions more aligned with the needs and susceptibilities of particular market segments. This research results in more efficiency, greater reach, and increased effectiveness for marketing activities aimed at targeted populations*." (NCI 2008, p171).

This section draws on three types of evidence about target marketing: (1) analyses of tobacco industry documents that described the development, intent, and consequences of marketing menthol brands, (2) analyses of the advertising environment that compared the quantity of menthol advertising either by neighborhood characteristics or by audience demographics, and (3) observational studies that compared advertising recall and recognition by audience demographics.

**Targeting: Youth and young adults**

In relation to tobacco use, brand image is especially important for adolescents because this is the age during which the vast majority of people take up smoking and brand choices are made. A recent review of tobacco marketing and its effects on tobacco use published by the National Cancer Institute (2008) concluded that "*much tobacco advertising targets the psychological needs of adolescents, such as popularity, peer acceptance and positive self-image. Advertising creates the perception that smoking will satisfy these needs.*"(NCI 2008, p280).

Tobacco companies frame their marketing efforts as being solely aimed at influencing brand switching in current users, and deny their advertising and promotional strategies promote youth smoking uptake. However, there is an abundance of empirical studies to show that the tobacco industry does target its marketing efforts towards youth and young adults and that youth are strategically important for the customer base. As concluded by Pollay et al. (1996), "*the battle of the brands for market share is waged largely among the young, for it is a brand's success among the* *young that leads to greater brand sales and profit in the long term*"(p.13). Despite restrictions on more traditional forms of tobacco marketing, youth notice and are influenced by tobacco marketing efforts in ways that increase their likelihood of taking up smoking (NCI 2008). The recent NCI review examined research studies linking tobacco advertising and promotion with smoking attitudes and behaviour, including qualitative, cross-sectional, experimental, cohort and time series studies. The review concluded that "*the total weight of evidence from multiple types of studies, conducted by investigators from different disciplines, using data from many countries, demonstrates a causal relationship between tobacco advertising and promotion and increased tobacco use, as manifested by increased smoking initiation and increased per capita tobacco consumption in the population*" (NCI 2008, p281).

***Industry documents research***

Ling & Glantz (2002), in a review of tobacco industry documents from Philip Morris, RJ. Reynolds and Lorillard, explored tobacco industry strategies for marketing to young adults aged 18 to 24 years. They concluded that tobacco advertising encourages regular smoking and increased consumption by integrating smoking into social activities and places that reflect life changes experienced by young adults, with menthol brands such as Newport being featured in example documents. Kreslake et al. AJPH (2008), in a review of tobacco industry documents, found evidence that younger smokers preferred milder brands with lower menthol levels, with R.J. Reynolds observing that "*the want for less menthol does indeed skew younger adult*"(Etzel 1993, cited in Kreslake 2008). The success of Newport among younger consumers—Newport has lower menthol levels than Kool and Salem brands—was attributed to this feature, and the authors noted that from the 1980s, all other major menthol brands actively pursued a low-level menthol formulation to attract this market (Kreslake et al. AJPH 2008). In Kreslake NTR (2008), industry documents indicated a clear acknowledgment of this low-menthol formulation being more attractive for those initiating smoking. For example, one Brown & Williamson document outlined that "*a successful starter cigarette would need to provide a low tobacco taste, low impact and irritation, low tobacco aftertaste, and low menthol content*"(Cantrell, 1987 cited in Kreslake NTR 2008). Kreslake et al. (NTR 2008) refer to several Lorillard documents that detailed studies finding lower satisfaction ratings among younger people in their twenties when given cigarettes with higher menthol levels. By comparison, smokers aged 45 and older had higher satisfaction ratings of cigarettes with higher menthol levels.

Klausner (in press), in her industry document review, concluded that youth were a target of menthol marketing. She notes Philip Morris was concerned in the late 1970s that it lacked a competitive menthol product at a time when menthol cigarette use was increasing among the young, women and African Americans. "*We knew that Blacks, females, and younger smokers were more likely to smoke menthol cigarettes than whites, males and older smokers. …These differences could have a profound effect on the future growth of the menthol share of the market. We know, for example, that males, whites and older smokers are more likely to quit smoking than females, Blacks and younger smokers*" (cited in Klausner, in press). Anderson's tobacco industry document review (in press) also noted the importance of young people as a primary target group for menthol cigarette marketing. For example, she found documents that indicated that the marketing strategy for Newport through much of the 1990s was to "*continue to improve Newport's appeal as the 'peer' brand among young adult smokers*"(cited in Anderson, in press). She concluded that menthol is targeted to young people in the U.S. and that although different menthol brands are associated with different "brand identities," menthol in general is perceived to be for females, younger smokers and lighter smokers. She concludes that marketing that emphasizes "*coolness, refreshing sensations, mildness, soothing taste and youth fun-loving imagery*" contributes to these perceptions (Anderson in press). As detailed further in a later section on targeting to African Americans, Hafez & Ling (2005) document how the company used music to appeal initially to African Americans with its Kool Jazz concerts and related music efforts, but initially failed in its aim to "*find an idea or symbol that was truly pan racial* (*universal racial*).” With its 2004 Kool Mixx campaign, which promoted elements of hip-hop culture through colorful cigarette packaging and related giveaways, such as radios, and music compact disks, the brand finally succeeded in reaching beyond its core target group of African Americans to young adults in general.

***Empirical studies***

Two empirical studies addressed the content and/or appeal of menthol marketing to adolescents or young adults. Unger et al. (1995) had 386 eighth-grade students in southern California rate each of 20 cigarette and alcohol ads that appeared in magazines or on television during early 1993. Brand name information was concealed on each ad. For Newport ads, 63.3 percent of students correctly identified the ad/s as being for cigarettes and 31.4 percent correctly identified the brand. For Kool ads, 10.5 percent correctly identified the ad/s as being for cigarettes and 11.6 percent identified the brand. This compared with correct identification of cigarette ad/s for Marlboro ads (87.8 percent) and correct identification of the brand (71.7 percent). Stage of smoking uptake (non-susceptible nonsmoker; susceptible non-smoker; user) was significantly associated with correct brand name recognition for all seven cigarette brands analyzed together and for Newport specifically, with users recognizing the ads significantly more than non-susceptible nonsmokers. Smoking susceptibility was positively associated with ad liking for the menthol brands Kool and Newport, and non-menthol brands Marlboro, Camel and Capri. These results were noted by the authors as consistent with the notion that cigarette advertising is attractive to susceptible nonsmokers as well and may influence them to experiment with the product.

Arnett & Terhanian (1998) showed 534 sixth- to twelfth-graders one print advertisement for each of five cigarettes brands—Marlboro, Camel, Kool, Benson & Hedges or Lucky Strike—and after each viewing they completed questions about the ad. Overall, 56 percent had seen the Kool ad more than six times, 38 percent liked it, 30 percent said it made smoking look appealing and 9 percent said it made them want to smoke that brand. Responses to these questions were higher for Marlboro and Camel and lower for Benson & Hedges and Lucky Strike. As for other brands, smokers more frequently indicated than non-smokers that they liked the Kool ad, and that the Kool ad made them want to smoke the brand.

Two studies provide ecological evidence that menthol marketing expenditures are related to adolescent cigarette brand preference. In a survey reported by Barker et al. (1994) the three most commonly purchased brands among adolescent smokers in 1993 (Marlboro, Camel and Newport) were the three most heavily advertised brands in 1993. This is despite the fact that Camel and Newport ranked seventh and fifth, respectively, in overall market share. Similarly, the increase from 1989–1993 in adolescents’ brand preference for Camel cigarettes and the decrease in preference for Marlboro cigarettes during that period were not explained by changes in overall market share for these brands. Rather, these changes mirrored the direction of changes in brand-specific advertising expenditures: from 1989–1993, Marlboro advertising decreased to $75 million from $102 million, while Camel advertising increased to $43 million from $27 million. In contrast, the increased preference for Newport menthol cigarettes did not reflect the decrease in Newport menthol advertising expenditures to $35 million from $49 million during the same period. The authors suggest that regional differences in brand preference of adolescents and changes in those preferences during 1989–1993 might be explained by further analysis of the relation between regional advertising expenditures and brand preferences.

Pollay et al. (1996) modeled the relationship between advertising expenditures for nine brands including Newport, Kool and Salem and youth and adult cigarette brand preference between 1974 and 1993. Brand preference data was sourced from population surveys of youth and from Maxwell Report market share data for adults. Using standard techniques to analyze market share involving

Koyck-type models, they found that brand choices among teenagers were related to the extent of brand-specific cigarette advertising. Furthermore, the relationship between brand choice and brand advertising was significantly stronger among teenagers than among adults, by a factor of almost three (Pollay et al. 1996). These findings were robust to different assumptions, including the removal from the model of the most popular brand, Marlboro. These findings suggest that advertising for cigarette brands, including menthol cigarette advertising, has a greater impact on the brand preferences of teenagers than on adults.

*Summary*. Taken together, the section on youthful imagery in menthol marketing and the studies of industry documents described in this section confirm that the industry developed menthol marketing to appeal to youth. This is particularly true of the Newport brand, but that strategy was also adopted by other tobacco companies. Marketing messages positioned menthol cigarettes as an attractive starter product for new smokers who are unaccustomed to intense tobacco taste and/or high levels of menthol. Empirical studies provide further evidence of targeting: youth pay attention to and are attracted to menthol cigarette advertising. Cigarette advertising, including menthol advertising, has a greater impact on the brand choice of adolescents than it does for adult smokers. Studies of the role of menthol cigarettes in smoking initiation are discussed in chapter 6.

**Targeting: Women**

The white paper by Rising & Alexander (2010) points out that neither of two reviews of tobacco use among women included information that was menthol-specific. However, four tobacco industry document reviews included information about menthol marketing to women and one empirical study was focused on menthol marketing to women.

Carpenter et al. (2005) reviewed tobacco industry documents to show that extensive research was conducted by the industry on female smoking patterns, needs and product preferences, including menthol brands. The industry took account of women's social and cosmetic concerns for cleanliness and freshness through menthol cigarette product design and marketing. Lorillard, for example, experimented with a lemon-flavored menthol brand to address female sensitivity to unpleasant odor and aftertaste while capitalizing on their greater willingness to experiment with flavored cigarettes (Carpenter et al. 2005).

In their review of menthol cigarette marketing which includes tobacco industry documents, Sutton & Robinson (2004) point out that female smokers were the first targeted population for menthol cigarettes, when a 1930's advertisement for Spud menthol cigarettes proclaimed that "*to read the advertisements these days, a fellow'd think the pretty girls do all the smoking*" (USDHHS, cited in Sutton & Robinson 2004). These authors also noted that advertisements for menthol cigarettes from the 1950s onward had a distinctly feminine aura, featuring images of romance, flowering fields and springtime.

Klausner's document review (in press), mentioned above, described examples of marketing efforts directed at young females. For example in 1976, R.J. Reynolds described Lorillard's marketing effort as follows: "*Newport is placing increased emphasis on both young female and young male publications reducing older female publications [magazines]. Trend is toward younger readers and more men although overall female skew continues*"(document cited in Klausner, in press). Anderson's document review (in press) found that the three largest stand-alone menthol brands had different brand identities in the mind of both manufacturers and consumers. R.J. Reynolds documents portrayed Salem as a brand for smokers who are "*passive, feminine,*" describing its Salem Slim Lights variant to be positioned for consumers "*who desire a refreshing, low tar cigarette with (a) stylish, unpretentious feminine image*" (cited in Anderson, in press). Although the menthol segment "*skews female*" (documents cited in Anderson, in press), the Kool brand has a more masculine image, described by Lorillard as "*a strong tasting, 'tough guy' cigarette*" (documents cited in Anderson, in press).

Fernandez et al (2005) conducted a descriptive analysis of menthol advertising in women's magazines compared to one men's magazine from 1988 to 2002. They found that the proportion of menthol ads out of all cigarette ads in each issue of magazines for white women did not differ from those for white men. However, as discussed more fully in the next section on ethnicity, there was a higher prevalence in magazines for Hispanic women.

<u>Summary</u>. Some menthol brands appear to be more targeted to women than men, while others have more masculine branding. However, there is more evidence that menthol marketing efforts are directed to youth and young adults in general, and to racial/ethnic subgroups of women (see also next section).

**Targeting: African Americans**

A large body of research has documented a disproportionate volume of cigarette advertising aimed at African Americans (cf. Primack et al. 2007). Only the subset of studies that categorized or quantified advertising for menthol cigarettes were examined for this section.

***Industry documents research***

The tobacco industry's internal documents illustrate sustained efforts to target African Americans through the development and advertising of menthol products and through corporate involvement in community-based organizations.

Balbach et al. (2003) reviewed 21,000 industry documents from a search string of terms related to R.J. Reynolds' launch of Uptown, a full flavor cigarette with lower levels of menthol than Salem, that was designed to appeal to young African American men. In a 1988 speech, a senior marketing official noted that the company had been using targeted marketing programs for decades: "*Reynolds tobacco has made a special effort to reach Black Smokers since the early 1960s…almost 70 percent of Black smokers choose a menthol brand. That's why special advertising and promotions for Salem cigarettes make a lot of sense in Black media and Black communities*" (Winebrenner 1988, cited in Balbach et al. 2003). The objective of R.J.Reynolds' Black Initiative Program was to regain its share of the African American market with a plan that featured "targeted Black print media (Jet, Essence, Ebony, key newspapers)" and a heavy "outdoor presence" (R.J. Reynolds 1990, cited in Balbach et al. 2003). Special packaging for Uptown reflected the company's beliefs that African American smokers opened cigarettes from the bottom and that a pack containing only 10 cigarettes would address the price sensitivity of the target audience. As a result of intense public pressure that followed R.J.Reynolds' press release, the company canceled the test marketing in Philadelphia and it abandoned the Uptown brand. A 1990 Philip Morris memorandum attributed this failure to its competitor's miscalculation: *"…marketing cigarettes to minorities was not new, saying so was."* (Philip Morris 1990, cited in Balbach et al., 2003) R.J. Reynolds' continued efforts to build brand share in the African American market were informed by the idea that "a highly visible commitment to social responsibility is fundamental to successful ethnic marketing" (R.J. Reynolds 1994, cited in Balbach et al. 2003). The authors noted that the company's strategy represented a combination of marketing existing menthol brands and building community relationships through support of local events and programs.

Hafez and Ling (2005) examined 210 industry documents related to music sponsorship and the Kool brand. Using music as the unifying element of an integrated marketing campaign aimed at young African American smokers was a proven formula for Brown & Williamson. Beginning with the first Kool Jazz concert in 1975, music promotions were used to maintain and augment market share in the

African American community. For example, a 1981 marketing document suggested that Kool's music campaign was originally developed "*on a strategy of more effectively reaching a major segment of our target audience, providing some kind of reward for this same group in the form of shows at bargain prices, and using the events to offset Black media availability deficiencies*." (Broecker 1981, cited in Hafez & Ling 2005). Vans equipped with loudspeakers, such as the "Kool Mobile Music Tour," were used to distribute free Kool cigarette samples in inner-city neighborhoods. Similar promotional techniques were the foundation of a 1981 Kool Market Development Program, which also encouraged the involvement of Brown & Williamson's sales representatives and managers in "*retail and community organizations that will assist in fostering positive relations in the Black community*." (Brown & Williamson,1982, cited in Hafez & Ling,2005).

Yerger et al. (2007) examined documents from the four companies (Brown & Williamson, Lorillard, Philip Morris, and R.J. Reynolds) whose menthol brands were the most heavily marketed in African American neighborhoods, using search terms related to African American, inner city, and urban. The analysis highlighted four strategies that were common to the industry's marketing programs in the inner cities from 1980 to the late 1990s: collecting psychographic and other data about African American consumers, using mobile vans to maximize the distribution of free cigarettes, developing specialized promotions for inner-city retailers, and engaging with local organizations to improve corporate image in the African American community. For example, Philip Morris sought to resolve problems with product availability and visibility in its "Black accounts," which were smaller liquor, grocery, and convenience stores in inner cities (Philip Morris 1984, cited in Yerger et al. 2007). The company redesigned product displays and paid retailers incentives to expand inventories and maintain visually prominent displays. First tested in Detroit, the program was later expanded nationwide to promote only menthol extensions of the company's most popular brands. Similarly, Brown & Williamson's "Kool Inner City Family Program" targeted the top 20 African American markets with free gifts for retailers and distributors, in-store advertising with African American models, and a variety of consumer offers (Lagreca 1987, cited in Yerger et al. 2007). R.J. Reynolds conducted interviews in inner-city zip codes with at least 50 percent African American residents and yearly household incomes under $20,000 in order to determine the boundaries of target neighborhoods for a "BYAS" (Black Young Adult Smoker) Initiative to increase market share for its Salem brand (Hawkins et al. 1989, cited in Yerger et al. 2007). Additionally, the value of the target audience for increasing brand share was described in the company's marketing report: "*The daring, flamboyant aspect of YA [young adult] Black smokers' personalities are evident in <u>the many trends they start</u>. And the fact that these trends often spread to the general population speaks to the <u>unrecognized power and influence</u> this subgroup yields on society…*" [emphases in original]. (Leferman Associates 1989, cited in Yerger et al. 2007). The authors concluded that geographically specific, aggressive, and intentionally disproportionate levels of marketing contributed to the tobacco-related health disparities that are evident among African Americans.
In their review of 144 industry documents, Johnson et al. (2008) identified similar targeting strategies, including industry-sponsored studies of African American culture, geographic targeting of urban areas, and investments in community, ethnic, and cultural events to enhance the industry's image in the African American community. For example, a 1976 marketing plan for Brown & Williamson reported: "*Kool is to develop programs which ingratiate themselves with the Black community. These programs are to show the makers of Kool as a community citizen, be backfire-proof and pave the way for supporting the brand*." (Brown & Williamson 1976, cited in Johnson et al. 2008).

Cruz et al. (2010) combined data from interviews with a former Brown & Williamson executive with analyses of tobacco industry documents to examine how a mix of marketing strategies was used to promote growth in menthol brand share among new and existing African American smokers in urban areas. According to the executive, Brown & Williamson used the term "focus" to refer to communities or stores in predominately low-income, African American areas that were identified as being critical to increasing market share. For example, a 2002 business plan stated: "*Kool is delivering a premium message to its anticipated audience and concentrating in 22 trend-setting urban cities where the majority of this audience lives. These cities house the 102 focus assignments that Kool has identified to be key to the growth of the brand*" (Kool USA 2002, cited in Cruz et al. 2010). The company placed a greater quantity of interior and exterior signs in focus stores, and installed pack displays that featured more shelf space for menthol than for non-menthol brands. In addition, a 2002 marketing report documented that a multi-pack discount offered in 1,600 stores resulted in a larger market share for menthol than was observed in stores that did not receive the promotion. The authors concluded that menthol is the lynchpin in a tightly integrated series of campaigns aimed at the urban poor, especially African Americans.

Anderson's (in press) analysis of tobacco industry documents highlighted the role of marketing in the growing popularity of menthol cigarettes among African American smokers. According to a history of menthol brands written by an R.J. Reynolds marketing official, Kool led this trend by advertising to African Americans before its competitors did: "*Kool ads were in Ebony consistently from at least 1962, when our records start….Kool became 'cool' and, by the early 1970s, had a 56 percent share among younger adult Blacks – it was the Black Marlboro*" (Burrows 1984, cited in Anderson in press). This sentiment was echoed in a 1968 document from Philip Morris, which observed that menthol cigarettes were "*especially suited to the needs, desires and tastes of Negro consumers*." (Philip Morris 1968, cited in Anderson in press). In a "Black Opportunity Analysis" conducted by R.J. Reynolds in 1985, the company's research observed that an "underclass" of African American smokers would remain reliable customers in spite of growing health concerns: "*Blacks simply have more pressing concerns than smoking issues*." (R.J.Reynolds 1985, cited in Anderson in press). A 1983 industry study of low-income African American smokers observed that recall of advertising for specific menthol brands had improved since 1979 and "*the use of menthol cigarettes among the 18–34 lower income Black segment is almost universal*" (Lorillard estimated 1983, cited in Anderson in press). The author concluded that heavy targeting of largely African American urban populations is reflected in the nearly exclusive preferences for menthol brands among these smokers. Indeed, survey data described in chapter 4 confirms that although more menthol smokers are non-Hispanic white than African American, African Americans disproportionately favor menthol brands.

All types of research methods are subject to limitations, including qualitative documents research. A separate peer-reviewed paper by Anderson et al. (in press) identified several limitations that pertain to the studies reviewed in this section and elsewhere in this chapter. The sheer volume of documents available (more than 60 million pages) makes it impossible for researchers to determine that all relevant data were included for each topic examined. Although researchers aim to identify the most important documents among similar results for combinations of related search terms, this "saturation" was not achieved in all studies. The prevalence of acronyms and evidence of code words for menthol suggests that researchers' understanding of the documents may be hampered if the context is unknown. In addition, evidence that the industry tried to conceal its findings and to destroy documents increases the chance that relevant documents could be missing and that a researcher's understanding of a topic might be incomplete. Despite these limitations, the studies reviewed here are noteworthy for a consistency of evidence about the tobacco industry's systematic efforts to promote menthol cigarettes to African Americans.

***Advertising environment***

The white paper by Rising (2010) identified six relevant peer-reviewed articles. In addition, this section included one peer-reviewed study that was published after the white paper (Seidenberg et al. 2010). The studies are organized by the type of advertising examined and then reviewed in chronological order.

Magazines

Three studies documented that advertisements for menthol cigarettes were overrepresented in magazines that are popular with African American readers. Cummings et al. (1987) compared ads that appeared in three magazines with a largely African American readership (Jet, Ebony, Essence) and four magazines with a largely non-Hispanic white readership (Newsweek, Time, People and Mademoiselle). Full-page ads appearing between June 1984 and May 1985 were classified according to product, and brand (menthol, non-menthol, or both). Compared to the other magazines, those targeting African Americans contained a larger proportion of cigarette ads (12.0 percent versus 9.9 percent) and larger proportion for menthol cigarettes (65.9 percent vs. 15.4 percent). Both comparisons were statistically significant.

Informed by hypotheses from an analysis of tobacco industry documents about R.J .Reynolds' Uptown brand, one study compared cigarette ads for R.J. Reynolds brands that appeared in the same three magazines targeted at African American readers (Jet, Ebony, and Essence) with those that appeared in People Weekly (Balbach et al. 2003). Ads were sampled from two time periods: the years surrounding the introduction of the Uptown brand (1989–1990) and one decade later (1999–2000). Compared to People Weekly, the magazines targeted to African Americans contained a significantly larger proportion of R.J. Reynolds' ads for menthol brands—100 percent vs. 31.6 percent in 1989-90 and 97.7 percent vs. 0 percent in 1999-2000.

Landrine et al. (2005) examined cigarette ads that appeared in one magazine targeted at African Americans (Ebony), one at Latinos (the Spanish language edition of People) and one at non-Hispanic whites (the English language edition of People). In issues sampled from January 1990 through August 2002, the proportion of ads for menthol cigarettes was 67.2 percent in the African American magazine, 35.3 percent in the Latino magazine, and 17.3 percent in the other magazine. Unadjusted odds ratios suggested that the African American magazine was 9.8 times more likely to contain a menthol ad than the white magazine; the Latino magazine was 2.6 times more likely to contain a menthol ad.

In a submission from Lorillard to FDA, the company stated that "Newport marketing expenditures have not been disproportionately weighted toward African American smokers or any other ethnic group or gender" (p. 44, Lorillard, July 2010). Although the company's advertising expenditures for general market magazines consistently exceeded its expenditures for African American magazines (see Figure 11, Lorillard July 2010), that difference does not preclude a pattern of targeted marketing that was documented in the studies of magazines. Assuming lower rates are paid to advertise in magazines with a smaller circulation, it would be possible to place a larger volume of ads in African American magazines at a substantially lower total cost. Lorillard increased its spending on African American magazines relative to general market magazines in 1993 (see Figure 11, Lorillard July 2010), but no studies examined the relative impact of that increase on the proportion of ads for menthol brands. Content analyses of magazine advertising for menthol and non-menthol brands after 2002 were not found.

Outdoor and retail advertising

All four studies on this topic found that menthol cigarettes were marketed disproportionately in areas with more African American residents. Altman et al. (1991) compared billboard advertising by the racial/ethnic demographics of census tracts in San Francisco, California. Each of the 901 billboards in the city was photographed between 1985 and 1987. Census tracts were categorized by the predominant racial/ethnic group and without regard to the proportion of non-Hispanic white residents. Thus, African American neighborhoods referred to census tracts where 30 percent of the residents were African American and they were the dominant ethnic/racial minority group, even if a larger proportion of residents were non-Hispanic white. The proportion of all billboards that advertised menthol cigarettes was 22 percent in African American neighborhoods, 17 percent in Hispanic, 11 percent in white and 10 percent in Asian neighborhoods. African American neighborhoods were significantly more likely to contain billboards advertising menthol cigarettes.

Pucci et al. (1998) described outdoor advertising for cigarettes in six Boston neighborhoods—two with the highest median household income, two with the lowest, and two in the middle range. In the two of the neighborhoods, 89.2 percent and 62.3 percent of the residents were African American. All outdoor ads for tobacco, including billboards, placards, posters, stickers, banners, neon and freestanding signs, were counted and categorized by brand. Ads for exclusively menthol brands, Newport, Kool, and Salem, made up 49 percent of the outdoor advertising for cigarettes in the two African American neighborhoods, compared to 38 percent in the Latino neighborhoods, and 22 percent in the non-Hispanic white neighborhoods. The proportion of all ads for menthol, regardless of brand, was not coded.

Laws et al. (2002) visited all stores in 10 demographically contrasting areas of Boston, Massachusetts and compared the proportion of all cigarette ads for menthol brands. To identify predominantly Latino and African American neighborhoods, the researchers selected census tracts of similar per capita income but different ethnic compositions. The comparison areas were predominantly non-Hispanic white and more affluent. Field observations were conducted in all 128 stores that sold cigarettes in 1999. Stores in the area with the highest proportion of African American residents contained the highest concentration of cigarette ads for menthol brands—32 percent in that area compared to 13 percent overall. The difference between the proportion of ads for menthol in predominantly minority areas (29 percent) and non-minority areas (12 percent) was statistically significant.

Similarly, Seidenberg et al. (2010) compared the proportion of all cigarette ads for menthol on storefronts in two Boston neighborhoods, one with predominantly African American residents (50.1 percent) and one with few African American residents (2.7 percent). To eliminate the large discrepancy in the number of retailers that sold tobacco in the two areas, the researchers visited all 59 stores that sold cigarettes in one zip code in the African American neighborhood with all 43 stores that sold tobacco in the comparison community. The proportion of cigarette ads for menthol brands was significantly greater in the African American neighborhood (53.9 percent vs. 17.9 percent). Adjusting for other characteristics of the ads (including size, proximity to school, and the presence of a price), the odds of finding an ad for menthol cigarettes was five times greater on storefronts in the African American neighborhood.

One weakness of the studies about outdoor and retail advertising is that they were limited to small geographic areas. In addition, some of the analyses did not control for neighborhood income, making it difficult to discern whether neighborhoods were targeted because they were predominantly low-income, African American, or both.

*Summary*. All of the tobacco industry document reviews provide evidence that the tobacco industry developed specialized brands and tailored marketing strategies to promote menthol cigarettes to African Americans. Studies of the advertising environment that have compared menthol and non-menthol advertising provide corroborating evidence of the target marketing strategies that were identified in the industry documents research. In all three empirical studies on the subject, menthol cigarettes were advertised disproportionately more than non-menthol cigarettes in magazines aimed at African American readers, compared to magazines with low African American readership. Both studies of outdoor advertising and both studies of retail store advertising showed a higher proportion of menthol ads out of all cigarette ads, in neighborhoods with more African American residents than neighborhoods with lower proportions of African American residents.

**Targeting: Other Race/Ethnicity**

Although there are many studies that confirm African Americans to be a particular target audience for menthol marketing efforts, there are fewer industry document reviews and empirical studies that point to the use of menthol advertising targeted towards particular ethnic groups, such as Hispanics, Asian Americans and Hawaiian/Pacific Islanders. Nonetheless, available studies generally show purposeful targeting towards these ethnic groups.

***Industry document reviews***

A review of tobacco industry documents on targeting of Asian Americans and Pacific Islanders described many tobacco marketing campaigns to reach these population subgroups, but marketing strategies for menthol cigarettes were not specifically mentioned (Muggli et al. 2002). A tobacco industry document review by Anderson (in press) identified menthol marketing campaigns specifically aimed towards Asians and Hawaiians/Pacific Islanders. For example, a study of an R.J. Reynolds' Kool cigarette marketing campaign targeting Hawaiians in 1988 remarked that the use of ethnic models "*could provide an opportunity for Kool to capitalize on being the first to employ ethnic advertising in Hawaii*" and "*display what islanders call the aloha spirit*" (Anderson in press). Anderson (in press) also documented that Philip Morris' Marlboro promotion plan in 1992 included "*special programs to menthol Hispanic and Asian smokers*" to increase its market share among young adult smokers.

***Empirical studies***

Altman et al. (1991) conducted a descriptive analysis of billboards by census neighborhood demographic characteristics during 1985-1987 in San Francisco. Overall, 19 percent of billboards featured ads for tobacco (and 13 percent for menthol cigarettes). Menthol cigarette billboards were more likely in African American (22 percent) and Hispanic (17 percent) neighborhoods than in Asian (10 percent) and white (11 percent) neighborhoods. Although no statistical analysis was undertaken, the rates appeared disproportionately lower for non-menthol cigarette billboards in African American (2 percent) neighborhoods, while being around half the rate in Hispanic (8 percent), Asian (4 percent) and white (6 percent) neighborhoods.

Two studies focused on magazine advertising were located. Landrine et al. (2005), in the same study described above in the section on targeting African Americans, Landrine et al. (2005) examined tobacco advertising in issues of Ebony, People magazine and People in Spanish between 1988 and 2002. In this study, ads for menthol brands were significantly more likely in the Spanish-language edition of People (35 percent of cigarette ads), compared to 17 percent of ads in the English language version of People magazine. A more recently published study reported on a descriptive analysis of cigarette ads in the English- and Spanish-language versions of Cosmopolitan and Glamour magazines from 1988 to 2002 (Fernandez et al. 2005). Despite these magazines having the same publisher, content, length and advertising policies, there were significantly more ads for menthol brands in the magazines for Spanish-speaking women (51.1 percent of cigarette ads) than in the versions for English-speaking women (28.3 percent of cigarette ads). In fact, magazines targeting Spanish speakers were 2.64 times more likely than the English language magazines to contain ads for menthol cigarettes. Sixty percent of the cigarette ads in the Hispanic versions were for Kool and Newport, compared to only 26 percent of the cigarette ads in the white magazine versions. Although this study was looked at just two women's magazines, it focused on popular titles. These studies both provide evidence of targeting of Hispanics through menthol magazine advertising.

The point of sale advertising study by Laws et al. (2002), described in a previous section, audited stores in Boston neighborhoods for tobacco advertising. They found 32.3 percent of all interior and exterior advertisements for menthol brands were in neighborhoods with the highest percentages of minority (African American and Hispanic) residents while 10 percent of all menthol cigarette ads were in neighborhoods with the lowest minority populations—a statistically significant difference. Another retail-focused study by Glanz et al. (2006) reported on an audit of tobacco advertising in 184 tobacco retail outlets in Hawaii in late 2002. Overall, advertisements for Kool menthol cigarettes were the most common of all tobacco ads identified, irrespective of whether ads were a straight count or were weighted by size. Kool also had the most outdoor ads using both outcomes. It had the largest number of indoor ads when a straight count was used, and was second to Marlboro when adjusted for size of ad. This retail advertising for Kool was thought to reflect the preference among Hawaiian youth for menthol cigarettes (especially Kool), which differs from youth preferences for Marlboro on the mainland (Appleyard et al. 2006; USDHHS USSG report 2004).

Summary. Comparatively fewer reviews and empirical studies examined whether menthol marketing has been targeted to racial/ethnic groups other than African Americans. Although no tobacco industry document reviews were available on the topic, all four empirical studies examining menthol and non-menthol advertising found a higher proportion of menthol ads out of all cigarette ads in Hispanic neighborhoods (2 studies)/magazines (2 studies), than in non-Hispanic white neighborhoods/magazines. A tobacco industry document review provided evidence that Asian Americans and Hawaiian/Pacific Islanders were targeted in menthol marketing. One empirical study showed a high prevalence of retail advertisements for Kool cigarettes in Hawaii.

**Does menthol marketing influence perceived taste and/or sensory experience of menthol cigarettes?**

Throughout TPSAC meetings, tobacco industry representatives consistently pointed to taste as being the main driver of preference for menthol cigarettes among menthol cigarette smokers (July 2010). However, taste is a complex perception, since it is the product of both flavor and other sensory attributes. Consumers can also be quite unclear as to what they mean by taste, often simply echoing descriptions given to them by tobacco branding, labeling and advertising (Pollay & Dewhirst 2002). Furthermore, there is evidence that consumers use elements of taste to infer the healthiness and other attributes of products. This is likely to be a natural human tendency, with some evolutionary advantages. For example, a key element of unpleasant taste is the perception of bitterness, thought likely to have evolved in animals to help them avoid eating plants and other foods containing toxins and other harmful chemicals.

This section is organized into two parts. First, it summarizes consumer research from other domains related to taste perception to document how branding and labeling can influence consumer taste perception and sensory evaluation. Subsequently, this section summarizes studies specifically pertaining to messages about cigarettes in general and menthol cigarettes in particular.

It should be noted that additional literature on the sensory experience of smoking menthol cigarettes compared to non-menthol cigarettes is summarized in chapters 3 and 6.

**Role of branding and labeling in taste perception and sensory evaluation**

Consumers have generally poor ability to discriminate between tastes, due in part to our taste buds' ability to detect only sweet, sour, bitter, salty and umami tastes. Multiple other senses are involved in taste perception, including smell, sound (when bitten or chewed) and touch (texture in the mouth and temperature) (Elder & Krishna 2009). Visual cues also contribute to the sense of taste by generating expectations about flavor. Evidence from the consumer science literature about the degree to which branding and labeling influence perceptions of the taste of food and drinks illustrates that taste perception is subjective and easily manipulated (Deliza & MacFie 1996). Use of branding, including use of color and descriptive names, results in an expectation or sensory halo effect, whereby the expectation halo influences how a person thinks a product might taste as well as taste perceptions and liking when the product is consumed.

There are several ways in which expectations might influence the sensory experience of products and their liking of the product (Deliza & MacFie 1996; Cardello 2007). One model predicts the existence of a contrast effect (or boomerang effect), which may occur if the consumer holds expectations that are vastly different from the eventual product performance. Under these circumstances, consumers who have very low (or very high) expectations about a product might be pleasantly surprised (or very disappointed) by the contrast when the product is actually consumed. However, contrast effects have rarely been observed in the literature, even when disconfirmation of expectation is arguably quite large (Cardello 2007). Another model, known as the assimilation model, predicts that evaluation of the product will change in the direction of expectations. In other words, an expectation can be a driver of sensory experience and liking. In studies where food and beverages have been used as test products, the vast majority of observed effects have been assimilation effects (Deliza & MacFie 1996; Cardello 2007).

For example, bitter coffee was appraised after sampling as tasting less bitter only among those consumers who were exposed beforehand to three advertisements asserting that the coffee was not bitter (Olson & Dover 1978). An early study found that a slice of turkey was rated more positively after tasting if consumers thought it was a popular brand rather than an unknown brand (Makens 1965). In a more recent study, people who were given an energy bar supposedly containing soy protein were more likely to rate it as 'grainy' and 'tasteless,' compared with identical bars that contained no mention of the word 'soy' (Wansink & Park 2002). In fact, neither bar contained soy. In another study in Illinois, evocative descriptive names of cafeteria meals (such as 'Succulent Italian Seafood Filet') led to meals being rated after consumption as more appealing, tastier and caloric, and eliciting more positive comments, than exactly the same meals with less descriptive names (such as 'Seafood Filet') (Wansink et al. 2005). Color and labeling influenced perceptions of otherwise identical M&M candies: brown M&Ms were rated as more 'chocolatey' than all other colors, and those labeled as *dark chocolate* were rated as more 'chocolatey' than those labeled *milk chocolate* (Shankar et al. 2009). Even children express the effects of branding on taste perception: a study of three to five year olds in California found that identical food products were appraised as tasting better when they were branded with McDonald's than when they were unbranded (Robinson et al 2007).

There is variability in the extent to which brand and label information influence evaluation of different types of products. For example, in another controlled cafeteria study, diet and health labels (e.g. , chocolate pudding vs. healthy chocolate pudding; pineapple soy muffins vs. diet pineapple soy muffins) improved the rated taste of desserts but not the rated taste of entrees (Wansink et al. 2004). In interpreting these findings, the investigators suggested that people might expect a dessert labeled as healthy or diet-related to not taste very good. When it tastes better than expected, it prompts an over-evaluation of taste ratings. By contrast, health labels had less ability to influence evaluation of the entrees offered, since they were already relatively healthy. This study suggests that for products that are less healthy, descriptive labels likely have greater capacity to promote positive taste evaluations.

In recent years, much progress has been made in understanding the neural basis of cognitive effects on taste and other sensory experiences. This research has used functional magnetic resonance imaging (fMRI) technology that measures blood flow in various regions of the brain in response to product consumption under varying conditions of expectation. In summary, these studies demonstrate that expectancies can change both the subjective evaluation of the product and the neural response to these products (Cardello 2007; Cardello & Wise 2008). For example, McClure et al. (2004) found that Coke was rated higher in a subjective taste test when consumed from a cup bearing the Coke logo than from an unmarked cup. Consistent with these subjective ratings, the study also found that the image of a Coke can presented prior to Coke tasting resulted in greater brain activity in the dorsolateral prefrontal cortex (DLPFC), hippocampus and midbrain, compared to unbranded Coke delivery (McClure et al 2004). This finding is important because the hippocampus and DLPFC have both been previously implicated in processing emotion and affect as it relates to behavior change. The investigators suggested that branding information biases preference decisions through the DLPFC, with the hippocampus engaged to recall the associated information (McClure et al 2004). In a more recent study, Nitschke et al. (2006) found that when people tasted a highly aversive (bitter) fluid, the level of activation in the bilateral taste cortex in the brain was reduced when they were told it would be only mildly aversive, compared to when they were told that it would be highly aversive. This misleading information also led to people rating the bitter fluid as less aversive than that same fluid when it was tasted following the truthful cue. Together, these studies imply that branding and labeling can lead people to hold more favorable expectations about a product, and these expectations influence brain functions in ways that result in an enhanced sensory experience.

The influence of branding on sensed experience when products are consumed is automatic, in that consumers are largely unaware of these processes. In part, this is likely to be because when consuming a product, consumers have limited time to make their evaluation and tend to rely on short-cuts – easily available information which is processed quickly and efficiently to assist their decision-making and guide their evaluation (also known as heuristic processing). Most consumers do not think that branding or labeling prior to tasting would change their sensed experience of products and are, in fact, unable to correctly predict the results of taste tests in which expectancies are manipulated in the ways described (e.g., Lee et al. 2006).

It is important to note that branding and labeling are not the only information available to form consumer expectations: the shared experiences and recommendations of others and one's own experience with the class of product to be tasted will also influence expectations and therefore one's subjective perceptions of taste. Individuals who have less experience with the class of products to be tasted and low involvement with the product tend to rely more on branding and labeling information (Deliza & McFie 1996; Cardello 2007).

Overall, this body of consumer sensory research suggests that a product that people may find unremarkable or even aversive, or that they know may be unhealthy, can be manipulated to be experienced as more pleasant by strengthening consumer's expectations that the product will offer a positive experience. Branding and labeling therefore have a critical role to play in raising consumer expectations about a product. As suggested by Cardello (2007), "*the opportunity exists to improve the acceptance of a product and its market share through creative marketing that establishes a positive image and expectation for a product. Here lies the heart of all advertising strategies aimed at improving product image*" (Cardello 2007, p.230). Those who have less experience with a class of products, including young people, may be especially vulnerable to the effects of marketing on product liking and sensory experience, and therefore, on its consequent influence upon product acceptance and use.

**Branding and labeling effects on subjective experience of cigarettes**

There is good evidence to show that branding and labeling modify the subjective perception of tobacco when it is consumed. Most of this research has been undertaken using cigarette packaging as the medium for branding. In a review of internal tobacco industry documents on tobacco packaging made public through litigation filed against major U.S. cigarette manufacturers, Wakefield et al. (2002) found that tobacco companies employed the concept of expectancy manipulation or 'sensation transfer' to assist them to design cigarette packaging. In the industry documents, the term 'sensation transfer' is used to refer to the phenomenon whereby brand elements on packaging create expectations of what the cigarette will be like when smoked—also referred to as the 'halo effect' of branding. Numerous tobacco industry studies were found whereby exactly the same cigarettes presented in different packs led consumers to evaluate them differently when they were smoked. Tobacco companies discovered that lighter colors on the pack promoted perceptions of lower cigarette strength. For example, identical cigarettes presented in blue packs were described after being smoked as 'too mild,' 'not easy drawing,' and 'burn too fast,' whereas when presented in a red pack, they were described as 'too strong' and 'harsher' (Wakefield et al. 2002).

A published empirical study randomly assigned 200 male and female smokers to smoke identical cigarettes that were branded either "April" or "Frontiersman" (Friedman & Dipple 1978). Female smokers who smoked the cigarettes with a feminine brand name rated all aspects of taste and enjoyment more favorably than the female smokers who tried the identical cigarettes with a masculine name. Similarly, male smokers favored the masculine brand, but the effect was less pronounced. In their industry document review on marketing imagery, Pollay & Dewhirst (2002) find that market researchers for the tobacco industry and its advertising agencies were not confident consumers knew what they were talking about when referring to 'taste' of a cigarette. As one document from 1975 detailed, *"[I]t is almost impossible to know if the taste smokers talk about is something which they, themselves, attribute to a cigarette or just a 'play-back' of some advertising messages."* (Marketing & Research Counselors Inc., cited in Pollay & Dewhirst 2002).

DiFranza et al. (2002) suggest that the process by which pack design communicates what consumers might expect from the cigarettes is subconscious. An R.J. Reynolds marketing department document indicated that "*on the first level a package serves to reinforce the brand's advertising in establishing a certain brand image or set of connotations, and in doing so it operates on a subconscious level. That is, the fact that it does this is not readily apparent to the consumer*" (Marketing Research Department 1969, cited in DiFranza et al. 2002). DiFranza et al. also note that the influence of pack design on the subjectively experienced qualities of the cigarette is of such a magnitude that when purely objective ratings of the cigarette qualities are desired, the test cigarettes are not branded (DiFranza et al. 2002). At the July 15, 2010 TPSAC meeting, tobacco industry representatives acknowledged that the presence of branding information does influence consumer evaluations of cigarettes when they are smoked (transcript p.183–185.) Thus, consumers' perceived taste and sensory evaluation of cigarettes are influenced not only by the product itself, but by related branding information, including color, pack design, and labeling.

In a review of tobacco industry documents, Wakefield et al. (2002) found that green colors in menthol packaging were predominantly used to influence expectations of menthol taste and sensory experience. For example, after smoking identical menthol cigarettes in a Philip Morris test, panelists consistently ascribed more menthol coolness to those presented in the darker of two shades of green, compared with the standard white paper cigarettes. There was no discernable difference between the lighter shade of green and white (Martin 1969, cited in Wakefield 2002). Another Philip Morris test found that the menthol brand Saratoga was perceived as having more menthol when the cigarette itself was wrapped with green paper than either production Saratoga, which had the same menthol level but was in a white wrapper, or the More brand, which had a higher menthol level but was in a brown wrapper—indicating that the green paper had an effect on the amount of menthol perceived (Howes 1976, cited in Wakefield 2002). A similar review of tobacco packaging by DiFranza et al. (2002) also commented on these sensation transfer tests, giving an example of an R.J. Reynolds pack test in which men strongly preferred the cigarette smoked when taken from an 'ice pack' over a cigarette smoked when taken from a 'green pack,' even though the cigarettes were identical in composition. The test concluded "*the cigarette related to the ice pack seems to be perceived as being* *a milder cigarette by the respondents. The ice on the ice pack connotes a cool/refreshing cigarette to the respondents*" (Magnus 1969, cited in DiFranza et al. 2002). Thus, manipulating elements of package design is sufficient to change smokers' expectations and evaluations of menthol cigarettes when they are smoked regardless of how much menthol they contain.

Consumer testing of cigarette packs was also undertaken to ensure that expectations of menthol content remained stable when lower tar and nicotine brand extensions were introduced. DiFranza et al. (2002) point to a consumer study by R.J. Reynolds in 1975 for three pack design options for Salem menthol cigarettes. Overall, the report concluded that "*the 'Green Line' design was the most effective in connoting lower tar and nicotine, especially among Salem smokers and female smokers. This package was also the least likely of the three alternatives to connote less menthol*" (Daniel 1975, cited in DiFranza et al 2002).

*Summary.* There is strong evidence from the general marketing literature that branding and labeling influence consumer expectations about a product and the subjective experience of product consumption. Tobacco company research and empirical studies demonstrate that elements of packaging such as branding, color and use of descriptive labels influence consumer beliefs about cigarettes, as well as the sensory experience when the product is smoked. There have been no peer-reviewed experimental studies specifically on the effects of menthol branding on consumer taste and sensory evaluation. However, consumer testing conducted by tobacco companies demonstrates that manipulation of elements of menthol cigarette packaging influences consumer sensory experiences of perceived coolness, amount of menthol, mildness, and overall preference. Thus, menthol packaging reflects the tobacco industry's knowledge about how color, labeling and other elements of branding will improve the consumer experience of the product's characterizing flavor.

## DO CONSUMERS PERCEIVE MENTHOL CIGARETTES AS SAFER OR LESS HARMFUL THAN NON-MENTHOL CIGARETTES?

As indicated in the section on Packaging, for both menthol and non-menthol cigarettes, different shades of the same color and the proportion of white space are commonly used to distinguish between variants of the same brand family. Two studies illustrate that color and other branding features influenced adults' and adolescents' (ages 12–17) expectations about perceived health risk (Hammond & Parkinson 2009); Hammond, Dockrell, Arnott, Lee & McNeill 2009). Using a paired comparison study design with one element of packaging manipulated, adult smokers rated cigarette packs that featured lighter colors, sensory descriptors (smooth, light, mild), and pictures of filters as delivering smoother taste, less tar and reduced health risks (Hammond & Parkinson 2009). In addition, beliefs about taste were positively correlated with beliefs about tar delivery and health risk. These studies did not include menthol packs, but they illustrate the extent to which branding elements about taste and sensory experience may contribute to beliefs that some cigarettes are less harmful than others. This section examines evidence from qualitative analyses of tobacco industry documents, qualitative focus group research, and survey research that examined consumer perceptions about the health benefits and relative risks of menthol cigarettes.

### Industry document reviews

Reviews of tobacco industry internal documents made public as a result of legal proceedings against tobacco companies provide a wealth of information about consumer perceptions of menthol cigarettes. The limitations of industry document reviews have been outlined in a previous section.

Giovino and colleagues (2004) identified tobacco industry documents in the late 1960s and 1970s which suggested that menthol smokers, including African Americans, perceived menthol cigarettes to be less hazardous than non-menthol cigarettes. Giovino et al. refer to a study from R.J. Reynolds called "Project Y" where menthol smokers were classified as 'more concerned' than smokers of non-menthol cigarettes. They point to a Philip Morris report on focus group discussions undertaken to assess the attitudes of African American smokers about menthol cigarettes, which states, "*There are indications that menthols tend to be considered generally better for one's health. That impression refers not only to the health of the respiratory tract, but the whole organism. The majority view is that menthols are 'less strong' than regular cigarettes, and that a cigarette which is 'less strong' is better for a person's health"* (Tibor Koeves, cited in Giovino et al. 2004). It was uncommon for consumers to openly assert that menthol cigarettes conferred an explicit health advantage; rather, that perception was more implicit and described indirectly by the use of terms such as strength, cooling, lower in tar, and less irritating. Consistent with the promises of early menthol marketing campaigns discussed in a prior section, tobacco industry documents indicated that individual sampling of menthol cigarettes often occurred because of a cold or sore throat, and during the winter months (Tibor Koeves, cited in Giovino et al. 2004), reflecting the higher seasonal rates of acute respiratory infection during this time. Another R.J. Reynolds document reported that African Americans were more likely than whites to believe menthol cigarettes were "*better when you have a cold,*" "*less likely to make you cough,*" and "*less irritating to the throat*" (R.J. Reynolds, cited in Giovino et al. 2004).

In their tobacco industry document review, Kreslake et al. NTR (2008) summarize some of the tobacco industry's extensive research to assess how product design influences consumer ratings of attributes of interest. They find that the way in which consumers describe product attributes differs between menthol and non-menthol smokers. For example, cigarette strength for menthol smokers is defined by menthol intensity, minty flavor and tobacco flavor, whereas for non-menthol smokers, it is defined by throat impact and throat scratch. Harshness is defined by amount of tobacco flavor for menthol smokers, but by throat impact, presence of a burnt or tarry flavor, and absence of added flavor for non-menthol smokers (Swaim, cited in Kreslake et al. NTR 2008). There was evidence in tobacco industry consumer research that consumers used menthol cigarettes as part of a purposive effort to change their smoking behavior in ways consistent with trying to reduce their exposure to the health harms. Kreslake et al. (NTR 2008) describe qualitative research with consumers undertaken by tobacco companies between 1972 and 1994. These studies suggest that some menthol smokers switched from non-menthols in an effort to maintain their smoking without the negative physical symptoms they attribute to non-menthols. These studies also describe consumers' use of menthols during a respiratory problem such as a cold, sore throat or bronchitis. Switching to menthols to try to cut down on the amount smoked was reported in qualitative interviews. Menthol cigarettes were perceived by consumers as milder than regular cigarettes, but were seen as distinct from 'light' cigarettes because they were viewed as not being compromised by the higher filter ventilation. A report by Roper (cited in Kreslake NTR 2008) on smokers of 'low tar' cigarettes concluded that "*menthol seems to compensate or make up for both few cigarettes and light cigarettes"* by providing *"an extra something.*" Kreslake et al. (NTR 2008) conclude that smokers who may otherwise quit because of the perceived harshness and health effects of 'higher tar' cigarettes, seek out menthol cigarettes for their 'substitute sensation' as they move to what they perceive is a lower tar cigarette with its associated implicit health reassurance. Tobacco industry document reviews on the role of menthol cigarettes in influencing quitting beliefs and intentions are discussed more fully in chapter 6 in the section on smoking cessation.

Anderson (in press) also analyzed industry documents on consumer perceptions of menthol cigarettes up to the mid 1990s. Consistent with Kreslake et al. NTR (2008) and Giovino (2004), Anderson also concluded that consumers view menthol cigarettes as safer, or less harmful, than non-menthol or full-flavor cigarettes. She notes that menthol smokers sometimes identify this perception explicitly (directly) and sometimes implicitly (indirectly), through the use of terms that suggest improved safety or health benefits, such as 'light,' 'mild,' 'cooling' or 'soothing.' For example, she cites an American Tobacco focus group study, which observed that "*there were indications that the menthol smoker subconsciously perceived menthol cigarettes as being healthier. There was somewhat of a 'health image' associated with menthol, related to its masking of the tobacco taste and its association with medicine, colds and sore throats*" (American Tobacco, cited in Anderson in press). Anderson found that menthol cigarettes have been marketed as, and are often perceived by consumers to be, milder and less irritating than regular cigarettes and therefore less of a health threat, in the same way that light/low tar cigarettes are mistakenly perceived to be safer. She concludes that menthol cigarettes provide psychological reassurance to consumers without providing any real health protection. This is exemplified in an R.J. Reynolds analysis of potential for share growth of menthol in 1997: *"[t]he health concern was perhaps the primary motive for switching to menthol in the first place. In the hierarchy of product benefits/attributes desired by menthol filter smokers, throat concerns rank just behind generic taste and satisfaction*" (RJR, cited in Anderson in press).

Klausner's (in press) tobacco industry document review was consistent with the findings of these other reviews in concluding that some young people smoke menthol cigarettes because they perceive them to be less harmful than non-menthol cigarettes, a notion they point out was encouraged through menthol advertising. Documents referred to young smokers choosing menthol cigarettes because they found the menthol "*less harmful*" or "*moving away from the problem [of smoking a harmful product]*" and "*a guilt-reducing mechanism…it manages in some small measure to subtly disguise the sin*" (cited in Klausner, in press). Klausner also notes that some youth use menthols for the first time when they have a sore throat or a cold because they perceive them to be less irritating than non-menthols. For example, a British American Tobacco study from 1982 found some smokers "*ascrib[e] medicinal properties to the mentholation*" and believe that "*menthols are somehow less intrusive or even less harmful than regular cigarettes.*"

**Empirical and qualitative studies**

The White Paper by Rising & Alexander (2010) found no published empirical studies of youth beliefs about of menthol cigarettes. Studies of adults' beliefs about of menthol cigarettes are discussed below. After first considering contextual and methodological interpretation issues, this section presents studies grouped by population surveys, clinic surveys, and focus group studies.

Surveys that compared menthol and non-menthol smokers' beliefs about the overall harm of smoking or disease risks of smoking (referred to in Lorillard's submission, July 2010) were not reviewed in this chapter. These surveys assessed the perceived harm or risk from smoking cigarettes, but not menthol cigarettes in particular. Over the years, a growing proportion of smokers agree that cigarette smoking is harmful (e.g., NSDUH surveys), as might be expected from the considerable investment in media campaigns about this important public health concern. Menthol smokers differ from non-menthol smokers on many demographic and psychosocial traits that would influence their beliefs about the harms of smoking. Comparing the beliefs about smoking for menthol and non-menthol smokers does not inform the research question about the perceived harm of menthol cigarettes in relation to non-menthol cigarettes.

Research about the relative harm of menthol cigarettes must be interpreted within the context of increased mass media education about the risks of smoking. During the 1990s, several states implemented tobacco education campaigns and after the MSA many more state-funded campaigns publicized the serious health harms of smoking and encouraged smokers to quit (NCI 2008). Over the past decade, a national media campaign from the American Legacy Foundation (Legacy) also broadcast messages about the misleading and deceptive practices of tobacco companies. Another Legacy media campaign emphasized the difficulty of quitting smoking and encouraged smokers to seek help. Media coverage about the deceptive marketing of "light" and "low tar" cigarettes is also relevant. A federal court order in 2006 prohibited the defendant tobacco companies from stating or implying any health benefits of a brand of cigarettes through the use of misleading terms such as "light," "mild," and "low tar." The FDA implemented a ban on these terms in the marketing and sale of cigarettes in June 2010. During the past decade, the public has been exposed to ongoing news coverage and media education that refutes tobacco marketing claims that some cigarettes are less harmful than others.

Against this backdrop it is increasingly unlikely that consumers would identify <u>any</u> cigarettes as offering explicit health benefits. In addition, questions that ask respondents about comparative risks are likely to elicit responses that different types of cigarettes are similarly risky. However, even in a population acutely aware of the harms of smoking, some studies reveal consumer perceptions that some cigarettes are safer than others (Hammond & Parkinson 2009; Hammond et al. 2010). When socially desirable responding is likely, studies that require consumers to choose between two or more products that differ on specific dimensions of interest are more sensitive indicators of consumer beliefs. Such studies typically compare two or more products with one element manipulated, or ask respondents to rank order products along particular dimensions. These kinds of comparative assessments are routinely used in consumer research, including in tobacco company consumer product testing, and in the cigarette pack testing studies by Hammond and colleagues (Hammond & Parkinson 2009; Hammond et al. 2010). To date, no published studies have used these methods to compare consumer perceptions of menthol and non-menthol cigarettes. However, reports from qualitative methods that permit more in-depth and indirect assessments of consumer beliefs about menthol cigarettes are included in this review. Assessment of implicit health benefits are particularly revealing, including aspects of taste and sensory experience, such as cooling, soothing, smoothness, mildness, low nicotine, lower strength, easing uncomfortable physical symptoms, or attributes such naturalness. As indicated earlier, smokers interpret these kinds of attributes to imply reduced harm (Pollay & Dewhirst 2002; Wakefield et al. 2002; DiFranza et al. 2002; Hammond & Parkinson 2009; Paek et al. 2010).

**Population-based surveys**

Two secondary analyses examined adults' perceptions of the explicit benefits or harms/risks of menthol cigarettes. Davis et al. (2010) examined responses of 4,556 adults to questions about menthol cigarettes from the HealthStyles survey that was mailed to a national consumer panel in 2009. The survey asked respondents "*Do you believe menthol cigarettes, such as Newport, Kool, Marlboro Menthol, Camel Menthol have beneficial health effects?*" Excluding 250 respondents who did not know what menthol cigarettes were or provided no answer, 76.8 percent of respondents (and 81.2 percent of smokers) believed menthol cigarettes had no health benefits, 18.9 percent (14.7 percent of smokers) did not know whether they did or not, and 4.3 percent (4.2 percent of smokers) thought they did have health benefits. African Americans (9.0 percent), those with up to high school education (8.6 percent) and those with annual incomes less than $25,000 (8.0 percent) were more likely to believe that menthol cigarettes had health benefits. However, there were no differences by age group.

The HealthStyles survey also asked whether "*menthol cigarettes such as Newport, Kool, Marlboro Menthol, Camel Menthol are: more harmful to my health than non-menthol/regular cigarettes; just as harmful to my health as non-menthol/regular cigarettes; less harmful to my health than non-menthol cigarettes or; I don't know*." The 248 respondents who did not know what menthol cigarettes were or gave no answer were excluded. Of the remaining respondents, 45.8 percent perceived menthol to be just as harmful as non-menthol cigarettes to their health, 40.9 percent did not know if menthol cigarettes were more or less harmful, 12.6 percent thought menthol cigarettes were more harmful and 0.6 percent, less harmful. Former smokers were more likely than never smokers to state that menthol cigarettes were more harmful (15.9 percent vs. 10.3 percent), but the comparison for current smokers (14.9 percent) was not significant. African Americans were more likely than whites to state that they did not know whether menthol cigarettes are more or less harmful than non-menthol cigarettes, but no interactions with smoking status were tested. Differences by age group were not reported as being significant. Although the survey achieved a 65 percent response rate, which is acceptable for a mailed questionnaire, the study was limited by the fact that the sampling frame was a pre-existing national panel that may not be representative of the national population. Also, no information was available about respondents' past or current use of menthol cigarettes. Odds ratios that compared beliefs by demographics were unadjusted, so the associations could be confounded.

Around 13 percent responded that menthol cigarettes were more harmful to health, but it was difficult to know if a perception of more harm to health might be due to menthol cigarettes being perceived to be more addictive or harder to quit. The survey did ask these two additional questions, and while again a majority (55 percent) responded that it was equally easy to get hooked on menthol and non-menthol cigarettes, or that they didn't know, 24.2 percent thought menthol cigarettes were more addictive. Similarly, while 82 percent thought both types of cigarettes were equally hard to quit, 12.1 percent thought menthols were harder to quit than non-menthols. However, the study did not explore the relationships between perceived harm and these variables.

Wackowski et al. (2010) examined data from a 2005 telephone survey of New Jersey adults, of whom 17.4 percent were smokers and 40.4 percent of smokers were menthol cigarette smokers (Wackowski et al. 2010). Smokers were asked "*compared to regular cigarettes, how risky do you think the following products are? Somewhat less, about the same, or somewhat more risky?"* Menthol cigarettes were included on a list of eight tobacco products (e.g., cigars, kreteks, bidis and light, herbal and flavored cigarettes). Question order was rotated. Overall, 70.1 percent of respondents reported menthol cigarettes posed the same risk as non-menthol cigarettes, 25.9 percent (and 30.2 percent of menthol smokers) reported that menthol cigarettes posed somewhat more risk, and 4 percent reported that menthol cigarettes posed somewhat less risk. Among menthol smokers specifically, 35.2 percent of African Americans and 46.3 percent of young adults (ages 18 to 24) believed menthol cigarettes posed somewhat more risk than non-menthol cigarettes. Independent of other demographics, young adult smokers were significantly more likely than the referent group of older smokers (age 65 or older) to believe that menthol cigarettes were somewhat more risky than regular cigarettes. Among menthol smokers, 46.3 percent of 18–24 year olds indicated menthol cigarettes were somewhat more risky than regular cigarettes, but the comparable responses for older menthol smokers were not reported.

A limitation of this study was that the response rate was 20.7 percent and the sample was sourced from only one US state. The study contained only one item about explicit health benefits of menthol cigarettes, and the authors pointed out that it is unknown how respondents interpreted the meaning of "somewhat less risky" and "somewhat more risky" than regular cigarettes. The authors speculated that the perceived ease of inhalation permitted by menthol may lead smokers to inhale more deeply and although this is interpreted as a benefit, it may also partly explain why menthols are perceived to be more risky. In addition, as for the Davis et al. (2010) survey, an alternative interpretation of "more risky" could be that menthol cigarettes were perceived as being more addictive and/or difficult to quit.

Given the aforementioned contextual factors, it is unsurprising that the vast majority of respondents attributed no explicit health benefits to menthol cigarettes and a small minority thought that menthol cigarettes were different than non-menthol cigarettes in explicit harms to health.

Two studies examined data from the same survey about perceptions of menthol cigarettes among African American smokers. Allen et al. (2010) developed a questionnaire based on focus groups with

African Americans. Items were also informed by the Castro (2004) literature review of biological, social, and cultural influences on the use of menthol cigarettes among African Americans and Hispanics. She cited examples of culturally relevant beliefs about the medicinal properties of menthol, including ingesting a menthol product (Vicks VapoRub) to treat congestion and colds. Castro concluded that health-related beliefs about menthol shared by lower-income African Americans and Hispanics are consistent with a view of menthol cigarettes as less toxic and addictive than regular cigarettes. The questionnaire developed and used in the Allen et al. study contained five multi-item scales, two of which assessed medicinal benefits and relative harm. The Medicinal Effects scale included statements that menthols are better than non-menthols for a sore throat, help to loosen up a stuffed up nose, help to cool a fever, and ease asthma problems; the Less Harmful scale included statements that menthol cigarettes contain fewer chemical additives, less nicotine, are less harmful and more natural than non-menthols. In other words, the Less Harmful scale was mostly comprised of items that assessed implicit harm. Another scale measured positive evaluations about the taste, cooling sensation and smell of menthols (Taste/Sensation). The remaining two scales measured the extent to which respondents endorsed beliefs that menthol cigarettes present an African American or stylish image (Image) and beliefs about menthol being frequently smoked by African Americans now and in the past (Tradition).

Allen et al (2010) surveyed 720 smokers in Los Angeles County who were recruited via street intercept methods from regions with high percentages of African Americans and interviewed between late 2006 and early 2007. Respondents were categorized as exclusively menthol smokers (57 percent), exclusively non-menthol smokers (15 percent), or smokers of both cigarette types (28 percent). Scale scores were derived from item responses to a 4-point scale with higher numbers indicating stronger agreement. Analyses compared scale scores for the three groups of smokers, adjusting for age, gender, education, and cigarettes per day. The three groups of smokers were equally likely to endorse the Image and Tradition scales. On the Taste/Sensation scale, menthol-only smokers scored higher than smokers of both types, who scored higher than non-menthol smokers. It was noteworthy that the scale scores for Taste/Sensation were positively correlated with scores for Medicinal Effects and Less Harmful. This finding is consistent with consumer research undertaken by tobacco companies, and with the findings of Hammond & Parkinson (2009), indicating that the concepts of taste, sensory experience and harm are related in the minds of consumers.

Compared to those who smoked exclusively non-menthols, menthol-only smokers and those who smoked both cigarette types had significantly higher scores on the Medicinal Effects and Less Harmful scales. Older participants and those with less education were also more likely to hold these beliefs. Compared to those who smoked exclusively non-menthols, smokers of both cigarette types had higher scores on the Medicinal Effects but not on the Less Harmful scale. The pattern of results suggests that menthol smokers were more likely than non-menthol smokers to perceive that menthol cigarettes provide medicinal benefits and reduced implicit health harms. Smokers ages 40 and older and less educated smokers were more likely to endorse these beliefs.

Unger and colleagues (2010) undertook a more detailed analysis of these data, including a larger set of covariates, such as perceived discrimination, depressive symptoms, anxiety symptoms, sensation-seeking, stress and reported frequency of exposure to menthol marketing. This ancillary analysis found Taste/Sensation to account for just over half the variance between menthol and non-menthol smoker subgroups. When excluded in order to evaluate the influence of other variables, it was found that compared with non-menthol smokers and adjusting for many covariates, those who smoked any menthol cigarettes were more likely to perceive medicinal benefits than others. Additional subgroup analysis showed that this was particularly the case among males ages 40 and older, although it should be noted that this subgroup analysis had low power to detect effects, with an approximate sample size of only 25 people who were regular smokers in each age/gender subgroup.

**Surveys of smokers seeking cessation treatment**

Hymowitz et al. (1995) administered a questionnaire to menthol cigarette smokers attending a smoking cessation program in New Jersey. Of 213 menthol smokers, 97 percent indicated menthol cigarettes "taste better", 61 percent thought they were "more soothing to my throat" than non-menthol cigarettes, and 51 percent indicated that "I can inhale menthol cigarettes more easily than regular cigarettes." Although menthol smokers endorsed these implicit health benefits, few of them (8 percent) reported that menthol cigarettes "are better for you than regular non-menthol cigarettes." There were few significant differences between African Americans and whites, and the small sample size limited these subgroup comparisons. Another limitation is that a convenience sample of smokers who are sufficiently motivated to quit to seek formal smoking cessation treatment likely differs from the general population of smokers. Despite the study limitations, it is notable that its findings are consistent with conclusions from reviews of tobacco company internal documents that consumers hold beliefs that menthol cigarettes offer a form of implicit or apparent health protection. This especially applies to menthol's throat-soothing qualities when inhaled in tobacco smoke, and the reduction of sensory barriers to inhaling the smoke. By comparison, few menthol smokers endorsed the statement that menthol cigarettes were explicitly healthier/safer than non-menthols.

Bansal et al. (2004) assessed smokers' beliefs about menthol cigarettes as part of an educational intervention about cigarette products. Of the 982 smokers who agreed to enroll in a cessation trial, 34.2 percent smoked menthol cigarettes and the sample was predominantly non-Hispanic white (72.8 percent). Prior to randomization to different educational conditions, participants rated their agreement with six statements about menthol cigarettes: "give you less tar than regular cigarettes;" "are cleaner than regular cigarettes;" "are safer than regular cigarettes;" "are easier to quit smoking than regular cigarettes;" "are smoother on your throat than regular cigarettes" and "feel easier on your chest than regular cigarettes." Respondents who agreed or disagreed also indicated the strength of their belief (somewhat or strongly). Respondents who were uncertain were assigned a value of 2 on a scale that ranged from 0 to 4. Higher scores reflected greater disagreement with beliefs that menthol cigarettes are less harmful than regular cigarettes. A mean of 3.28 out of 4 (standard deviation was not reported) suggests that on average, smokers enrolled in a cessation trial disagreed that menthol cigarettes were less harmful than regular cigarettes. The high level of internal consistency of the scale suggests that ratings about sensory experience (smoother and easier on the chest) were positively correlated with other items about relative harm. In addition, lower scores were observed for the two items about sensory experience, indicating more agreement with these items than others. In this respect, the pattern of findings was consistent with other studies (Allen et al. 2010; Hymowitz et al. 1994). However, differences between item responses were not tested and separate scores for menthol and non-menthol smokers were not reported. As noted previously, a convenience sample of smokers seeking cessation treatment likely holds different perceptions of menthol cigarettes than the larger population of smokers.

**Focus groups**

Richter and her colleagues undertook two studies of health risk perceptions of menthol cigarettes. In 2002, Richter et al. (2006) conducted 16 focus groups in Dallas and Chattanooga with young adult smokers (ages 18–22 years) who had tried or currently used non-traditional tobacco products (NTPs), such as bidis, shisha, and herbal cigarettes. All participants rated light, regular and menthol cigarettes against each other and against each of the NTPs on a six-point scale from 'much safer' to 'much more harmful.' Non-Hispanic whites (the largest participant group), perceived menthol cigarettes as less harmful than regular cigarettes and more harmful than light cigarettes. Among Hispanics, light cigarettes were consistently rated as safer than regular cigarettes, but there was inconsistency in comparative menthol ratings. Among African Americans, light cigarettes were rated as either the same or safer than regular and menthol cigarettes, whereas menthol and regular cigarettes were perceived to pose the same risk. A strength of this study was repeated use of the rating exercise in all groups. A limitation was that results were not presented overall, but rather by race/ethnicity and college/non-college attendance, which limited the stability of estimates. It was noteworthy that the group with the largest sample size (non-Hispanic whites) more clearly rated menthol cigarettes as being in between light and regular cigarettes on the harmfulness scale.

In 2005, Richter et al. (2008) conducted six focus groups with African American menthol smokers aged 45 to 64 years old in Atlanta. Among the main discussion themes was a belief that smoking menthol cigarettes leads to fewer negative health effects. Taste was described as a prime reason for smoking menthol cigarettes, although this appeared to be closely linked to perceptions of harm. Menthol cigarettes were commonly described as being 'refreshing,' 'soothing' or 'smooth,' while non-menthols were 'strong' or 'harsh.' As one participant explained: "*A regular cigarette is too strong. If I smoke that, I mean, I just start coughing because it's too strong. Menthol is lighter*." Some participants described unpleasant reactions to smoking non-menthol cigarettes in comparison with menthol cigarettes. "*I can't smoke non-menthol cigarettes because I wind up with a headache and a dry mouth. It dries my tongue out. And a menthol cigarette doesn't. I can enjoy it, especially after I eat,*" one said. Another person commented: "*It'll hurt your head and hurt your chest if you try to smoke a non-menthol.*" Participants in a group asked to rank brands from most to least dangerous placed full flavor menthol brands in an intermediate position between brands described as 'light' or 'slim,' which were perceived to be least dangerous, and full flavor non-menthol brands, perceived to be most dangerous. Two additional themes that were related to each other were that non-menthol smokers were considered to be hard-core smokers with less interest in quitting, and that switching to non-menthol cigarettes was perceived as a strategy that menthol smokers used to try to quit smoking. Participants' preference for menthol cigarettes were strong and non-menthol cigarettes were viewed as a cessation aid. Some described switching to non-menthols as a strategy to help them quit, whereas others indicated that switching to menthol delayed quitting. "*The reason I started smoking menthol was because the regulars were so strong and instead of me quitting, I was trying to find some means to get around that, so I went to menthol*," one participant said.

Limitations of focus groups are that individuals may be influenced by other group participants, and skilled group moderation is required to ensure that dominant views do not skew responses of other participants. Focus groups are unlikely to be representative of the population from which participants are drawn, but are designed to capture a range of views and permit in-depth discussion of concepts, which requires synthesis using careful qualitative analysis. Conducting focus groups in multiple cities is a strength of the research reported here. In addition, the results from the comparative ranking task and the qualitative findings are consistent with tobacco industry consumer research on perceptions of menthol cigarettes.

*Summary*. Taking the tobacco industry's document research and empirical studies into account, the evidence suggests that consumers perceive that menthol cigarettes offer some form of implicit health protection or medicinal benefit that non-menthol cigarettes do not provide. This was reported in all four industry document reviews. These reviews also pointed to consumer beliefs about explicit health benefits of menthol cigarettes, reflecting early advertising messages that more explicitly promoted the health benefits of menthol cigarettes (see messaging section). Evidence from focus groups and several surveys also suggested that consumers perceive implicit health benefits of menthol cigarettes (Hymowitz et al. 1994; Richter et al. 2006; Richter et al. 2008; Allen et al. 2010; Unger et al. 2010). Two studies that used multi-item scales (Allen et al. 2010; Bansal et al. 2004) also found positive correlations between beliefs about taste/sensation, medicinal benefits, and relative harm, as was found or suggested in other studies (Pollay & Dewhirst 2002; Wakefield et al. 2002; DiFranza et al. 2002; Hammond & Parkinson 2009).

In studies that addressed both implicit and explicit health benefits, smokers were more likely to endorse the former than the latter (Hymowitz et al. 1994; Bansal et al. 2004). Indeed, few smokers endorsed any statement that menthol cigarettes are explicitly safer or less harmful than non-menthol cigarettes (Bansal et al. 2004; Davis et al. 2010; Hymowitz et al. 1994; Wackowski et al. 2010). In the large population-based surveys, some smokers reported that menthol cigarettes were more harmful/risky than non-menthol cigarettes (Davis et al. 2010; Wackowski et al. 2010), but the meaning of this response is difficult to interpret.

Notably, much of this research focused predominantly or exclusively on African American smokers (Allen et al. 2010; Unger et al. 2010; Richter et al. 2008, Hymowitz 1994), which raises the question of whether these consumers are substantially more likely than others to endorse implicit health benefits of menthol cigarettes. The two survey studies of African Americans (Allen et al. 2010; Unger et al. 2010), together with the focus group study of older African Americans (Richter et al. 2008), and the earlier clinic population survey of Hymowitz et al. (1994) which included a large proportion of African Americans, all found the respondents to hold beliefs about the medicinal benefits of menthol cigarettes and other implicit health benefits pertaining to menthol cigarette strength, constituents, smoothness and ease of inhalation. These studies asked about implicit health benefits in addition to explicit health harms or risks, and employed research methods that entailed the completion of multi-item scales, required respondents to make comparative rather than absolute judgments about products, or used qualitative techniques. The studies that included sample sizes large enough to compare African Americans with other racial/ethnic groups did not use these methods.

**EVIDENCE SYNTHESIS**

Chapter 5 set out to answer six questions relating to the marketing and consumer perception of menthol cigarettes. The responses to those questions are provided below. These answers assisted TPSAC in addressing the nine overarching questions listed and discussed in chapter 1 that are the subject of this report. Specifically, these responses address TPSAC's population-based questions: *Does tobacco company marketing of menthol cigarettes increase the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?* TPSAC considered this information, along with the other evidence gathered, reviewed and synthesized in this report, to assess the overall public health impact of menthol cigarettes and to make its recommendations to the FDA.

**How is menthol marketing different from and similar to non-menthol marketing, in terms of product, place, price, promotion and packaging?**

The evidence is sufficient to conclude that menthol cigarettes are marketed in similar ways to non-menthol cigarettes, in that the same general marketing principles are employed.

However, there may be an important difference in practice in relation to retail marketing and pricing. Overall, menthol cigarettes are slightly more expensive than non-menthol cigarettes, although a larger proportion of retail sales for menthol than non-menthol cigarettes are promoted. More menthol smokers than non-menthol smokers take advantage of such promotions and this difference was greater for African American smokers. There was limited information available on pricing and promotions by neighborhood demographics, in relation to tobacco tax increases, and in relation to brands. This precluded a more detailed understanding of how the tobacco industry and consumers use price promotions of menthol vs non-menthol brands to undermine the potential benefits of tobacco tax increases and other tobacco control policies on quitting, particularly among key population subgroups. While the prevalence of smoking has declined in the past several years, the proportion of smokers who prefer menthol cigarettes has increased. Thus, the rate of decline in smoking prevalence is slower for menthol than for non-menthol smokers. This phenomenon has coincided with a substantially increased emphasis on tobacco marketing and price promotions at the point of sale. Existing evidence is insufficient to conclude that retail marketing practices may be responsible for recent increases in the proportion of smokers who smoke menthol cigarettes. Research is needed to examine the relationship between the move towards retail-based marketing, especially price promotions, and the increase in the proportion of smokers who smoke menthol cigarettes.

**What health reassurance messages were/are used in menthol marketing messages?**

The evidence is sufficient to conclude that menthol cigarettes have been and continue to be marketed with a set of associated branding elements and labels that connote health benefits. These originally included claims of explicit medicinal benefits such as soothing a sore throat or clearing a blocked nose, but moved over time towards more implied health benefits, with the use of powerful images of coolness and refreshment, the use of phrases and labels stressing sensory experience such as 'refreshing' and 'smooth,' and the use of the color green which is associated with nature and healthiness. While contemporary tobacco marketing efforts have been constrained by legislation that restricts advertising in traditional media, the powerful advertising messages used in the past are reinforced and continued by the ongoing use of menthol brand names and menthol marketing messages such as 'smooth' and 'fresh' that are implicitly linked to health benefits.

**What other messages were/are conveyed to potential consumers by menthol marketing messages?**

The evidence is sufficient to conclude that other menthol marketing messages feature youthful imagery and themes to appeal to youthful audiences, as well as socially and culturally relevant messages about in-group identity to appeal to different market segments. Different in-group identities are emphasized in marketing for different brand families, so there is no single brand image that signifies a menthol smoker.

**Who are the target populations for menthol marketing? Is there evidence to show that youth, women, and specific racial/ethnic groups were targeted?**

Identification of primary target groups for marketing is basic marketing practice. NCI's Monograph 19 provides abundant evidence of targeting of youth, young adults, racial/ethnic groups, women and other population subgroups in cigarette marketing (NCI 2008).

Evidence presented in this Chapter and chapters 4 and 6 indicates that menthol smoking is higher among youth and young adults, compared with older adults. There is sufficient evidence to conclude that menthol cigarettes are marketed disproportionately to younger smokers. There is evidence from tobacco industry documents that the tobacco industry designed menthol cigarettes with lower menthol yields, with an awareness that, at these lower menthol levels, the sensory effects of menthol reduce the harshness of cigarettes for new smokers. In addition to messages that implied health reassurance, menthol cigarette marketing has promoted a more youthful brand image than for non-menthol cigarettes, and has emphasized the role of menthol cigarettes in peer group acceptance.

Chapter 4 demonstrates that menthol use is higher among women than men. While there is evidence from industry document reviews and empirical studies that women have been targets of tailored menthol marketing efforts, there is insufficient evidence that menthol marketing was targeted proportionately more to women per se than non-menthol marketing.

The evidence is sufficient to conclude that menthol cigarettes are disproportionately marketed per capita to African Americans. African Americans have been the subjects of specifically tailored menthol marketing strategies and messages. Billboard advertising and point-of-sale advertising for menthol cigarettes has been over-represented in neighborhoods with a high percentage of African Americans and in magazines with high African American readership, and more so than non-menthol cigarette advertising. Consistent with these targeted marketing efforts, menthol cigarettes are disproportionately smoked by African American smokers. The evidence is sufficient to conclude that it is at least as likely as not that menthol cigarettes have also been disproportionately marketed to Hispanics. Menthol smoking is higher in Hispanics than in non-Hispanic whites. Although Asian Americans, Hawaiian/Pacific Islanders and females have been the subjects of tailored menthol marketing messages and menthol smoking is higher in all these population subgroups, there is insufficient evidence to conclude that they have been proportionately more targeted by menthol than non-menthol advertising.

**Does menthol marketing influence perceived taste and/or sensory experience of menthol cigarettes?**

The evidence is sufficient to conclude that menthol branding and messaging influences the perceived sensory experience of menthol cigarettes, contributing to consumer's overall subjective evaluation and liking of the product.

**Do consumers perceive menthol cigarettes as safer or less harmful than non-menthol cigarettes?**

The evidence is sufficient to conclude that, consistent with marketing claims, consumers hold beliefs about the medicinal benefits of menthol and beliefs about other implicit health benefits, and that this is especially the case among African Americans. However, in the context of widespread public education about the health harms of tobacco use, it is uncommon to state an explicit belief that menthol cigarettes are safer or less harmful than non-menthol cigarettes.

## CHAPTER 6: EFFECTS OF MENTHOL CIGARETTES ON INITIATION, ADDICTION AND CESSATION

### INTRODUCTION

The Family Smoking Prevention and Tobacco Control Act charges the Tobacco Products Scientific Advisory Committee (TPSAC) with developing a report and recommendations that address " the impact of the use of menthol in cigarettes on the public health including such use among children, African Americans, Hispanics, and other racial and ethnic minorities." This chapter is concerned with the effects of menthol cigarettes on smoking initiation, addiction and cessation. Put another way, do menthol cigarettes—when compared to non-menthol cigarettes—make it more or less likely that someone will start smoking, become addicted, or quit?

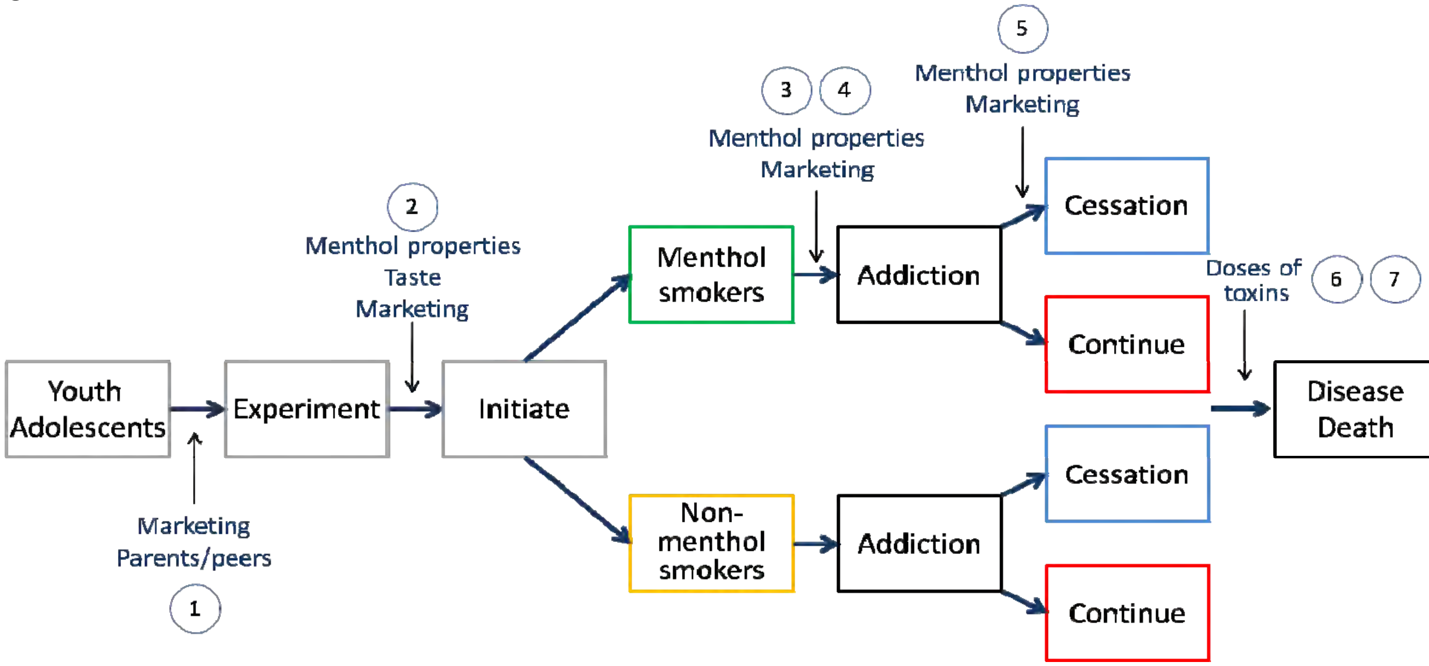
This chapter builds on information presented in previous chapters about the influence of menthol cigarette marketing (chapter 5) and the physiological effects of menthol cigarette smoking, including the cooling sensation that menthol imparts and the ability of menthol to counter the harshness of nicotine (chapter 3). Chapter 4 explored the broad patterns and trends of menthol cigarette use by age, race, gender and income. In order for TPSAC to execute its charge, it also addressed the impact of menthol cigarettes on smoking initiation, addiction and cessation.

The first chapter of this report presented nine questions relevant to TPSAC's consideration of the public health impact of menthol cigarettes; seven are related to individual menthol cigarette smokers and two are related to the population effects of smoking menthol cigarettes. The information and analysis provided in this chapter are relevant to five of the seven questions that relate to individual cigarette smokers. They are:

- Does availability of menthol cigarettes increase the likelihood of experimentation?
- Does availability of menthol cigarettes increase the likelihood of becoming a regular smoker?
- Does inclusion of menthol in cigarette increase the likelihood of the smoker becoming addicted?
- Does inclusion of menthol in cigarettes increase the degree of addiction of the smoker?
- Are smokers of menthol cigarettes less likely to quit successfully than smokers of non-menthol cigarettes?

In accordance with the public health model presented in chapter 1 (see Figure 1, below), this chapter is divided into three sections: (1) experimentation and initiation, (2) addiction, and (3) cessation. As indicated in Figure 1, several factors may moderate each stage within this model. The marketing of menthol cigarettes and their availability from peers or family members may influence experimentation with menthol cigarettes. Experimentation—and the continued influences of peers and marketing, coupled with the sensory effects of menthol cigarette smoking—may lead to smoking initiation. Nicotine pharmacokinetics, the sensory properties of menthol cigarettes (e.g., a cooling sensation) and beliefs transmitted by marketing messages or social groups about menthol cigarettes (e.g., relative safety), may promote regular smoking and eventually addiction. The same biological, social and commercial factors that lead to initiation and addiction may also affect the increased or decreased likelihood of menthol cigarette smoking cessation compared to non-menthol cigarettes.

Figure 1




**METHODS**

Chapter 2 provided the general framework for this report and the TPSAC's approach to gathering, reviewing and weighing the evidence. Using this framework, chapter 6 draws on sources that provide information about menthol cigarette smoking experimentation, initiation, addiction and cessation, or provide necessary background information. Four sources of documents were examined: (a) peer-reviewed articles obtained from the search conducted by the FDA and from additional studies identified from these articles; (b) white papers and secondary analysis of existing datasets either written or commissioned by the FDA; (c) tobacco company presentations and written submissions; and (d) public comments that provided relevant evidence.

**EXPERIMENTATION AND INITIATION**

The experimentation and initiation section covers five topics: (1) the rates of menthol vs. non-menthol cigarette use among youth and young adults compared to older adults; (2) the rates of menthol vs. non-menthol cigarette use in recent initiators and established smokers; (3) the age of cigarette initiation of menthol vs. non-menthol cigarette smokers; (4) switching between and among menthol and non-menthol cigarette smokers; and (5) the characteristics of menthol cigarettes that may enhance the abuse liability or appeal of the product (sensory experience, reduction of harshness, cooling sensation, beliefs about relative safety). This chapter draws on population-level information in chapter 4 in addition to multiple datasets, surveys and analyses that provide in-depth information about the experimentation and initiation of menthol cigarette smoking. This chapter also draws on information about the sensory experience of smoking menthol cigarettes presented in chapter 3.

**Patterns of smoking menthol cigarettes in adolescents and young adult smokers**

***Age gradient of proportion of menthol cigarette use across the age spectrum***

Most smokers start smoking during adolescence before the legal age for purchasing cigarettes or during their young adult years (Institute of Medicine, 1994; Substance Abuse and Mental Health Services Administration, 2009; U. S. Department of Health and Human Services, 1994). Thus, examining patterns of menthol cigarette smoking among adolescents and young adults is informative to understanding the role of menthol cigarettes in initiation.

In data collected in 2008, almost half of adolescent smokers between 12–17 years old (47.7 percent) reported past 30-day use of menthol cigarettes and 40.8 percent of young adults aged 18–25 years smoked menthol cigarettes (http://www.oas.samhsa.gov/2k9/134/134MentholCigarette.htm; Substance Abuse and Mental Health Services Administration, 2009). The rate of initiation with menthol cigarettes compared to non-menthol cigarettes is not well characterized. However, a greater pattern of menthol smoking has been observed among youth and younger adults compared to older adult smokers (Hymowitz et al. 1995; Substance Abuse and Mental Health Services Administration, 2009; Sidney, Tekawa, & Friedman 1989, among African Americans and Asians; Fernander et al. 2010; see chapter 4). For example, based on analysis of pooled cross-sectional 2004-2008 NSDUH data, a higher proportion (44.7 percent) of adolescent smokers ages 12–17 smoke menthol cigarettes than among young adults ages 18-25 years old (36.1 percent) or adults 26 years old or older (30.2 percent) (Rock, Davis, Thorne, Asman, & Caraballo 2010). When separated by different race/ethnicities, the proportion of menthol smokers is higher in adolescent smokers 12–17 years old compared to smokers 18–25 years or 26 years and older among whites (41.0 percent vs. 28.8 percent vs. 21.9 percent, respectively), Hispanics (47.0 percent vs. 38.2 percent vs. 29.5 percent), Asians (51.5 percent vs. 35.8 percent vs. 28.6 percent) and American Indian/Alaska Native (34.7 percent vs. 27.4 percent vs. 23.0 percent). By contrast in the African American population, 71.9 percent of adolescent smokers smoke menthol cigarettes compared to 82.2 percent of adult menthol smokers.

Giovino (2010, unpublished submission) conducted a fine grain analysis of NSDUH data to determine if an age gradient existed when smokers were divided into two categories: those who smoked fewer than 10 cigarettes a month (less established smoking) and those who smoked 10 or more cigarettes a month (more established smoking). He observed a statistically significant age gradient among those menthol smokers aged 12–34, with the highest prevalence observed among the 12–17 year olds for both categories of smokers.

As discussed in detail in chapter 4, TPSAC received public submissions that criticized and clarified NSDUH survey data. TPSAC reviewed these submissions and concludes that the issues raised in Curtin et al. (submission to the FDA, June 2010) are addressed in Giovino et al. (2010, unpublished submission) and do not affect TPSAC's interpretation of the NSDUH data.

***Age gradient of propotion of menthol cigarette use within youth***

Studies have also been conducted examining age gradients within an adolescent group. According to an analyses of the 2004, 2006 and 2009 National Youth Tobacco Survey (NYTS), a slightly higher portion of current middle school smokers than current high school smokers used menthol cigarettes within the past 30 days (49.4 percent vs. 44.9 percent; Caraballo & Asman, in submission). These results are concordant with the Appleyard et al. study (2001) using the 2000 NYTS and the study of Hersey et al. (2006), using the 2000 and 2002 NYTS among whites and Hispanics, but not among Blacks/African Americans (Appleyard, et al. 2001; Hersey, et al. 2006), and among Asian and Native Hawaiians/ Pacific

Islanders (Appleyard, et al. 2001). Giovino (2010, unpublished submission), analyzing the 2003 National Youth Smoking Cessation Survey, observed that menthol cigarette use was highest among smokers ages 12–15 years (53.5 percent), followed by ages 16–17 years (47.0 percent), ages 18–21 years (40.5 percent) and ages 22–25 years (34.6 percent). A statistically significant age gradient was observed overall and within males, females and whites. In an analysis of the 2006 NYTS, Curtin et al. (2010b) found a statistically significant higher percentage for "current smokers aged 9–13 years (59.3 percent) and lower percentage for current smokers aged 17–21 years (38.3 percent) reporting menthol vs. non-menthol cigarette smoking." The smoking rate among 14–16 year olds was 45.8 percent.

In an analysis of 2004–2008 pooled NSDUH data, (February 10, 2011 presentation (*Comparative Rates of Initiation of Menthol and Non-menthol Cigarette*s), Hersey observed that younger adolescents were more likely to smoke menthol cigarettes than older adolescents. The percentages of menthol smokers in each gradient, with confidence intervals in brackets, were: 12–13 years old, 48.6 percent (42.4, 54.8); 14–15 years old, 46.3 percent (43.6, 49.0); 16–17 years old, 43.9 percent (42.1, 45.6); 18–25 years old, 36.3 percent (35.5, 37.1). Age gradients were observed regardless of whether the groups analyzed were all current smokers or smokers who identified their menthol or non-menthol status. Similar age gradients were observed among whites (12–14 years old, 42.7 percent [39.0, 46.3]; 15–17 years old, 38.1 percent [36.4, 39.8]) and Hispanics (12–14 years old, 47.1 percent [37.3, 57.0]; 15–17 years old, 42.2 percent [37.5, 46.9]). The age gradients were reversed among African American adolescents (12–14 years old, 50.9 percent [40.8, 61.0]; 15–17 years old, 70.4 percent [65.3, 75.4]) and other racial/ethnic groups (12–14 years old, 37.2 percent [24.7, 49.7]; 15–17 years old, 46.4 percent [39.9, 53.0].

(See Table 1 for studies on age gradients associated with menthol smoking).

***Brand preference among youth: age gradient and trends***

The most popular menthol brand smoked by youth is Newport, which is manufactured by Lorillard. Along with the non-menthol brands Marlboro and Camel, Newport ranks among the top three brands purchased by adolescents. These brands are used by 81.3 percent of smokers aged 12–17 years old and 82.4 percent of smokers aged 18–25 years old (SAMSHA 2005, (see Caraballo & Asman, in submission). Internal tobacco documents show that as early as 1976, Lorillard had noted that Newport had a strong appeal among young or new smokers (Klausner, 2011 in press, page 16).

The findings from the product preference studies are congruent with the age gradients found in the prevalence of menthol cigarette users among adolescents. In the 1993 Teenage Attitudes and Practice Survey (TAPS), 70 percent of current smokers reported that they usually bought their own cigarettes and younger smokers (aged 12–15 years) were more likely than older smokers (aged 16–18) to purchase Newport cigarettes (19.4 percent vs. 10.6 percent) and less likely to buy Marlboro cigarettes (49.5 percent vs. 63.1 percent, Barker, 1994). Similarly, the 1999 Monitoring the Future Survey found fewer adolescents in higher grades compared to lower grades reporting preference for Newport cigarettes (eighth grade. 22.5 percent; tenth grade, 17.7 percent, twelfth grade, 13.3 percent) (Johnston, O'Malley, Backhan, & Schulenberg 1999).

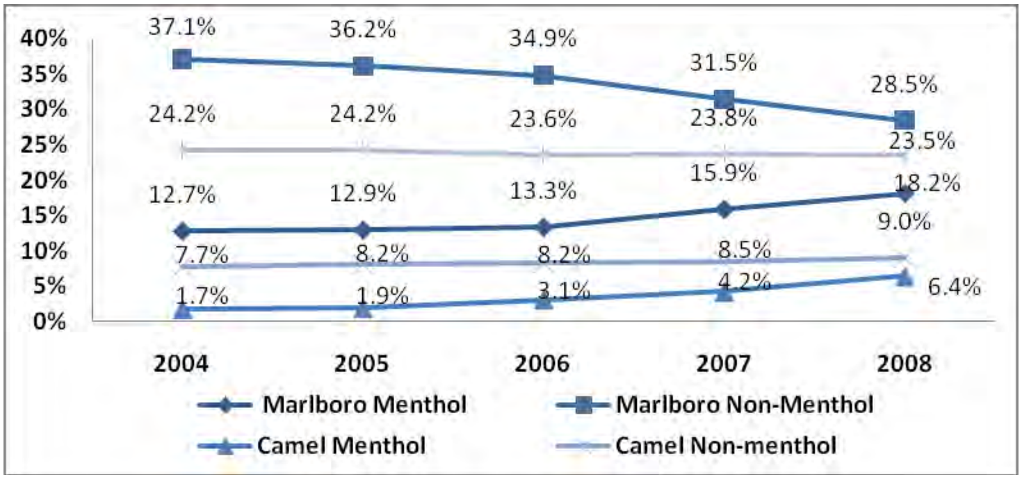
Giovino et al. (2004), in an analysis of 2000 NSDUH data by racial/ethnic group, found the age gradient was dependent on the brand of menthol cigarettes. Among African American smokers, more than three-fourths of adolescents (79.2 percent, ages 12–17) and young adults (76.7 percent aged 18–25 years) but less than one-third of those age 26 and older (31.5 percent) smoked Newport. African American smokers age 26 and older smoked Kool (14.1 percent) and Salem (6.9 percent) more than African American smokers ages 12–17 (2.1 percent and 1.6 percent for Kool and Salem, respectively) and

African American smokers ages 18–25 (4.6 percent and 1.6 percent for Kool and Salem, respectively). Among white smokers ages 12-17, nearly one of five (18 percent) smoked Newport but less than one of 10 older smokers smoked Newport (9.3 percent of 18–25 year olds and 2.9 percent of 26 years and older). White smokers ages 26 and older, smoked Kool (1.8 percent) and Salem (3.0 percent) more than white adolescent smokers ages 12–17 (0.7 percent and 0.3 percent for Kool and Salem, respectively). Among Hispanic smokers, nearly one of three adolescents age 12–17 (31.4 percent), one of six young adults ages 18–25 (16.7 percent) and less than one of fourteen adults ages 26 years and older (7.1 percent smoked Newport cigarettes. The age gradient for Kool (0.3 percent vs. 0.9 percent vs.3.6 percent for adolescents, young adults and adults, respectively) and Salem (no data vs. 0.2 percent vs. 3.4 percent for adolescents, young adults and adults, respectively) were the inverse of the gradient for Newport.

Studies suggest an increasing trend in menthol use among youth both historically and more recently, depending on the menthol brand (see Table 2 for trends in menthol smoking among youth). TAPS showed a substantial change in brand preferences among the adolescents from 1989 to 1993, with a 55 percent increase in the purchasing of Newport cigarettes (4.5 percentage points) in spite of the unchanged market share for Newport and a decrease in Newport advertising expenditures to $35 million from $49 million during this time (Barker, 1994). Similarly, Kaufman et al. (2004), analyzing data from three nationally representative cross-sectional surveys of adolescents (1996 National Survey of Tobacco Price Sensitivity, Behavior, and Attitudes Among Teenagers and Young Adults; and the 1989 and 1993 TAPS), found that percentages of white and Hispanic adolescents who usually bought Newport doubled between 1989 and 1996, The percentage of white adolescent Newport buyers grew to 10.4 percent from 5.3 percent and the percentage of Hispanic adolescents who usually bought Newport increased to 25.9 percent from 12.8 percent, with dramatic increases among those ages 12–14 (from 4.8% percent to 19.2 percent). Increases in Newport purchases were observed among both males and females. More recent data show that the percent of past month Newport smokers in grades 8, 10 and 12 has remained stable from 1998 to 2008 (see Caraballo & Asman, in submission, FDA white paper), although a decreasing trend has been observed with Marlboro cigarettes (see Figures 3–5 in paper).

Hersey presented an analysis of the percent of 12–17 year olds smoking different brands of menthol cigarettes from 2000 to 2008 using the NSDUH survey (Presentation to TPSAC February 11 2011; see Figure 2). Although the percent of this age group who used Newport cigarettes did not increase between 2000 and 2008 (23.4 percent and 23.5 percent, respectively), the percent who smoked Marlboro Menthol increased to 18.2 percent from 12.7 percent and Camel Menthol increased to 6.4 percent from 1.7 percent. On the other hand, non-menthol Marlboro cigarettes decreased to 28.5 percent from 37.1 percent.

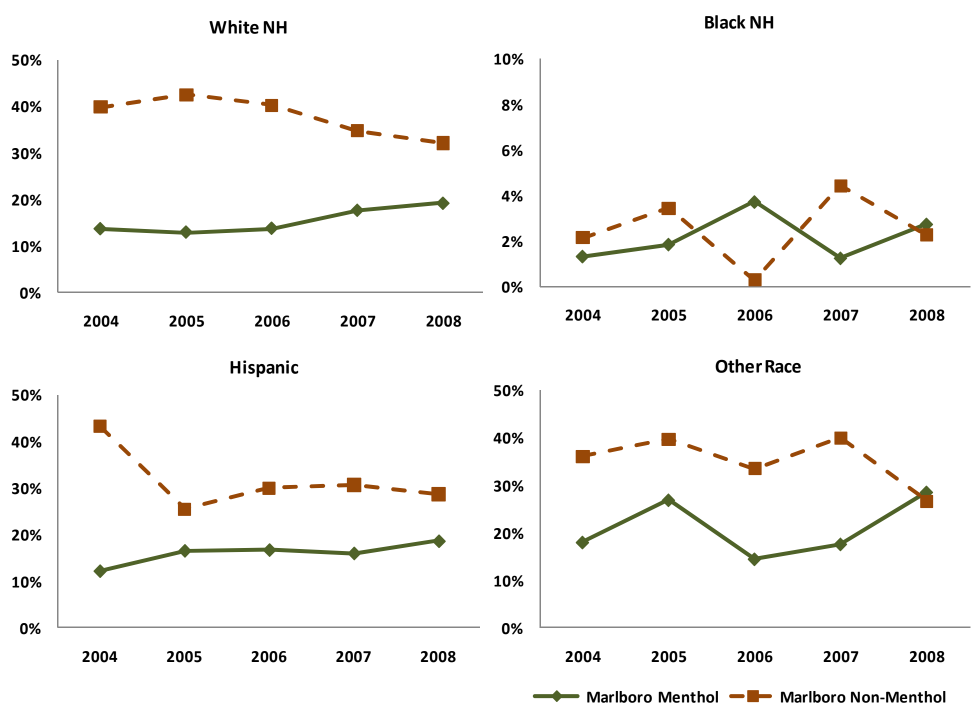
**Figure 2. Trends in the Percentage of Brand Use among 12-17 Year-Old Current Smokers in the National Household Survey of Drug Use and Health (NSDUH): 2004 to 2008**




**Note: This figure shows percentage of current smokers aged 12 – 17 who smokeda particular brand and type of cigarettes. Data were analyzed by RTI from the National Household Survey on Drug Use and Health (NSDUH). The number of current smokers aged 12-17 in this analysis by year was 2004: 2,225; 2005: 2,221; 2006: 1,996; 2007: 1,907; and 2008: 1,759. Source: RTI analysis of the National Survey on Drug Use and Health (NSDUH) 2004 -- 2008**

In their analysis of the NSDUH surveys from 2004 to 2008 among 12–17 year olds across different racial/ethnic groups, Hersey et al. observed an increase in Marlboro menthol use and decrease in Marlboro non-menthol use among whites, Hispanics and the other category, but not among African Americans (Presentation to TPSAC February 11 2011, see Figure 3).

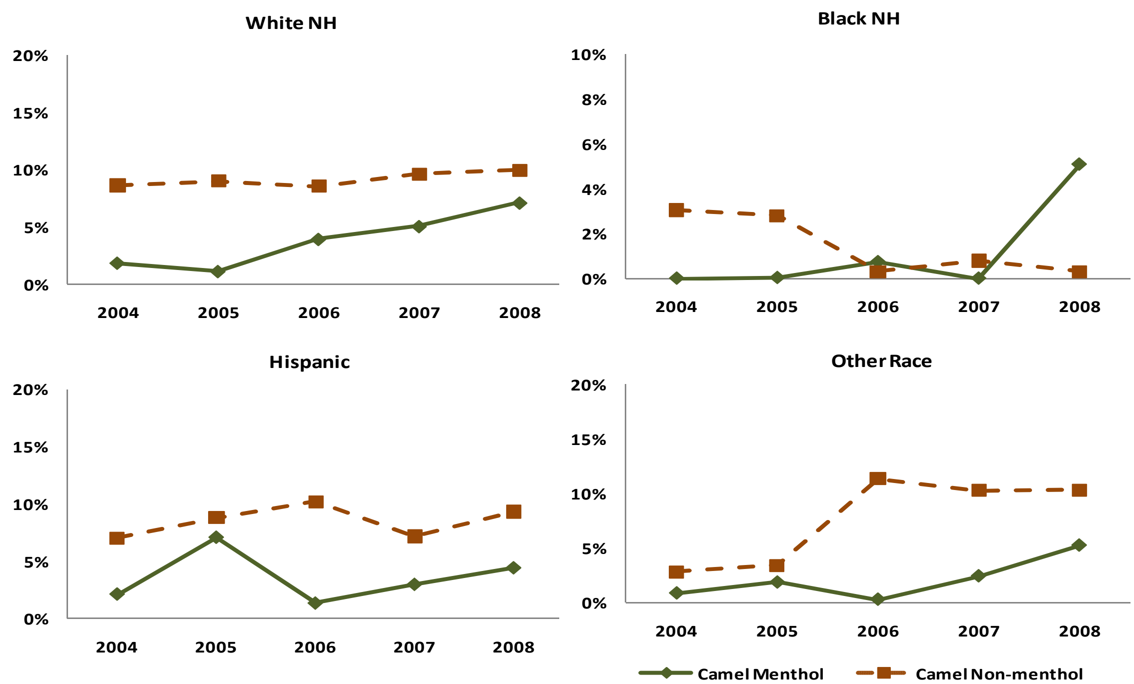
**Figure 3. Percent of Smokers, Aged 12 – 17, Smoking Marlboro Menthol and Marlboro Non-Menthol from 2004 to 2008 by Race/Ethnicity**




**Source: RTI analysis of the National Survey on Drug Use and Health (NSDUH) 2004 -- 2008**

For the Camel menthol brand, increases were seen for all racial/ethnic groups, whereas non-menthol Camel use decreased among African Americans, did not change among whites and Hispanics, and increased among smokers in the other category (see Figure 4). On the other hand, Newport cigarette use remained relatively flat between 2004 and 2008, as observed by Caraballo and Asman (in submission, FDA white paper).

**Figure 4. Percent of Smokers, Aged 12 – 17, Smoking Camel Menthol and Camel Non-Menthol from 2004 to 2008 by Race/Ethnicity**



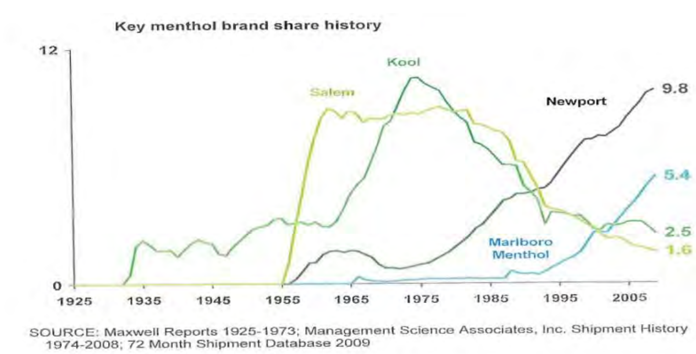

**Source: RTI analysis of the National Survey on Drug Use and Health (NSDUH) 2004 -- 2008**

The data were also examined by age and level of experience with smoking, as assessed by those who had smoked less than 100 cigarettes (novice smokers) and those who had smoked 100 cigarettes or more (experienced smokers). The percentage of Marlboro Menthol smokers increased among novice and experienced smokers ages 12–17 (+6.1 percentage points and +4.1 percentage points, respectively) and among novice and experienced smokers ages 18–25 year olds (+5.6 percentage points and +3.3 percentage points). Greater increases were observed in the youngest group.

Altria Client Services provided information intended to counter the hypothesis that the availability of menthol cigarettes increases cigarette initiation. In a June 30, 3010 submission (Page 100), Altria said the rate of cigarette purchases among underage adolescents had decreased dramatically since 1995. According to the Youth Risk Behavior Survey, 54.5 percent either purchased (38.7 percent) or had someone else purchase cigarettes (15.8 percent) compared to 42.1 percent who either purchased (14.0 percent or someone else purchase cigarettes ( 28.1 percent) in 2009. This document also refers to studies indicating that most adolescents obtain their cigarettes from peers and potentially family members, rather than purchasing the cigarettes themselves (articles cited include: Croghan, Aveyard, Griffin, & Cheng, 2003; Emery, Gilpin, White, & Pierce, 1999; Forster, Chen, Blaine, Perry, & Toomey, 2003; Harrison, Fulkerson, & Park, 2000; Ma, Shive, Legos, & Tan, 2003; Substance Abuse and Mental Health Services Administration, 2007; S. S. Williams & Mulhall, 2005). Concordant with these findings, Allen and Unger (2007) examined factors associated with menthol and non-menthol cigarette use among a convenience sample of 432 adult African American smokers in lower income neighborhoods in Los Angeles in 2001. After controlling for age and employment, and significant correlates of menthol use, including parents' menthol cigarette smoking (among females) and among both men and women, the belief that most African American smokers smoke menthol, suggesting that social and cultural norms contribute to menthol cigarette smoking. As noted in chapter 5, "Menthol marketing…uses socially and culturally relevant messages about in-group identity to appeal to different market segments." Marketing cigarettes as part of the youthful or African American culture would be increase the appeal and availability of cigarettes among peers within this social network.

A submission by Altria (June 30, 2010, page 30) showed a significant increase in the market share of Marlboro menthol cigarettes from 1975 to 2005 (5.4 percent share of US market in 2005, see Figure 5) as well as Newport cigarettes (9.8 percent of market share in 2005). It was noted that this increase in market share could not be explained by any change in levels of menthol yield in cigarettes (Lorillard Tobacco Company, submission, June 30, 2010 for Newport Full Flavor, Lights and Mavericks). Although the menthol content in cigarettes has increased, the yield has stayed the same through increased ventilation of cigarettes.

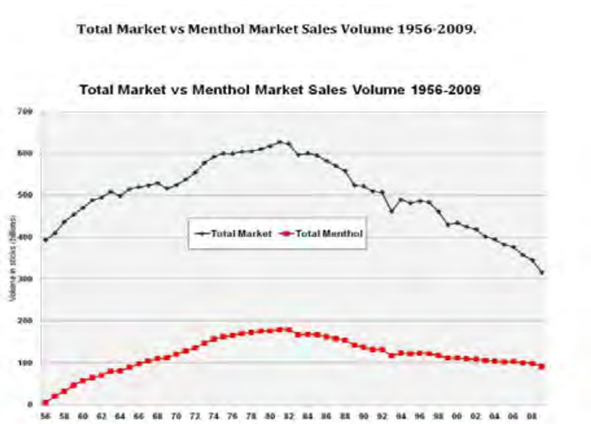
Figure 5. Trends in market share of menthol cigarettes




In order to examine the association between market share and youth smoking rates, the June 30, 2010 submission from Lorillard correlated menthol market share with youth smoking rates by state (2009 data of youth smoking rates obtained from Campaign for Tobacco Free Kids, Key State-Specific Tobacco-Data and Rankings). The data show an inverse association of menthol market share with youth smoking rates (see page 49 and 50, Figures 13 and 14). This analysis did not explore potential ecological confounding by such factors as race.

To further support the lack of relationship between youth smoking and the availability of menthol cigarettes, the June 30, 2010 document submitted by Altria points to the significant declines in underage smoking since peak levels in the late 1990s. However, by contrast, Giovino (2010 unpublished submission) showed that the rate of decrease is less among menthol cigarette smokers compared to non-menthol cigarette smokers. In fact, among young adults (18–25 year olds), no change in the rate of menthol use has been observed from 2004 to 2009 (14.0 percent vs. 14.5 percent) compared to a decrease in non-menthol use (25.7 percent vs. 20.4 percent). This finding follows the market share pattern observed for menthol vs. non-menthol cigarettes (see Figure 6, [Figure 9 from Lorillard June 2010 submission]). Furthermore, while the rate of smoking has been declining among adolescents (although the most recent Monitoring the Future report shows that smoking rates have stopped declining, with a slight increase in eighth and tenth graders from 2009 to 2010, www.monitoringthefuture.org), the proportion of adolescent cigarette smokers who report using menthol cigarettes increased significantly from 2004 to 2008 (Rock, et al., 2010). Specifically, Rock et al. (2010) noted that the 2004 to 2008 NSDUH data showed that menthol cigarette use increased significantly among white smokers aged 12–17 (from 40.3 percent in 2004 to 46.0 percent in 2008, p <0.01) and among menthol smokers aged 18–25 years old for both Hispanics (from 33.9 percent in 2004 to 42.4 percent in 2008) and in whites (from 26.7 percent to 32.5 percent, p < 0.01).

Figure 6.




Finally, the suggestion has been made that menthol cigarettes are not likely to contribute to the initiation of smoking because African American youth have a higher prevalence of smoking menthol cigarettes compared to whites, yet they experience a lower rate of smoking and a later age of onset compared to whites (presentation by Hunt, July 15-16, 2010, Altria). Hunt did not address other factors such as the role of cultural norms and ethnicity and race, which needs to be taken into consideration. Menthol cigarettes may still facilitate initiation of smoking in the African American culture even if they experience different patterns of initiation than whites.

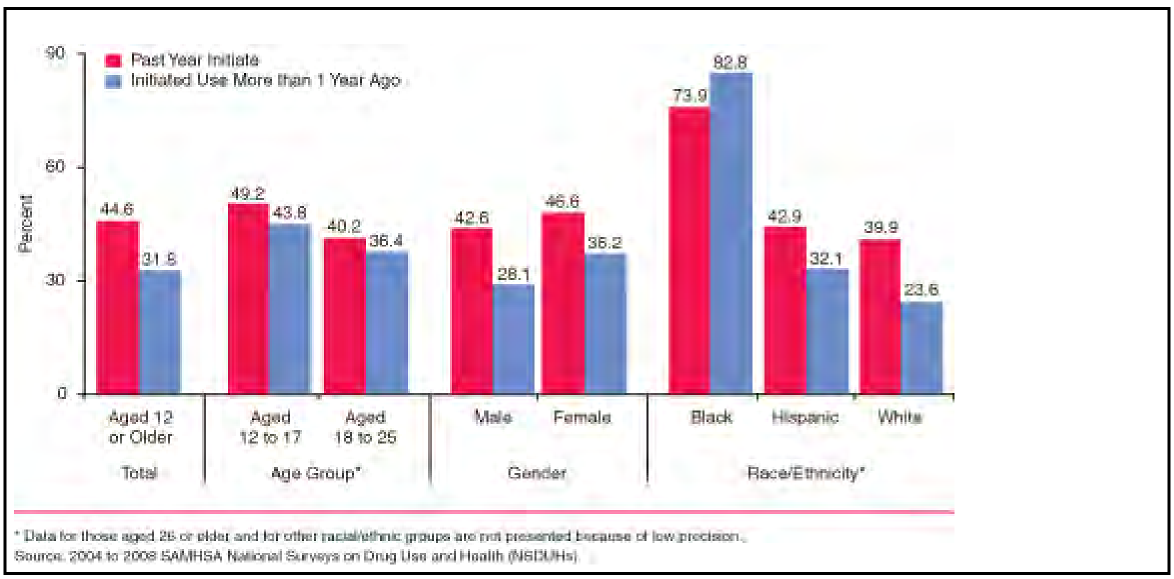
<u>*Summary:*</u> The evidence strongly suggests a higher prevalence of menthol cigarette use among adolescent smokers compared to adult smokers, except among African Americans. This finding is concordant with the trend and prevalence data presented in chapter 4. The discrepant results observed in some studies using national surveys, particularly in the analysis presented by Curtin et al. 2010 (see chapter 4), may be reflect the small subject sample (e.g., NHANES had only 20 menthol smokers in the 12-17 year old category) or subjects less than 18 years and older were not interviewed (e.g., NHIS). The results also show that a higher proportion of younger adolescent smokers tend to smoke and prefer menthol cigarettes compared to older adolescent smokers. The data show that while adolescent smoking has been declining among menthol and non-menthol smokers, the rate of decline is greater among non-menthol smokers and the proportion of adolescent smokers smoking menthol cigarettes, particularly Camel and Marlboro menthol cigarettes, has been increasing among both experimenting smokers (<100 cigarettes in a lifetime) and more established smokers (smoking 100 or more cigarettes

in a lifetime). It is unclear whether a greater proportion of younger adolescents initiate and experiment with cigarette smoking with menthol cigarettes compared with older adolescents.

**Pattern of menthol smoking in recent smokers versus established smokers**

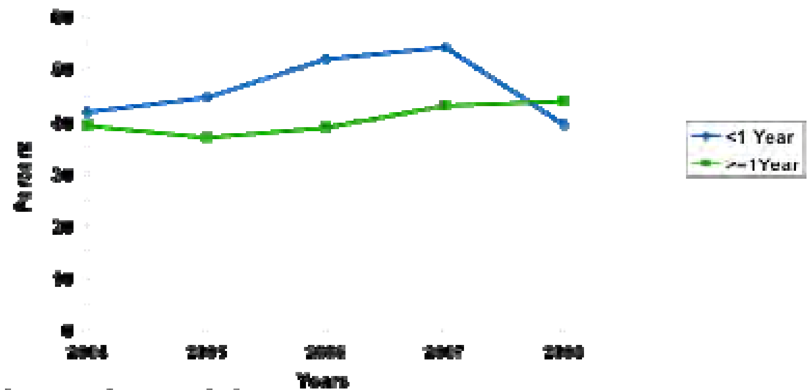
Two peer-reviewed articles, three white papers and three public comments were identified and reviewed by TPSAC. Peer-reviewed studies of national survey data show that recent adolescent smokers are more likely to smoke menthol cigarettes than more established adolescent smokers (Hersey, et al., 2006; Substance Abuse and Mental Health Services Administration, 2009), although the trend was reversed in 2008 among smokers aged 12–21 (Rising et al. 2010). Hersey et al. (2006) analyzed data from the 2002 NYTS that examined middle and high school students who smoked for one or more times in the past 30 days and who described the brand and/or the menthol status of the cigarettes they usually smoked. A significantly higher percent of menthol smokers was found among middle school students who had been smoking for less that 1 year compared with middle school students who had been smoking for more than 1 year (62.4 percent vs. 53.3 percent, $p < 0.002$). This same pattern was observed for high school students, but the difference was not statistically significant (45.9 percent vs. 41.9 percent, respectively). In an analysis of the 2004 to 2009 NSDUH data, the proportion who smoked menthol cigarettes compared to non-menthol cigarettes among those who had been smoking less than 1 year was higher among smokers aged 12–17 years (49.2 percent vs. 43.3 percent) and among smokers aged 18–25 years (40.2 percent vs. 36.4 percent) as well as among whites (39.9 percent vs. 23.0 percent), Hispanics (42.9 percent vs. 32.1 percent), but not among African Americans, although no statistical analysis was provided (See Figure 7, NSDUH Report Menthol Cigarettes,2009).

**Figure 7. Past Month Menthol Cigarette Use among Past Month Cigarette Smokers Aged 12 or Older, by Recency of Cigarette Initiation and Demographic Characteristics: 2004 to 2008**




In the white paper submitted by Rising et al. (2010), unpublished data on the use of menthol cigarettes by young smokers (aged 12–21 years) from the 2004 to 2008 NSDUH was described that showed a higher prevalence of menthol use among smokers who smoked less than one year compared to smokers who smoked for more than one year, but this pattern was reversed in 2008 (see Figure 8).

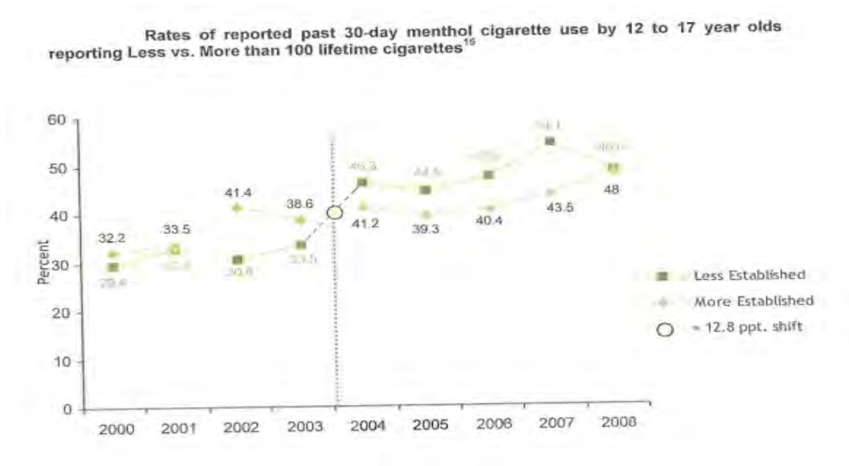
**Figure 8. Menthol cigarette use by new smokers (age: 12-21)**




National Survey on Drug Use & Health
Substance Abuse and Mental Health Services Administration

In the submission dated June 30, 2010 (page 110), Altria raised the issue that the findings from the 2004 to 2008 NSDUH may reflect how the question is phrased. They pointed out that prior to 2004, the question was phrased as: *During the past 30 days, did you smoke (insert brand name if identified) menthol or regular cigarettes **most often***. After 2003, the question was phrased: *Were the (insert brand name if identified) cigarettes smoked during the past 30 days menthol* (which thereby assessed any use of menthol cigarette smoking). Altria contended that few differences were observed in the percent of menthol smokers among current initiates (current smokers who had indicated that they had smoked for the first time in the past year) vs. prior initiates (current smokers who said they initiated smoking in prior years) prior to 2004, but after the change in phrasing, higher rate of recent smokers were observed to smoke menthol compared to more established smokers. TPSAC found it is difficult to attribute the differences in the data after 2003 to changes in the survey question. Even before the change, menthol smokers were beginning to account for a larger percentage of recent smokers. However, Altria (June 2010) pointed out that the jump in percentage was more than expected after the change in how the question was framed (see Figure 6.6, page 109). On the other hand, as pointed out by Giovino (2010, unpublished submission), Altria failed to note that the survey after 2003 included a question prior to the menthol cigarette inquiry which asked for the brand ***most often used*** and then an inquiry was made as to whether this brand of cigarettes (most often) smoked during the past 30 days was menthol. Relatively few smokers do not answer the question about the cigarettes most often smoked. For example, in 2008, only 4 percent of the sample responded to the question of whether they smoked menthol cigarettes in the past month without naming a usual brand of cigarettes.

Altria (June 2010 submission) conducted another analysis in which adolescent subjects were divided into those who had smoked less than 100 cigarettes cumulatively (novice smokers) and those who had smoked more than 100 cigarettes cumulatively (experienced smokers) (see Figure 9). The results showed a lower percentage of menthol smokers vs. non-menthol smokers in the novice smoker category during the earlier time period. However, it is important to note that the more recent survey data showed a higher percentage of menthol smokers in the novice smoker category, except in 2008.




In a study combining data from the 2004, 2006 and 2009 NYTS, differences were not observed in potential stages and prevalence of smoking menthol cigarettes (Caraballo & Asman, in submission). Among adolescents who smoked <1 cigarette per day (CPD) on 1–5 days of the past 30 days, 30.9 percent reported smoking menthol cigarettes, a rate similar to or slightly lower than among adolescents who smoke 1–5 CPD on 1–5 days, 6–9 days, 20–29 days and all 30 (45.3 percent to 49.7 percent). These data suggest that adolescents are not more likely to initiate smoking with menthol cigarettes. Similarly, using the NSDUH 2004-2008 surveys, Giovino (2010, unpublished submission) also found no differences in proportions of use of menthol cigarettes among smokers of all ages who smoked 1–5 days in the past 30 days (36.1 percent), 6 to 9 days (38.3 percent) or 10 days of more (31.9 percent). Among those aged 12–17 years, the proportions were 52.8 percent, 54.5 percent and 46.3 percent, respectively.

Another way to examine whether or not greater initiation in smoking occurs with menthol smokers is to compare the rate of menthol cigarette use vs. non-menthol cigarette use among less established smokers. In the February 11th presentation, Hersey examined data from 2000 to 2008 using the NSDUH survey and observed that a higher percent of menthol vs. non-menthol smokers smoking fewer than 100 cigarettes among youth. For example, 51.7 percent of Marlboro menthol smokers aged 12–17 reported smoking fewer than 100 cigarettes in their life vs. 38.1 percent of Marlboro non-menthol smokers. Similarly, 62.1 percent of Camel menthol smokers reported smoking fewer than 100 cigarettes versus 40.3 percent of Camel non-menthol smokers. For Newport, the rate was 46.8 percent. Because of the cross-sectional nature of the study, the causal direction is hard to interpret (smokers initiating on menthol cigarettes vs. those smoking menthol cigarettes tend to smoke fewer cigarettes).

(See Table 3 for rates of recent vs. established smokers among menthol smokers.)

*Summary:* These studies are limited by being cross-sectional and we can only infer that recent users as opposed to more established users are representative of those who initiated smoking with menthols. Nonetheless, there is some evidence to show that more recent smokers have a higher prevalence of smoking menthol cigarettes than established smokers in studies of adolescents that examined duration of smoking. However, there is mixed evidence to show that smokers of a few cigarettes (who might represent experimenters) tend to smoke more menthol cigarettes than smokers of a higher number of cigarettes.

**Age of initiation for menthol vs. non-menthol cigarettes**
Nine peer-reviewed articles, two unpublished submissions, and one white paper on internal tobacco documents were identified. Nine peer-reviewed studies and one unpublished secondary analysis

showed no differences in age at which the first cigarette was smoked (Allen & Unger, 2007; Okuyemi, Ebersole-Robinson, Nazir, & Ahluwalia, 2004; Pletcher et al., 2006), age of initiation (Cubbin, Soobader, & LeClere, 2010) or started smoking (Hyland, Garten, Giovino, & Cummings, 2002; Hymowitz, et al., 1995)(Hyland November 2010) or age of regular smoking (Lawrence et al., 2010; Okuyemi, et al., 2004; Okuyemi, Faseru, Sanderson Cox, Bronars, & Ahluwalia, 2007), comparing smokers of menthol and non-menthol cigarettes. The types of studies examined ranged from cross-sectional surveys (Cubbin, et al., 2010; Lawrence, et al., 2010; Okuyemi, et al., 2004), multicenter cohort studies (Hyland, et al., 2002; Hymowitz, et al., 1995; Pletcher, et al., 2006) to a treatment study (Okuyemi, et al., 2007). Two studies specifically examined African American populations (Okuyemi, et al., 2004; Okuyemi, et al., 2007). Three of the studies used the COMMIT database but with analyses of different time periods (Hyland, et al., 2002; Hyland & Rivard, 2010 b; Hymowitz, et al., 1995). One study that examined risk factors for menthol status showed marginal statistical significance for age of regular smoking, with delayed initiation associated with menthol status (Fernander, Rayens, Zhang, & Adkins, 2010). Tobacco documents also do not reveal any evidence to show the menthol smokers start earlier than non-menthol smokers (Klausner, 2011 in press).

In a submission from R.J. Reynolds, Curtin et al. (2010b) examined self-reported age of initiation in four national surveys: first whole cigarette smoked (NHANES <20 years old; NYTS), age started smoking regularly (NHANES, age < 20 years; NHIS), age first began smoking cigarettes (NSDUH) or age at first cigarette (NSDUH). The authors concluded that in general, based on NHANES, NHIS and NSDUH data, older age of initiation was observed among current menthol compared to non-menthol smokers, especially among females and individuals 30 years or older. However, significant differences were not observed with control for race, age and gender. On the other hand, the NYTS showed the age of first whole cigarette smoked was younger among the menthol compared to the non-menthol smokers, even when controlling for race, age and gender. The average initiation age was 0.52 years younger in current menthol smokers vs. non-menthol cigarette smokers ($p<0.05$).

*Summary:* The preponderance of evidence shows that menthol cigarette smokers do not report an earlier age of initiation of cigarette use (age of onset of first cigarette or regular smoking). However, the one study that examined an adolescent sample observed an earlier age of first smoking a whole cigarette among menthol vs. non-menthol smokers.

**Rate of switching from menthol to non-menthol cigarettes and from non-menthol to menthol**

Switching rate was considered important to consider because greater switching from menthol to non-menthol compared to non-menthol to menthol suggests that menthol may serve as a starter product. Two peer-reviewed articles, four unpublished secondary analysis (one of which was a public comment and submission) were identified for this topic and one white paper on internal industry documents. Data are conflicting on the extent of switching from menthol to non-menthol compared to non-menthol to menthol cigarettes. In the 15-year CARDIA cohort study that enrolled 1,535 healthy African American and European white men and women aged 18 to 30 years old in 1985, no differences were observed in the percent of young adult smokers (18 to 30 years old at the time of enrollment) who switched types of products (12 percent menthol to non-menthol switchers, 11 percent non-menthol to menthol switchers; Pletcher, et al., 2006). In another study of 29,037 current smokers and members of the Kaiser Permanente Medical Care Program followed for 4.5 years, more African American smokers under the age of 40 years switched from non-menthol to menthol cigarettes (14.6 percent) than from menthol to non-menthol cigarettes (3.6 percent), even when adjusting for age and sex (Sidney, et al., 1989); however, this study was conducted in the early 1980s and the follow-up rate was quite low (28 percent to 32 percent).

Hyland and Rivard (submission to FDA, November 2010b) explored the characteristics of menthol smokers and rates and correlates of switching to and from mentholated products using data from the COMMIT (Community Intervention Trial for Smoking Cessation) study. The percentage of 2,095 smokers using menthol tobacco in 1988 through 2001 by different demographic and smoking-related characteristics was calculated. Like other studies, they found that switching between menthol and non-menthol cigarettes is uncommon for all smokers, regardless of race. About 6.4 percent (out of 2,095) switched from menthol to non-menthol and 4.2 percent switched from non-menthol to menthol. Logistic regression was used to examine the correlates of switching from menthol to non-menthol cigarettes and vice versa in 1993 and in 2001. Smokers age 55 and older, as well as those who started smoking at 15 years or younger, were most likely to switch from menthol to non-menthol cigarette in 1993 or 2001. Smokers who report smoking fewer than 25 cigarettes per day were most likely to switch from non-menthol to a menthol cigarette in 1993 or in 2001.

Hyland and Kasza (November 2010 a submission) conducted another secondary analysis of epidemiological studies using the International Tobacco Control Four Country Survey (ITC-4), which collected information from 7,532 subjects 18 and older between 2002 and 2008 (annual assessments) from four different countries. Current smokers were defined as having smoked at least 100 cigarettes during their lifetime, and currently smoking at least monthly, and menthol status was determined by the brand that they presently smoke. Among whites, the probability of switching from menthol to non-menthol cigarettes (7.63 percent) was higher than switching from non-menthol to menthol (1.74 percent). Similarly, among Hispanics, the probability of switching from menthol to non-menthol cigarettes was higher (17.39 percent) than switching from non-menthol to menthol (6.72 percent). Among African Americans, the probability of switching from menthol to non-menthol (7.8 percent) was lower than non-menthol to menthol (14.78 percent).

(b) (4)

[redacted]

Two studies examined adolescents or young adults. One report analyzed the 2003 National Youth Smoking Cessation Survey. This survey examined 2,582 16-24 year olds who had ever smoked 20 lifetime cigarettes and had smoked at least once during the previous 30 days. After 24 months, 1,045 out of the 2,582 initially enrolled participants were still smoking. Menthol status was determined at baseline and at follow-up. Results showed that more 16-24 year old smokers switched from smoking menthol cigarettes to non-menthol cigarettes than vice versa after a two-year assessment period (15.0 percent vs. 6.9 percent, Giovino, 2010 unpublished submission). Nonnemaker et al. (November2010 submission to the FDA) analyzed a three-year longitudinal cohort school-based study of 12-18 year olds using the American Legacy Longitudinal Tobacco Use Reduction Study. This school-based survey of 47,237 middle school and high school youth was conducted in three waves from 2000 through 2003 in 83 schools in seven communities and five states. The analyses were restricted to youth who participated in all three waves of the survey (N=16,396 out of 35,352 interviewed at baseline). Youth who initiated smoking prior to baseline or who were older than 18 were dropped from the study. Analyses were estimated using weights that account for baseline characteristics as well as attrition. Data was analyzed excluding and then including youth who initiated smoking in Wave 3. Including Wave 3 initiates because of the larger sample size, the results showed that 5.9% switched from menthol to non-menthol and 8.0 percent from non-menthol to menthol, a direction opposite from that observed from Giovino (2010).

(See Table 4 for rates of switching)

*Summary:* There is some evidence to suggest that more menthol smokers switch to non-menthol cigarettes within certain populations of smokers. This may help explain some of the age trends in menthol smoking (lower prevalence among older adults), where more subjects are are switching from menthol to non-menthol. It is notable that relatively few smokers switch brands thereby demonstrating brand loyalty even among yIt is notable that relatively few smokers switch brands thereby demonstrating brand loyalty even among youth and young adults.

**Sensory experience of menthol cigarettes**

Several articles have described characterizing menthol as facilitating the uptake of cigarettes because it reduces the harshness of tobacco and provides a cooling sensation thereby increasing the appeal of the product (Henningfield et al., 2003) (Lawrence, Cadman and Hoffman, white paper 2010). As described in chapter 3, these effects from menthol makes it biologically plausible that menthol enhances the addictiveness of cigarettes.

Because of the limited amount of research in this area, internal tobacco industry documents may reveal the industry's thinking about menthol cigarettes as a product for initiators or non-established smokers. In research that assesses relevant documents from 1965 to 2000, two types of menthol smokers emerge—those who cannot tolerate the harshness and irritation of non-menthol cigarettes, and those who seek out the flavor and physical sensation of menthol (Kreslake et al. 2008).

For the first type, menthol reduces the negative sensory characteristics associated with smoking. This type includes a large proportion of occasional smokers or young smokers, or smokers who switched to menthol cigarettes because the harshness or perceived negative health effects of their non-menthol cigarettes. The tobacco industry documents show that they were aware of how to manipulate menthol levels to appeal to cigarette smoking initiates. The author (Cnatrell, 1987 in Kreslake 2008, page 710) of an internal Brown & Williamson memo noted that a "successful starter cigarette would need to provide a low tobacco taste, low impact and irritation, low tobacco aftertaste and low menthol content." A Lorillard document noted that among younger subjects (aged 21-29), ratings of overall satisfaction were lower when the levels of menthol increased. Thus, Newport Lights, which had less menthol loading, was more appealing to younger respondent than cigarettes with higher menthol loading (Kreslake et al., 2008, page 711). The second type of smoke includes individuals who seek out specific menthol flavors associated with physical sensation. These established menthol smokers appear to be tolerant of or seek out stronger sensory characteristics and tend to be African American and male.

A search of internal tobacco industry documents commissioned by the FDA using the Legacy Tobacco Document Library addressed properties of menthol and the smoking experience. The review found properties menthol contribute to the that "menthol has cooling and anesthetic properties that are dose-sensitive and that can moderate the harshness and irritation of tobacco." (conclusion from R.J.Reyonlds Tobacco Co. study, page 8, Yerger, in press). This finding is congruent with a search conducted by Wayne and Connolly (2004) who reviewed the archival database maintained at Tobacco Documents Online, ranging in date from 1920s through1990s. These authors reported that documents indicate that tobacco companies thought that mentholation led to "altered perception of tobacco smoke and its constituents via cooling, smoothing and anesthetic effects; increased impact through stimulation of trigeminal receptors and interaction with nicotine controlling its perception, delivery and uptake." The FDA commissioned report (Yerger, in press) page xx) further observed, "By making cigarettes smoother and less harsh, menthol alleviates nicotine's irritating effect. For decades, the tobacco industry has known that younger, inexperienced smokers have lower tolerance for irritation and tobacco taste than do older and more experiences smokers."

The white paper commissioned by the FDA (Klausner, 2011 in press) on menthol initiation concluded that their analyses indicate that youth and experimenters choose menthol cigarettes because they are easier to smoke, are more soothing on the throat and cooler, milder and less harsh or burning. Further, the author describes an early study that was conducted by Philip Morris, which showed that what menthol smokers report they like about menthol is due to effect rather than taste. The key effects that appear to appeal to menthol smokers include "cooling effects clean, antiseptic effects, slightly numbing, anesthetic effects and heady, lifting effects (page 6)." The author points to a Brown & Williamson document that surmised the beginning smoker's familiarity with mint-flavored candies contributed to the acceptance of menthol. Similar to the Kreslake study, the author describes the tobacco companies' knowledge that initiators of smoking prefer cigarettes with a hint of menthol but as the smokers age, they prefer cigarettes with more menthol. In addition, the documents also showed that some youth smoke menthol cigarettes because they perceive them to be less harmful than non-menthol cigarettes. The tobacco companies also found the family and peer influences to be important in determining use of menthol cigarettes by young and new smokers. Other tobacco companies believed that the choice of menthol was haphazard. Industry presentations and associated documents suggest that individuals have different taste preferences and taste is what drives them to smoking mentholated cigarettes (July 2010 TPSAC meeting).

*Summary:* Based on review of internal tobacco documents, the evidence suggests that youth choose menthol cigarettes, particularly at lower menthol yields, mainly because of the relative ease of smoking a menthol cigarette for the naive smoker and because they perceive menthol to be less harmful than non-menthol cigarettes. These internal document findings converge with the studies on the physiological effects of menthol conducted both internally and externally to the tobacco companies and possibly the finding that adolescent smokers tend to prefer Newport cigarettes, which tend to have lower menthol in cigarette as percent of tobacco weight and lower menthol in smoke than brands like Kool or Salem (June 30, 2010 Altria submission, Table 1.3). Taken together, the various lines of evidence support an appeal of menthol cigarettes to youth and starting smokers because of their sensory effects.

**REGULAR SMOKING AND ADDICTION**

This section examines whether menthol cigarette use is more likely to lead to regular smoking or nicotine addiction compared to non-menthol cigarette use. TPSAC looked at evidence in three relevant areas: abuse liability, the trajectory of addiction, and the intensity of addiction. Abuse liability addresses whether menthol interacts with nicotine or enhances the experience of smoking to make menthol cigarettes more addictive than non-menthol cigarettes. Trajectory of addiction explores the likelihood and speed with which menthol cigarette smokers become addicted to nicotine compared to non-menthol cigarette smokers. Intensity of addiction assesses whether menthol cigarette users are more or less dependent on nicotine or cigarette smoking than non-menthol cigarette users.

**Abuse liability assessment**

***Menthol's effects on the nicotine pharmacokinetics***

Nicotine pharmacokinetics are important because the reinforcing strength of cigarettes is based on the amount and speed of nicotine delivery as well as the rate of nicotine clearance (U. S. Department of Health and Human Services, 1988, 2010). As noted in chapter 3, the preponderance of evidence shows no differences in the amount of acute nicotine delivered by a single cigarette to menthol vs. non-menthol cigarette smokers. Although evidence presented in chapter 3 suggests menthol may slow the clearance of nicotine from the bloodstream, the effect is small and not likely to affect pharmacokinetics significantly. Therefore, most likely, menthol does not alter the pharmacokinetics of nicotine in a way that would enhance the development addiction beyond that of a non-menthol cigarette. Chapter 3 reports that menthol may act on nicotinic receptors and may modulate pharmacologic effects of nicotine, but the functional consequence of such effects with respect to addiction is unknown.

***Abuse Liability Laboratory Studies***

To date no formal animal or human abuse liability assessment has been conducted with menthol cigarettes. In the absence of such research, TPSAC examined four peer-reviewed studies on smoker responses to menthol and non-menthol cigarettes; one peer-reviewed analyses of internal tobacco company documents, and two peer-reviewed studies on behavioral economic analysis of menthol and non-menthol cigarette smokers.

<u>Smoker responses to menthol and non-menthol cigarettes</u>

Several studies have examined the effects of menthol containing cigarette substitutes and cigarettes on subjective response, which may provide insight into whether a product containing menthol may be more rewarding. The within-subject, laboratory studies and their findings are summarized below.

Levin et al. (1990) used cigarette substitutes to examine smokers' taste reactions to five flavors, three tobacco flavors and two menthol-like flavors. Each flavored cigarette substitute was rated on several dimensions and compared to placebo. Cigarette substitutes with menthol-like flavors received statistically significantly higher ratings on liking and satisfaction than placebo and were among the highest ranked in both menthol and non-menthol smokers.

Pickworth et al. (2002) examined smokers' reactions to high-nicotine yield (2.5 mg nicotine yield) and low-nicotine yield (.2 mg nicotine yield) menthol and non-menthol laboratory cigarettes and two menthol (Kool, Newport) and two non-menthol (Winston, Marlboro) commercial cigarette brands. Menthol cigarette smokers used menthols in the study; non-menthol cigarette smokers used non-menthols. No statistically significant differences in most subjective responses (strength, satisfaction, psychological reward, negative effects) were observed between the menthol and non-menthol smokers. Nicotine yield, not menthol, had effects on subjective measures.

Pritchard et al. (1999) compared responses of smokers to "denicotinized" (0.06 mg nicotine yield) menthol (4.1 mg menthol/cigarette) and non-menthol cigarettes. In this study, menthol and non-menthol smokers tested both types of cigarettes. As in Pickworth et al. (2002), no significant differences in subjective responses (mental alertness, anxiety/nervousness, muscular relaxation) were observed between menthol and non-menthol cigarettes. In addition, little evidence of pharmacological effect, as assessed by EEG and heart rate, were observed between menthol and non-menthol cigarettes.

These laboratory studies are limited by their small sample sizes, unbalanced distribution of race/ethnicity among menthol and non-menthol smokers, and focus on established smokers and other inclusion criteria, limiting the generalization of these finding.

Only one study has examined reactions associated menthol vs. non-menthol cigarettes during the first smoking experience. No differences in subjective reaction to the first inhaled cigarettes by mentholation were observed (DiFranza et al., 2004). The DiFranza et al. study is limited due to the small sample size and retrospective recall of their experiences with their first inhaled cigarette. Furthermore, just over half could recall the brand of their first inhaled cigarette.

<u>Analyses of internal tobacco company documents</u>

One recent peer-reviewed study of internal tobacco industry documents reveals experiments that indicate menthol has a significant impact on low-nicotine and denicotinized cigarettes.

Yerger (in press) writes that during the late 1980s, Philip Morris scientists conducted tests on various prototypes of “alkaloid (nicotine) reduced tobacco” (ART). The non-mentholated ART prototypes were described as lacking impact (e.g., “kick” or “grab” in the back of the mouth and throat when inhaling a cigarette, a sensory experience believed to contribute to immediate smoking satisfaction). Yerger writes (page 8): “Phillip Morris found the mentholated prototypes of ART to be ‘subjectively superior’ to non-mentholated versions because they were the only ART prototypes that provided any impact.” She further states, “When further testing the mentholated ART prototypes, Phillip Morris scientists found menthol provided this perceived impact because it produced some nicotine-like effects.”

Yerger (in press) additionally writes that Philip Morris conducted a study that combined four levels of menthol with three levels of nicotine. The results showed that cigarettes without nicotine were preferred more when menthol was added; low or intermediate menthol levels were preferred over high menthol levels in cigarettes. Yerger describes other Phillip Morris studies that confirmed the observation that “menthol increased impact for the low-nicotine delivery cigarettes…The effect of menthol was most pronounced for the cigarette with the lowest nicotine delivery” (page 11, quote by Gerry Nixon from Phillip Morris).

Yerger (in press) further describes tobacco industry studies conducted by Phillip Morris and Brown and Williamson in the 1970s of different menthol concentrations on low-tar delivery cigarettes to maximize customer appeal and increase market demand for these cigarettes. During that time, these low-tar/nicotine brands were believed to address concerns about the health effects of smoking and were considered to represent a growth area.

Yerger (in press) also writes of human studies conducted by Phillip Morris that found menthol produces some nicotine-like central nervous system and subjective effects (e.g., mental alertness, muscular relaxation), making menthol a “partial replacement” for nicotine (page 15). This observation is likely to be due the stimulation of the trigeminal nerve or nerve fibers, which is considered “essential to eliciting ‘liking’ response to tobacco products” (page 15). Yerger writes that because of the nature of the documents, no information was provided on the specifics of study designs or who comprised the subjects for this study.

Behavioral economic models

The relative abuse liability of a product can be determined by the extent to which another product can be substituted for it. Tauras et al. (2010) observed that smokers do not find menthol and non-menthol cigarettes to be close substitutes. Using data from the 2003 and 2006/07 Tobacco Use Supplements to the Current Population Survey (n=57,387, aged 18 and older), they developed a regression model that estimated the probability of being a menthol smoker, conditional on being a current smoker who reported a preference for menthol or non-menthol cigarettes. Cigarette prices, smoke-free air laws and socioeconomic and demographic characteristics were examined as covariates. The results showed that non-menthol cigarettes were less of a substitute for menthol cigarettes than vice versa. A 10 percent increase in menthol cigarette prices would cause 2.36 percent of menthol smokers to switch to non-menthol cigarettes. By contrast, a 10 percent jump in non-menthol cigarette prices would cause 4.75 percent non-menthol cigarette smokers to switch to menthol cigarettes. This difference was more pronounced among African Americans and young adults. Furthermore, these investigators found relatively more use of menthol cigarettes in states that have stronger laws restricting smoking. Both these findings suggest that menthol cigarettes may be more reinforcing or addicting than non-menthol cigarettes.

Farrelly et al. (2007) examined the effect of price increases on the purchase of stronger cigarette types (cigarettes with higher tar and nicotine yields). Scanner data (ScanTrack licensed from ACNielsen) on cigarette prices and sales were obtained from supermarkets (with at least $2 million in annual sales) across the United States from 1994 to 2004. Using multivariate regression models, price elasticities suggest that the average inflation-adjusted price increase of 55.8 percent for menthol cigarettes was associated with an increase of 1.73 percent in sales-weighted tar yields and 1.28 percent increase in sales-weighted average nicotine yields. A 50.5 percent price increase of non-menthol types of cigarettes over the same period produced an estimated increase of 1 percent in tar per cigarette but no statistically significant increase in nicotine yields. Thus, these findings show that an increased probability that stronger cigarettes are smoked as price of cigarettes is increased and this effect is larger among menthol than non-menthol smokers. Concordant with the prior study, these results also suggest addiction to cigarettes may be stronger among menthol smokers, although the study results do not show if more exposure to tar and nicotine occurs as a result of the smoking higher tar and nicotine yield cigarettes. However, one of the strengths of these studies is that they are nationally representative samples and examine actual behavior of consumers.

*Summary:* No animal and relatively few human studies have been conducted directly examining the relative abuse liability of menthol vs. non-menthol cigarettes. Reviews of internal tobacco industry documents show studies conducted by the tobacco industry that demonstrate that menthol is associated with greater impact or “throat grab” when added to denicotinized or lower nicotine yield cigarettes. As suggested in chapter 3, abuse liability of menthol cigarettes may be higher because of potentially strong conditioned cue response with menthol cigarettes. Finally, studies using behavioral economic models, which have been used to assess abuse liability of other drugs, suggest greater reinforcing effects from menthol cigarettes.

**Trajectory from initiation to regular smoking or dependence**

To date, only Nonnemaker et al. (2010) has examined if early menthol cigarette use was more likely to be associated with regular smoking or dependence than early non-menthol cigarette use. As previously described, this unpublished research analyzed data from the American Legacy Longitudinal Tobacco Use Reduction Study, a three-year longitudinal cohort school-based study of 12–18 year olds. Progression to greater smoking was determined in three ways: (1) a transition from smoking less than 100 cigarettes to smoking more than 100 cigarettes; (2) a transition from smoking on less than 20 days per month to smoking 20 or more days per month; and (3) a transition from non-daily smoking to daily smoking. Nicotine dependence was measured in response to the following questions: (a) *How soon after you wake up do you usually smoke your first cigarette on weekdays? during the weekend?* (b) *If you are sick with bad cold or sore throat, do you smoke cigarettes?* (c) *How true is this statement for you? When I go without a smoke for a few hours, I experience cravings*; (d) *How true is this statement for you? I sometimes have strong cravings for cigarettes where it feels like I'm in the grip of a force that I can't control*. The higher the score on this dependence measure, the greater the extent of dependence. Key explanatory variables included an indicator for reporting the first cigarette smoked was menthol (n=1100), and indicators for pattern of menthol use: menthol to menthol (n=3930): menthol to non-menthol (n=55); non-menthol to menthol (n=82); and non-menthol to non-menthol (n=459). Analysis includes adolescents who initiated in Wave 3 to provide a larger sample size and also because some ethnic/racial groups do not start smoking until a later age. All regression analysis was controlled for gender, age, and race/ethnicity. Key findings follow (see Appendix A for tables).

Among Wave 3 smokers, 43.0 percent reported menthol use at initiation. A large majority of current smokers at Wave 3 maintained a preference for the type of cigarette they started on across survey waves—36.8 percent began smoking menthols and still smoked menthols at Wave 3, and 49.3 percent began smoking non-menthols and still smoked non-menthols in Wave 3. As previously noted, only a small percentage reported going from menthol to non-menthol (5.9 percent) and from non-menthol to menthol (8.0 percent).

Initiation to menthol is positively associated with smoking daily (OR: 1.99, 95% CI: 1.42–2.80), established smoking (OR: 1.94, 95% CI 1.41–2.66) and lifetime cigarette smoking (OR:1.94, 95% CI: 1.40–2.68) at Wave 3 compared to non-menthol reference group initiators.

Respondents who switched from menthol cigarettes to non-menthol cigarettes were significantly more likely to qualify for smoking daily (OR: 3.30, 95% CI 1.59–6.87), established smoking (OR:3.25, 95% CI: 1.58–6.66) and lifetime cigarette smoking (OR: 3.41, 95% CI: 1.59–7.31) compared with the non-menthol reference group initiators. The greater likelihood of smoking regularly or lifetime smoking may be a function of switching rather than menthol status. For example, respondents who switched from the non-menthol to menthol group were also significantly more likely to qualify for established smoking (OR: 2.05, 95% CI: 1.08–3.87) and Lifetime Cigarette Smoker (OR:1.98 95% CI: 1.03–3.78). However, menthol to menthol respondents were also more likely to qualify for daily smoking (OR: 2.09, 95% CI: 1.45–3.03), established smoking (OR: 2.07, 95% CI: 1.47–2.93) and lifetime cigarette smoking (OR: 2.08, 95% CI: 1.47–2.94) than for the non-menthol reference group.

Most importantly, for all three outcomes—daily smoking, established smoking and lifetime cigarette smoking—the models that include Wave 3 initiators reveal a positive and statistically significant association between menthol at initiation and transitions to higher levels of smoking (smoking daily, OR: 2.11, 95% CI: 1.47–3.03; established smoking, OR: 2.02, 95% CI: 1.44–2.84; and lifetime cigarette smoking, OR: 2.32, 95% CI: 1.64–3.28)

> Respondents who switched from menthol cigarettes to non-menthol cigarettes were statistically significantly more likely to transition to increased smoking for each transition outcome compared with the non-menthol reference group (smoking daily, OR: 3.65, 95% CI: 1.46–9.16; established smoking, OR: 4.72, 95% CI: 1.86–11.99; lifetime cigarette smoking; OR: 7.42, 95% CI: 2.73–20.22). Transitions for each outcome were also more likely for menthol-to-menthol respondents (smoking daily, OR: 2.12, 95% CI: 1.44–3.12; established smoking, OR: 2.09, 95% CI: 1.45–3.00; lifetime cigarette smoking, OR: 2.27, 95% CI: 1.57–3.28). Respondents who switched from non-menthol to menthol were not more likely to transition to increased smoking for any of the transition outcomes.
>
> Menthol cigarette use at initiation is positively and statistically significantly associated with nicotine dependence, according to the results of the ordinary least square regressions for the nicotine dependence (OR:1.04, 95% CI: 0.26–1.82). Menthol-to-non-menthol smokers were significantly more likely to have higher dependence scale scores (OR: 2.33, 95% CI: 1.08–3.59) than non-menthol to non-menthol smokers. However, menthol to menthol smokers have significantly lower scale scores (0.96, 95% CI: 0.08–1.83) than the non-menthol reference group. This latter finding is not robust. No statistically significant results were found in the non-menthol to menthol group.

Klausner (2011 in press) found no evidence in internal tobacco company documents to indicate that people who start smoking menthols compared to non-menthols progress more quickly toward established smoking. No study has primarily examined the rapidity with which people initiate smoking and become regular smokers. Okuyemi et al. (2004), in a study of African American treatment seekers found menthol smokers report three years between their first cigarette and the start of regular smoking was compared to two years for non-menthol smokers. The generalizability of this data is limited.

*Summary*: In order to specifically determine if menthol cigarettes play a significant role in the initiation of smoking, the best study would be to examine the rates of continued or established smoking and dependence among those who initiated smoking with menthol vs. non-menthol cigarettes. There are limitations to the Nonnemaker et al. (2010) study including: (a) a small sample size of ethnic/racial minority groups, (b) inclusion of subjects who only completed all three waves of the study, (c) the lack of national representativeness of the sample, and (d) long intervals between assessments. While replication of these results would be important and an establishment of a longitudinal cohort study would be valuable, the currently presented evidence is persuasive in demonstrating that initiating with menthol cigarettes is associated with increased risk for transitioning to more established smoking.

**Degree of addiction**

There are several ways to assess the degree of addiction to a tobacco product. These include examining the (1) the number of cigarettes smoked, with higher levels of smoking denoting greater dependence,(2) biomarkers of exposure (e.g., urinary total nicotine equivalents (NE), plasma or saliva cotinine, total NE/cigarette, cotinine/cigarette), (3) alterations in the 3 hydroxycotinine (3OH) to cotinine ratio, with higher ratio potentially indicating greater risk for dependence, and (4) self-report measures of dependence which include using the Fagerstrom Test for Nicotine Dependence, a component of the FTND (time to first cigarette or TTF), other measures of dependence, waking up in the middle of the night to smoke and severity of withdrawal symptoms. The majority of these measures have been validated with each other or other indicators of addiction (USDHHS 2010). The section reviews studies using these indices of addiction to assess whether adults and adolescents who smoke menthol cigarettes are more addicted to nicotine than those who smoke non-menthol cigarettes.

***Adults***

Cigarettes per day

The number of cigarettes smoked per day (CPD) has been found to be a strong indicator of nicotine dependence (U. S. Department of Health and Human Services, 2010). TPSAC identified 28 studies that measured CPD by cigarette type. Of these studies, one was excluded because of its small sample size (Ahijevych, Dai, & Chan, 2002). Of the remaining 27 studies, 16 found no CPD differences between menthol and non-menthol cigarette smokers. The studies are summarized below.

Eleven peer-reviewed studies found that menthol cigarette users reported smoking fewer cigarettes per day. The statistical significance of the results varied by race/ethnicity in some of the studies, but the results related to race/ethnicity were not consistent from one study to the next. A limitation of many of the studies is that they did not control for age, race/ethnicity, or income. Results of the 11 studies follow.

- Wang et al. (2010), analyzing a cross-sectional, multi-site, observational study, reported 15.0 vs. 16.3 CPD for menthol vs. non-menthol cigarette users, respectively ($p < 0.01$). Although CPD was statistically significantly higher in white menthol vs. non-menthol cigarette smokers (18.1 vs. 17.2 CPD), there was no difference in African Americans (10.9 menthol vs. 12.1 non-menthol CPD).

- Giovino et al. (2004), analyzing the U.S. component of the International Tobacco Control Policy Evaluation survey, found a statistically significant difference of 18.1 vs. 19.8 CPD ( $p<0.01$) in white menthol vs. non-menthol smokers, respectively. No difference was observed in African Americans.

- Curtin et al., (2010 dependence) analyzing 2003 NHIS, found borderline significance for lower intensity of smoking among menthol vs. non-menthol cigarette smokers overall ($p=0.06$), a statistically significant difference in white menthol vs. non-menthol cigarette smokers (15.5 vs. 16.98 CPD, respectively, $p < 0.05$), but not among African Americans or "other" ethnic group. In an analysis of 2007 NSDUH, white menthol cigarette smokers also showed a lower smoking intensity than white non-menthol cigarette smokers ($p < 0.01$), but this difference was not seen among African Americans or other racial/ethnic groups.

- Stahre et al. (2010), analyzing the 2005 National Health Interview Survey, found 14.6 vs. 17.5 CPD ($p < 0.0001$) in menthol vs. non-menthol cigarette smokers, respectively.

- Analyzing data from the 2002 and 2006/07 Tobacco Use Supplement-Current Population Survey (TUS-CPS), Fagan et al. (2010) found 13.1 vs. 15.0 CPD ($p < 0.001$) in menthol vs. non-menthol cigarette smokers, respectively; Lawrence et al. (2010) found 51.9 percent of menthol cigarette smokers consumed fewer than 10 cigarettes per day compared to 42.3 percent of non-menthol cigarette smokers.

- Pletcher et al. (2006), examining a longitudinal cohort study with young adults examining risk in cardiovascular disease (CARDIA) reported 10 vs. 15 CPD ($p < 0.001$) for menthol and non-menthol cigarette smokers, respectively

- Hyland et al. (2002) examining a national community-based intervention trial found menthol smoking was associated with smoking five cigarettes or less a day compared to smoking more than this amount at baseline after controlling for covariates.

- Gandhi et al. (2009), examining a large sample of treatment seekers, reported 19.0 vs. 23.1 ($p < 0.001$) overall, 15.7 vs. 20.3 CPD ($p<0.001$) in African American menthol vs. non-menthol cigarette smokers, respectively, and 17.0 vs. 22.1 CPD ($p=0.017$) in Hispanic menthol vs. non-menthol cigarette smokers, respectively. No differences were observed in whites ($p=0.09$) or "other" ethnic group.

- Fu et al. (2008), in a multi-site study of Veterans Administration multi-ethic treatment seekers, observed 20 vs. 30 CPD ($p < 0.001$) in menthol vs. non-menthol cigarette smokers, respectively. Subjects were asked to recall CPD for the two years prior to study entry.

- Muscat et al. (2002), in a cross-sectional analysis of a case-control study on smoking and lung cancer, found 28.0 vs. 29.3 CPD in white menthol vs. non-menthol cigarette smokers, respectively (prevalence odd ratio, POR, for smoking $\geq$ 21 CPD vs. smoking $\leq$ 20 CPD= 0.9, 95% CI=0.8-1.0), and 18.2 vs. 20.9 CPD in African American menthol vs. non-menthol cigarette smokers, respectively (POR for smoking $\geq$ 21 CPD vs. smoking $\leq$ 20 CPD= 0.7, 95% CI=0.3-0.9).

Ten peer-reviewed studies showed no differences in CPD between menthol and non-menthol cigarettes. These studies included:

- Treatment studies (Fu, et al., 2008; Mustonen, Spencer, Hoskinson, Sachs, & Garvey, 2005; Okuyemi et al., 2003; Okuyemi, et al., 2007). Okuyemi et al. (2003; 2007) were conducted only in African Americans.

- Community based, cross-sectional studies (Hyland, et al., 2002 at follow-up; Muscat et al., 2009; Okuyemi, et al., 2004 ). Okuyemi et al. (2004) was conducted only in African Americans.

- A cross-sectional analysis of longitudinal cohort and intervention study for smoking and lung health (Murray, Connett, Skeans, & Tashkin, 2007).

- National surveys, including a secondary analyses of the 2005 NHIS and Cancer Control Supplement (Cubbin, et al., 2010) and the 2006/07 TUS-CPS (Ahijevych & Ford, 2010). The latter study found no differences in CPD by menthol status among daily and non-daily cigarette smokers.

Two non-peer-reviewed secondary analyses of cross-sectional surveys also found no CPD differences in menthol vs. non-menthol cigarette smokers.

- Hyland et al. (2010 a) examined the International Tobacco Control Four Country Survey (ITC-4) involving data collection from 7532 individuals between 2002 and 2008. No differences were observed in number of cigarettes within racial/ethnic and gender strata.

- Curtin et al. (2010c) conducted cross-sectional secondary analyses of 2005/06, 2007/08 NHANES and 2007 NSDUH. After controlling for sex, race/ethnicity and age, no overall differences in smoking intensity between menthol and non-menthol smokers were observed with NHANES and no differences were seen with NSDUH. When examining the NHANES data within racial/ethnic groups, no CPD differences were found among whites, African Americans or the "other" ethnic group.

Four non-peer-reviewed treatment-related studies also found no CPD differences between menthol and non-menthol cigarette smokers. The first study examined the response to pharmacological treatments for nicotine addiction (King, Cao, & Matthews, 2010), the second study looked at the efficacy of a motivational treatment for smoking-relapse prevention in pregnant mothers, the third study examined the efficacy of palmtop computers for smoking cessation and the fourth study probed the social determinants of smoking cessation. The latter three studies involved both unadjusted and adjusted analyses (Reitzel, 2010 a, 2010 b) (2010c)

<u>*Summary:*</u> The evidence for differences in number of cigarettes smoked between menthol and non-menthol smokers is mixed. There some evidence to support the finding that menthol cigarette smokers consume fewer cigarettes per day than non-menthol cigarette smokers, particularly in some race/ethnicity groups compared to others, but the evidence within races is also mixed.

<u>Biomarkers of exposure</u>

Cigarettes per day may not be the most precise measure of actual exposure to nicotine (Caraballo et al., 1998). Determining actual nicotine exposure requires measurement of either total nicotine equivalents or cotinine (a metabolite of nicotine). These biomarkers of nicotine exposure can be examined in two ways: overall levels or per cigarette smoked.

*Biomarkers of exposure overall*

As described in chapter 3, TPSAC identified 14 peer-reviewed studies that measured and compared overall levels of biomarkers of nicotine exposure in menthol and non-menthol cigarette smokers. Results of these studies are summarized below.

Four studies found menthol cigarette smokers had statistically significantly higher levels of cotinine compared to non-menthol smokers. These studies were primarily experimental laboratory studies conducted with African American and white smokers (342 vs. 230 ng/ml, p=0.019, Ahijevych, Tyndale, Dhatt, Weed, & Browning, 2002; 239 vs. 180 ng/ml, p=0.02, Ahijevych & Parsley, 1999), smokers with schizophrenia as well as normal smokers (294 vs. 240 ng/ml, p=0.041, J. M. Williams et al., 2007) or African American and white smokers (478.2 vs. 249.1 ng/ml, significant even after adjusting for race, cigarettes per day and mean amount of each cigarette smoked, p=0.03, Clark, Gautam, & Gerson, 1996).

One study (Benowitz, Herrera, & Jacob, 2004) found higher cotinine levels in African American when they smoked menthol compared to non-menthol cigarettes, and lower cotinine levels in white smokers when the smoked menthol vs. non-menthol cigarettes. Cigarettes smokers who had experience in smoking both menthol and non-menthol cigarettes smoked menthol or non-menthol cigarettes with same machine-determined yield and nicotine content for one week before crossing over to smoke the other cigarette type for the second week. Subjects were confined to a residential unit 3 days out of each week. During this stay, subjects were instructed to smoke 20 CPD every 45 min, blood levels of nicotine were measured throughout the day and an intravenous infusion of deuterium labeled nicotine and cotinine were administered to determine rate of rate and pathways of nicotine clearance. Systemic intake of nicotine was not affected by menthol cigarettes. Plasma cotinine averaged over 24 hours was not significantly different between menthol and non-menthol smokers overall. However, there was a condition x race interaction, where $AUC_{nicotine}$ and average cotinine concentrations were higher in African Americans when smoking menthol cigarettes compared to non-menthol and the opposite was observed for whites. Although the sample size in this study was very small (n=14), the results emphasize the importance of examining race x menthol interactions.

Two studies detected a trend toward higher cotinine levels in menthol cigarette smokers compared to non-menthol cigarette smokers. Mustonen et al. (2005) found that African American and white menthol smokers had higher levels of cotinine compared to respective non-menthol smokers in a treatment study, but the differences were not significant (p=0.18). Muscat et al. (2009), in a cross-sectional, community-based study, observed slightly higher plasma cotinine in African American menthol vs. non-menthol smokers, but results were not statistically significant (p=0.09).

Seven studies found no differences in levels of cotinine and total nicotine equivalents (NE) between menthol and non-menthol smokers. These studies are:

- Wang et al. (2010), a cross-sectional, observational multi-site study, involving 24-hour urine collection and adjusted for covariates (lower NE levels were found in unadjusted analysis, 12.8 mg/24 hr vs. 13.5 mg/24hr, p < 0.05);
- Heck (2009), a parallel-arm study with subjects matched for machine-measured tar and balanced for sex, age and race, involving 24 hour urine collection;
- Signorello et al. (2009), a community-based cohort study on cancer occurrence;
- Murray et al. (2007), a community-based cohort intervention study among smokers at risk for COPD;
- Allen and Unger et al. (2007), a cross-sectional survey of African Americans living in an urban area (stratified by gender and controlled for age and employment status);
- Okuyemi et al. (2003; 2007), treatment studies with African American smokers; and
- Ahijevych et al., (1996) a laboratory smoke-exposure studies with female African Americans and whites, balanced for menthol status and race.

*Biomarkers of exposure as measured per cigarette*

The above studies measure overall levels of nicotine exposure; it is also possible to measure nicotine exposure per cigarette. Higher cotinine or nicotine equivalent levels per cigarette may be associated with greater reinforcing effects from each cigarette and subsequently a higher potential for addiction. TPSAC identified six peer-reviewed studies that measured and compared either cotinine per cigarette (cotinine/cigarette) or nicotine equivalents per cigarette (nicotine/cigarette) in menthol and non-menthol smokers.

Four studies showed higher levels of nicotine exposure per cigarette in menthol cigarette smokers compared to non-menthol cigarette smokers.

- Mustonen et al. (2005) found higher cotinine/cigarette in a treatment study of 307 white and African American smokers (23.3 ng/ml vs. 19.4 ng/ml, p=0.004), particularly black male menthol vs. non-menthol smokers.
- Ahijevych et al (2002) reported cotinine/cigarette levels of 20.7 ng/ml vs. 12.4 ng/ml (p=0.05) in an experimental laboratory study of a small number of African American and white female smokers. In a similar sample stratified for race and menthol status, Ahijevych et al. (1999) reported cotinine/cigarette levels of 17.8 ng/ml vs. 13.1 ng/ml, but found no race x menthol interaction.

- Wang et al (2010), using unadjusted statistical analysis, found higher nicotine equivalents (NE)/cigarette overall (0.96 vs. 0.90 mg/cigarette, $p < 0.05$) and within the African American (1.10 vs. 1.00 mg/cigarette, $p<0.05$) but not white (0.86 vs. 0.89 mg/cigarette) menthol cigarette smokers compared to non-menthol cigarette smokers, in a large cross-sectional, observational, ambulatory, multi-site study. When data was adjusted for covariates, no significant differences were observed.

Two studies found no differences in cotinine/cigarette in menthol vs. non-menthol cigarette smokers. One of these studies examined African American and white female smokers enrolled in smoke-exposure laboratory study (Ahijevych, et al., 1996). The other study examined smokers with schizophrenia and smokers without mental illness. These subjects were participants in either a treatment or experimental study in which cotinine/cigarette was adjusted for cigarettes per day, group (with and without mental illness) and ethnicity (J. M. Williams, et al., 2007).

*Summary:* There is conflicting evidence regarding the effects of menthol on nicotine exposure levels as measured by cotinine or 24-hour nicotine equivalents. Four studies found menthol cigarette smokers had statistically significantly higher cotinine levels; one study found higher cotinine levels in African American but not white menthol smokers; two studies detected a trend toward higher cotinine levels in menthol smokers; and seven studies found no difference in nicotine exposure between menthol and non-menthol smokers. The results are also mixed for the effects of menthol cigarette smokers on nicotine levels per cigarette (four of six studies supportive of higher levels, with one study finding effects in unadjusted analysis). Unfortunately, the majority of these studies did not control for race, income or gender, factors that may the affect number of cigarettes smoked or extent of nicotine exposure. In addition, as described in chapter 7, smokers who smoke fewer than 10 cigarettes per day may be a group where menthol effects may be observed.

Subjective measures of dependence

*Fagerstrom Test for Nicotine Dependence (FTND)*

The Fagerstrom Test for Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) is the most widely used dependence measure (U. S. Department of Health and Human Services, 2010). TPSAC identified seven studies with FTND measures—five peer-reviewed, one unpublished secondary analysis, one unpublished submission by Altria. Six found no differences in FTND scores between menthol and non-menthol cigarette smokers. These studies were a cross-sectional survey of African American smokers seen at an inner-city health center generally catering to a low income population (Okuyemi, et al., 2004), a cross-sectional survey of African Americans living in an urban area (Allen & Unger, 2007), a community-based, cross-sectional study aimed at studying smoke exposure and nicotine dependence, adjusted for age, race, sex and education (Muscat, et al., 2009), a community-based, cohort study examining interventions for smoking cessation and lung health in smokers with mild and moderate airflow obstruction (Murray, et al., 2007), a cross-sectional , observational, multisite study (findings after adjusting for age, race, gender, education and tar yields; Altria Client Services on behalf of Philip Morris USA, 2010, June 2010 submission, p. 135) and a treatment study of African American smokers (Okuyemi, et al., 2003).

One study found statistically significantly higher FTND scores in menthol versus non-menthol smokers participating in a treatment study (5.56 ± 1.83 vs. 4.97 ± 1.81 years, $p = 0.007$). This study also found a greater smoking urge at baseline (first study visit) using the Brief Questionnaire of Smoking Urge in menthol vs. non-menthol cigarette smokers (total 33.32 ± 13.79 vs. 30.17 ± 12.63, $p = 0.043$) (King, et al., 2010 secondary analysis, November ). This study was limited by its small sample of African American non-menthol cigarette smokers and white menthol cigarette smokers.

*Time to first cigarette (TTFC)*

A potentially better measure of dependence than FTND is time to first cigarette (TTFC)—the amount of time that lapses between waking and smoking the first cigarette of the day. This item has been found to be highly associated with physical dependence measures such as withdrawal symptoms and relapse to smoking after a cessation attempt (Piper et al., 2008; U. S. Department of Health and Human Services, 2010). Sixteen studies were identified with TTFC measures. Seven of them—six peer-reviewed studies and one unpublished secondary analysis—showed a shorter TTFC with menthol cigarettes. Eight studies—four peer-reviewed and four unpublished secondary analysis—showed no difference in TTFC between menthol and non-menthol cigarette smokers. One unpublished secondary analysis showed menthol cigarette smokers had a longer TTFC than non-menthol smokers.

The seven studies showing a shorter TTFC among menthol vs. non-menthol cigarette smokers follow.

- Ahijevych et al. (1999), in an experimental, laboratory smoke-exposure study in African American and white females, found TTFC of 19.9 vs. 37.4 minutes for menthol vs. non-menthol cigarette smokers, respectively, ($p$=0.02). The sample was stratified for race and menthol status.

- Okuyemi et al. (2003), in a smoking cessation treatment study in African Americans, found 81.7 percent of menthol vs. 69.8 percent of non-menthol cigarette smokers endorsed smoking $\leq$ 30 minutes after waking.

- Gandhi et al. (2009), in a smoking cessation treatment study in African American and white smokers, found 24.3 percent of menthol vs.19.9 percent of non-menthol cigarette users smoked within five minutes of waking.

- Muscat et al. (2009) measured TTFC in a community-based, cross-sectional study of smoke exposure and nicotine dependence in African American and white volunteers. Menthol cigarette smokers were more likely than non-menthol cigarette smokers to have a first cigarette 30 minutes or less after waking (OR: 2.1, 95% CI: 1.0-3.8). The results were adjusted for age, sex, race and education.

- Fagan et al. (2010), in a secondary analysis of pooled 2003 and 2006/07 TUS-CPS data on smokers of six to 10 cigarettes per day, found menthol cigarette smokers were more likely than non-menthol cigarette smokers to have a first cigarette within 5 minutes of waking (OR: 1.22, 95% CI: 1.05, 1.43 after controlling for a number of covariates such as gender, age, race/ethnicity and income).

- Ahijevych and Ford (2010), in a secondary analysis of the 2006/07 TUS-CPS among young adult, non-daily smokers using random effects model, found first cigarette within 30 minutes of waking associated with menthol smoking ($p<0.05$). Non-daily smokers were defined as those who smoked between one and 29 days in the last 30 days.

- Hyland and Kasza (2010 a November submission), in a non-peer-reviewed secondary, multivariate analysis of adult smokers who were interviewed as part of the International Tobacco Control Four Country Survey (ITC-4), found that when considering all respondents, menthol smokers reported fewer minutes to first cigarette compared to non-menthol smokers ($p < 0.01$). The analysis was adjusted for age, education, income, and quitting indicators. The strength of this relationship differed between racial/ethnic groups, with Hispanic respondents (particularly men), experiencing the greatest difference between menthol and non-menthol smokers (significance for menthol X white/Hispanic interaction term <.05).

No differences were observed in eight studies:

- A secondary analysis of the 2006/07 TUS-CPS among daily, young adult smokers (using random effects model, Ahijevych & Ford, 2010); a secondary analysis of pooled 2003 and 2006/07 TUS-CPS among smokers who smoked fewer than six cigarettes per day or more than 10 cigarettes per day (after controlling for a number of covariates such as gender, age, race/ethnicity and income; Fagan, et al., 2010); and a secondary analysis of the pooled 2003 and 2006/07 TUS-CPS when using multivariate logistic regression model (Lawrence, et al., 2010).

- A cross-sectional, multisite observational study (first cigarette < 5 minutes or within 30 minutes, after adjusting for gender, age, race, income, tar yield, smoking amount, etc., Altria Client Services on behalf of Philip Morris USA, 2010 June submission).

- A large multi-site clinical trial comprised of a multi-ethnic sample to test a repeat tobacco cessation treatment found no differences between menthol and non-menthol cigarette smokers who had their first cigarette 30 minutes or less after waking. The study used retrospective recall of both menthol status and TTFC two years prior to study enrollment (Fu, et al., 2008).

- Three studies conducted by Reitzel (2010 a, 2010 b; 2010 c November submissions) also showed no difference by menthol status in time to the first cigarette of the day ≤ 5 minutes using adjusted analysis. These studies include research on the efficacy of a motivationally-based treatment for smoking relapse prevention in racially diverse pregnant mothers (Reitzel, 2010 c November) and palmtop computers used for smoking cessation among African American smokers (Reitzel, 2010 b November). The third study examined social determinants of smoking cessation in a racially diverse population (Reitzel, 2010 a November). In the randomized pregnant female smokers of diverse race, menthol was nearly statistically significantly associated with the time to the first cigarette of the day ≤ 5 minutes in unadjusted analyses (OR : 0.73, 95% CI: .54-1.00, p=0.05; (Reitzel, 2010 c November).

Conversely, in a secondary analysis of the 1988 telephone use surveys from COMMIT (Hyland, et al., 2002), increased menthol use was associated with greater than 60 minutes compared to less than 10 minutes to the first cigarette in the morning (OR: 1.16, 95% CI: 1.00-1.35 after adjusting for such covariates as for sex, age, race/ethnicity, education, amount smoked). Menthol users were slightly less likely to report smoking with 10 minutes after waking (RR: 0.90, 95% CI: 0.81- 0.99).

*Waking up in the middle of the night*

A recently validated measure of dependence is whether a smoker wakes up in the middle of the night. This measure has been related to smoking within 30 minutes of awakening, number of cigarettes per day and has been shown to be a predictor of treatment outcome (Bover, Foulds, Steinberg, Richardson, & Marcella, 2008; Foulds et al., 2006). Two studies have shown an association between menthol smoking and this measure. Gandhi et al. (2009) examined smokers who attended a specialist smoking cessation service and found a higher percent of menthol cigarette smokers vs. non-menthol cigarette smokers endorsed waking up in the middle of night to smoke (55.3% vs. 44.9%, p<0.001). Bover et al. (2008) also examined cigarette smokers who sought treatment as a specialist smoking cessation clinic. In multivariate analysis, night smoking was associated with smoking menthol cigarettes (AOR: 1.50; 95% CI: 1.20-1.87, p=0.0004).

Other dependence measures

Five treatment studies (two peer-reviewed studies and three unpublished secondary analyses) use two other dependence measures to analyze nicotine addiction by menthol status: Nicotine Dependence Syndrome Scale (NDSS) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68). None of these studies showed a consistent menthol effect.

The Nicotine Dependence Syndrome Scale is multidimensional validated measure for nicotine dependence that provides a total score and score for several factors: Drive (craving and withdrawal and compulsion to smoke), Priority (behavioral preference of smoking over other reinforcers), Tolerance (reduced sensitivity to the effects of smoking); Continuity (regularity of smoking) and Stereotypy (invariance of smoking) (Shiffman, Waters, & Hickcox, 2004). Okuyemi et al. (2007) used NDSS to assess dependence in a treatment study of African American light smokers. No significant difference was observed between menthol vs. non-menthol cigarette smokers. In another survey (Florida Behavioral Risk Factor Surveillance System), using six items from the NDSS, non-menthol cigarette smokers reported greater dependence compared to menthol cigarette smokers, but multivariate analysis showed that the odds of menthol smoking were not related to nicotine dependence (Hooper et al., 2011).

The Wisconsin Inventory of Smoking Dependence Motives (WISDM-68) is a comprehensive, multi-dimensional measure of dependence that yields an overall smoking dependence score (WISDM-68 total score) as well as subscale scores for critical dimensions of dependence, including non-physical indices of dependence e.g., affiliative attachment, automaticity, social/environmental goals (Piper et al., 2004). Higher scores on the WISDM-68 are indicative of greater tobacco dependence. Three non-peer-reviewed secondary analysis of treatment studies using WISDM-68 were conducted by Rietzel (2010 a, 2010 b; 2010 c November).

In the first study, Reitzel (2010 b November) used WISDM-68 to measure dependence in a smoking cessation trial designed to determine the efficacy of using palmtop computers for cessation in African American smokers. Menthol cigarette use was not statistically significantly associated with the WISDM-68 total score in unadjusted analyses or in analyses adjusted for age, sex, partner status, income, employment status, and educational achievement. When examining each of the 13 subscales of the WISDM-68, in unadjusted analyses, menthol cigarette use was significantly associated with WISDM-68 Craving ($\beta$= .46, SE = .21; $p$ = .03) and marginally associated with Taste/Sensory Processes ($\beta$= .41, SE = .22; $p$ = .06). Specifically, menthol cigarette use was associated with more craving and taste/sensory-related dependence than non-menthol use. In adjusted analyses, the only significant association was between menthol cigarette use and WISDM-68 Taste/Sensory Processes ($\beta$= .52, SE = .24; $p$ = .03).

Reitzel (2010 c November) also examined dependence with the WISDM-68 in a study that randomized racially diverse pregnant female smokers of diverse race in clinical trial designed to test the efficacy of a motivationally based treatment for smoking relapse prevention. Menthol cigarette use was not statistically significantly associated with the WISDM-68 total score in unadjusted analyses or in analyses adjusted for age, race/ethnicity, partner status, income, and educational achievement. When the association between menthol use and each of the 13 subscales of the WISDM-68 was examined, in unadjusted analyses, menthol cigarette use was significantly associated with WISDM-68 Cue Exposure/Associative Processes ($\beta$= -.52, SE = .21; $p$ = .01) and Tolerance ($\beta$= .38, SE = .20; $p$ = .05). Specifically, menthol cigarette use was associated with less dependence in response to cue exposures/associative processes, but more tolerance-related dependence relative to non-menthol use. However, these significant associations were not maintained in adjusted analyses.

In the third study that utilized the WISDM-68, Reitzel (2010 a November submission) conducted a longitudinal cohort study designed to examine the social determinants of smoking cessation in 424 racially/ethnically diverse adult smokers. Menthol cigarette use was again not statistically significantly associated with the WISDM-68 total score in unadjusted analyses or in analyses adjusted for age, sex, race/ethnicity, partner status, income, employment status, and educational achievement. None of the 13 subscales of showed any significant relationships in unadjusted or adjusted analyses.

<u>Withdrawal symptoms</u>

Another measure of physical dependence is the extent to which menthol vs. non-menthol cigarette smoking leads to more severe withdrawal symptoms. Only one study examined this topic. Okuyemi et al. (2007), in a treatment study of African American smokers, found no differences in reported withdrawal symptoms between menthol and non-menthol cigarette smokers.

*<u>Summary</u>*: The evidence is conflicting regarding the effects of menthol on subjective measures of dependence in adult smokers. This conflicting evidence is observed whether they studies are population-based surveys, longitudinal cohort studies or treatment studies.

***Adolescents***

TPSAC identified six peer-reviewed articles and three unpublished secondary analyses that examined indications of nicotine dependence in adolescent menthol and non-menthol smokers. Five peer-reviewed studies and the three unpublished secondary analyses showed higher indicators of dependence.

Hersey et al. (2006), who examined data from 2000 and 2002 NYTS, conducted one of the most solid adolescent studies. This study controlled for demographic background (i.e., age, gender and race/ethnicity) and smoking behavior (i.e., length, frequency, and level of smoking) and used the validated Nicotine Dependence Scale for Adolescents (NDSA). Smokers were classified as menthol or non-menthol cigarette smokers based on their usual brand. The study found that adolescent menthol cigarette smokers were 45 percent more likely to score above the median on the NDSA than adolescent non-menthol cigarette smokers ($p=0.006$).

In another recent study, Hersey, Nonnemaker and Homsi (2010) examined the 2006 NYTS, using a logistic regression model that controlled for background (i.e., school level, gender, race/ethnicity) and smoking behavior (i.e., length, frequency, and level of smoking). Smokers whose usual brand was menthol had a significantly greater likelihood of endorsing needing a cigarette within 1 hour than among non-menthol smokers (OR=1.86, $p=0.003$). This relationship was also observed among established smokers (smoking > 100 cigarettes in a lifetime; OR=2.06, $p=0.001$). Among established smokers, smoking a menthol brand was significantly associated with feeling restless and irritable without smoking (OR=1.39, $p=0.049$) and with experiencing craving after going without smoking for a few hours (OR=1.35, $p=0.035$).

Wackowski and Delnevo (2007) also analyzed 1345 "established" adolescent smokers (smoked in the past 30 days and smoked at least 100 cigarettes in a lifetime) from the 2004 NYTS. Those who usually smoked menthol cigarettes had higher odds of endorsing two of four dependence related statements, even after controlling for demographic characteristics and smoking pattern. Compared to non-menthol cigarette smokers, menthol cigarette smokers were 2.6 times more likely to go less than an hour before needing a cigarette and 1.6 times more likely to experience cravings after not smoking for a while ($p<.05$). No significant differences were found for items inquiring the extent to which they feel restless or irritable after not smoking for a while and their perception about their ability to quit smoking now if they wanted to.

Muilenburg and Legge (2008) surveyed middle and high school students in six public institutions in a large metropolitan area in southeastern U.S. Respondents included 2068 adolescents who had used or at least experimented with smoking. Compared to non-menthol cigarette users, menthol cigarette users smoked significantly more cigarettes based on various indicators of amount (total cigarettes smoked ever, days smoked in month, cigarettes smoked in month and ever smoked daily, OR: 3.41 to 5.35, $p \leq 0.01$), irrespective of race. Menthol cigarette smokers were statistically significantly more likely to report a shorter length of time since their last cigarette (OR=3.22, $p \leq 0.01$). It was important to note that only 18.6 percent of respondents reported smoking menthol cigarettes, though the population was predominantly African American. African American adolescent smokers have a much higher prevalence of menthol cigarette smoking (see chapter 4).

Collins and Moolchan (2006) assessed adolescent smokers (531 menthol and 41 non-menthol smokers) who were being recruited for a smoking cessation study. A higher percentage of menthol cigarette smokers endorsed smoking within the first 5 minutes of awakening compared to non-menthol smokers (45 percent vs. 29 percent). No differences were observed for FTND scores or smoking rate. This study did not describe the racial/ethnic composition of the menthol and non-menthol groups, which could be a potential confounding factor.

A non-peer-reviewed study, Nonnemaker et al. (2010) analyzed a three-year longitudinal cohort, school-based study of 12–18 year olds using the American Legacy Longitudinal Tobacco Use Reduction Study. As noted above (see *Trajectory from initiation to regular smoking or dependence*), this study demonstrated that initiation to menthol cigarettes was positively associated with smoking daily (OR: 1.99, 95% CI: 1.42-2.80), established smoking (OR: 1.94, 95% CI 1.41-266) and lifetime cigarette smoking (OR: 1.94, 95% CI: 1.40-2.68). Menthol use at initiation was also positively and statistically significantly associated with nicotine dependence (Beta: 1.04, 95% CI: 0.26-1.82).

Hersey, Nonnemaker, Homsi and Allen (November 2010) examined a 2002 survey of 5,511 youth in 48 U.S. schools sponsored by Legacy for Health. Analyses were conducted with 587 youth who had smoked cigarettes over the past three days and had a cotinine level of 5 ng/ml or higher. The study provided descriptive analysis and used multiple regression to model cotinine levels, or score on the Nicotine Dependence Scale for Adolescents controlling for age, sex; race/ethnicity, and the length, frequency, and level of smoking. Some of the more interesting results were the following: (1) Over all youth, in models that included cigarettes per day smoked, smoking menthol cigarettes did not have greater association with cotinine levels than smoking non-menthol cigarettes. (2) Among youth who smoked for less than one year, there was a statistically significant interaction between menthol use and the mean number of cigarettes smoked per day—menthol cigarette use was associated with increased cotinine levels among youth who smoked more heavily ($p=0.048$ to $p<0.001$). (3) Among youth who smoked for less than one year, smoking menthol cigarettes rather than non-menthol cigarettes was associated with statistically significantly higher levels of nicotine dependence ($p=0.049$). (4) Findings were similar for whites and non-whites, although samples sizes were quite small in some ethnic/racial groups.

Curtin et al. (June 2010c) conducted cross-sectional secondary analyses of NYTS. With regard to smoking intensity, current menthol cigarette smokers compared to non-menthol cigarette smokers were significantly ($p < 0.001$) more likely to be overrepresented in the higher use categories (>20 cigarettes, 13.1 percent vs. 5.1 percent) and less represented in the lower use categories ($\leq$ 10 cigarettes per day, 73.3 percent vs. 82.9 percent). This observation was statistically significant in both genders and among whites and other racial/ethnic groups, but not African Americans. When controlling for age, gender and race/ethnicity, current menthol cigarette smokers were more likely to smoke 11–20 cigarettes (OR: 1.43, 95 percent CI: 0.97-2.10) and >20 cigarettes (OR: 2.25. 95 percent CI: 1.32-3.85) compared to non-menthol smokers.

DiFranza et al. (2004) found no differences in dependence measures between menthol and non-menthol smokers in a study that followed 267 seventh graders in the Boston area for 30 months. Students were asked at the end of the study if the first cigarette they had smoked was menthol or non-menthol. There were no differences in responses to the Hooked on Nicotine Checklist between menthol and non-menthol smokers. It is important to note that about 50 percent of this population did not know if the first cigarette they smoked was menthol or non-menthol. It was not known what cigarette type subjects continued to smoke.

(See Table 5 for summary of results on adolescence and dependence.)

*Summary*: There is strong evidence to support that adolescent menthol cigarette smokers are more dependent on nicotine than adolescent non-menthol cigarette smokers. Seven of the nine studies reviewed by TPSAC involved multivariate analysis that controlled for demographic characteristics and smoking history. Differences were found on a dependence measure (Hersey, et al., 2006) and on items related to smoking urgency (e.g., needing a cigarette within 1 hour, shorter time to needing a cigarette, inability to go for less than one hour before feeling like they need a cigarette, shorter length of time since last cigarette), and craving or feeling irritable/restless for a cigarette after not smoking for a while (among established smokers) (Hersey, Nonnemaker, & Homsi, 2010; Muilenburg & Legge, 2008; Wackowski & Delnevo, 2007). Furthermore, studies showed greater cigarette use among menthol smokers (Curtin, et al., 2010c June 2010 Muilenburg & Legge, 2008; Nonnemaker, et al., 2010). Hersey et al. (November 2010) observed greater cigarette use among specific populations of menthol smokers, but less cigarette use among menthol smokers overall. A study that did not conduct a multivariate analysis found more menthol cigarette users smoked within five minutes of waking than non-menthol cigarette users—a measure of smoking urgency (Collins & Moolchan, 2006). Only one small study did not find significant differences on a dependence measure, but this study was limited by problems of recall and small sample size (DiFranza, et al., 2004).

**CESSATION**

This section examines whether menthol cigarette smokers are more or less likely to successfully quit than non-menthol cigarette smokers. Three types of research were reviewed: cross-sectional population surveys, longitudinal cohort studies (e.g., community tobacco intervention, health effects) and clinical trials of cessation treatments. TPSAC also assessed the effectiveness of approved pharmacologic treatments in menthol cigarette smokers compared to non-menthol cigarette smokers. This section first presents the evidence on cessation in adults, followed by the evidence on cessation in adolescents.

**Cessation in adults**

Twenty-five studies were identified and based predominantly on the results that adjusted for confounding factors, 13 showed no effect on cessation rates by menthol status, two studies showed a better outcome among menthol smokers, and 12 studies showed a detrimental effect. These studies are summarized below.

***Studies showing no significant differences in cessation between menthol vs. non-menthol smokers***

Population surveys

Alexander et al. (2010) used the 2006 TUS-CPS (n=30,146 current everyday or some day smokers 18 years or older) to determine differences in quitting behaviors between menthol and non-menthol cigarette smokers among groups with different occupational status. The results showed a trend toward a greater number of menthol cigarette smokers ever quitting smoking for one day or longer (70.9 percent vs. 69.5 percent, p=0.09), a statistically significantly higher number of menthol smokers quitting smoking for one day or longer *in the past 12 months* (55.0 percent vs. 50.3 percent, p<0.001). No differences between menthol and non-menthol cigarette smokers were seen in number of quit attempts in the past 12 months (mean=4.0, SE=0.2 vs. mean=3.8, SE=0.1) or longest length of time (months) they stopped smoking (mean=2.0, SE=0.2 vs. mean=2.2, SE=0.2). For blue-collar workers, menthol smokers were more likely to ever stop smoking for one day or longer compared to non-menthol smokers (71 percent vs. 65 percent, p=0.0008) and to stop smoking for one day or longer *in the past 12 months* (56 percent vs. 49 percent, p=0.002). Among service workers, menthol smokers were less likely to ever stop smoking for one day or longer compared to non-menthol cigarette smokers (65 percent vs. 71 percent, p=0.007). Using logistic regression to control for occupational status and workplace policies, no significant difference was seen in the likelihood of menthol vs. non-menthol cigarette smokers ever to quit smoking for one day or longer (OR: 0.98, 95% CI: 0.83-1.15).

Fagan et al. (2010) conducted a secondary analysis with the pooled 2003 and 2006/07 TUS-CPS. Data was analyzed among current daily smokers (n=46,273, 18 years or older). Statistically significant differences were observed for number of quit attempts made for one day or longer among those who made quit attempts in the past 12 months, with the higher number observed for the menthol cigarette smokers (mean=2.23, SE=0.04 vs. mean=2.14, SE=0.02, p <0.05). There were no differences in the length of abstinence in the past 12 months between menthol and non-menthol cigarette smokers who tried to quit (mean=0.32, SE= 0.01 for both groups). Bivariate and multivariate models did not show any significant association between usual cigarette brand (either menthol vs. non-menthol) and quit attempts in past 12 months (OR: 0.92, 95% CI: 0.83-1.02 to OR: 1.10, 95% CI: 0.91-1.34) or duration of quit attempts > 2 weeks in the past 12 months across various number of cigarettes categories (OR: 0.93, 95% CI: 0.79-1.12 to OR: 1.05, 95% CI: 0.82-1.36).

Longitudinal cohort studies

Murray et al. (2007) examined smokers (n=5,887 smokers aged 35-60 years) with evidence of mild to moderate airflow obstruction who enrolled in the Lung Health Study from 1986 to 1989. Menthol status was determined by inquiring whether the type of cigarettes they smoked was plain or menthol. Participants were randomly assigned to one of three intervention groups to determine their effects in preventing COPD: (a) smoking cessation and ipratropium, an inhaled bronchodilator, (b) smoking intervention and placebo inhaler and (c) usual care. For the smoking cessation analysis, data for the five years after enrollment was examined. At annual follow-up visits, an inquiry was made on whether participants had smoked cigarettes in the past 12 months. Menthol vs. non-menthol differences were examined for three classifications: (a) sustained quitters (participants who were biochemically confirmed as quitters at the five annual visits and could recall no month with mean smoking greater than one cigarette/day at any annual visit; (b) intermittent smokers (participants who were biochemically confirmed as quitters at some annual visits and as smoking at other annual visits, (c) continuing smokers (participants who were identified as smoking at all annual visits). No significant differences between menthol vs. plain cigarette smokers were observed in the percentage of participants who were sustained quitters (male: 16.6 percent vs. 17.2 percent; females: 13.8 percent vs. 15.4 percent) intermittent (male: 26.0 percent vs. 26.9 percent; females: 30.4 percent vs. 28.7 percent) or continuous smokers (male: 57.3 percent vs. 55.9 percent; female: 55.9 percent vs. 55.9 percent) by use of menthol cigarettes.

Hyland et al. (2002) examined smokers (n=13,268 smokers 25-64 years old) enrolled in the Community Intervention Trial for Smoking Cessation (COMMIT), which involved selecting a random sample of smokers from a representative sample. COMMIT was a randomized community-based intervention trial for smoking cessation in 11 matched pairs of communities. These smokers completed a telephone tobacco use survey in 1988 and were re-interviewed in 1993. Use of menthol cigarettes (determined by report of whether the type of cigarettes of the brand that the participant smoked was menthol or plain) was analyzed at baseline and in 1993 when six-month cessation was assessed. Successful cessation was measured by a no response to the questions, *Do you smoke now?* and *Have you smoked any cigarettes in the past 6 months?* Multivariate regression was used to assess association with menthol use with outcomes controlling for other factors related to dependence (e.g., age, sex, education, cigarettes per day, time to first cigarette, history of past serious quit attempts). No association was observed between menthol and cessation both overall (RR: 1.00, 95% CI: 0.90-1.11) and in race-specific analysis (whites RR: 0.94, 95 percent CI: 0.83-1.05; African Americans RR: 1.04, 95 percent CI: 0.73-1.47; Hispanic RR: 1.22, 95 percent CI: 0.80-1.87). However, the data showed greater number of more than two quit attempts among menthol smokers (OR: 1.16, 95% CI: 1.03-1.30).

In a non-peer-reviewed study, Hyland et al. (2010 b submission to FDA) conducted another analysis of the COMMIT data set. A total of 2,095 cohort members was included in the analysis. The association between cessation as determined in 2005 and use of menthol cigarettes in 1988 through 2001 was examined using logistic regression models which controlled for gender, age, race, education, frequency of alcohol consumption, age started smoking, amount smoked, time to first cigarette, number of past quit attempts, other smokers in the household, and desire to quit smoking. There were three key cessation indicators.

> (a) Quit Attempts in 2005: *Since 2001, how many times have you made a serious attempt to quit smoking?* A response of 1 or greater was considered a quit attempt.
>
> (b) Cessation in 2005*: Have you smoked any cigarettes in the last six months?* A current smoker was defined as a person who smoked in the six months before the survey; a quitter was defined as a person who was a current smoker in 2001 and a former smoker in 2005.
>
> (c) Cessation in 2005 among those who attempted.

Menthol smokers were equally as likely as non-menthol smokers to try to quit smoking in the overall population (OR: 0.91, 95% CI: 0.72-1.15, 57.5 percent vs. 60.3 percent), among African Americans (OR: 1.24, 95% CI: 0.27-5.67, 55.3 percent vs. 62.5 percent) and among whites (OR: 0.91, 95% CI: 0.71-1.17, 58.8 percent vs. 61.0 percent). Menthol smokers were equally likely to be successful in quitting in the overall population (OR: 0.84, 95% CI: 0.61-1.15, success rates 14.7 percent vs. 18.5 percent) and in whites (OR: 0.79, 95 percent CI: 0.56-1.11, 14.7 percent vs. 19.1 percent). The odds ratio for successful quitting could not be calculated for African Americans because of the small sample size. For African Americans, success rates we were 17.0 percent for menthol and 9.4 percent for non-menthol. Menthol smokers were also equally likely as non-menthol smokers to be successful in quitting among those who had made a quit attempt as observed in the overall population (OR: 1.03, 95% CI 0.71-1.48, success rates 22.1 percent vs. 24.5 percent) and among whites (OR: 0.96, 95% CI: 0.65-1.41, success rates 22.0 percent vs. 25.2 percent). Among African Americans, the success rate was 26.9 percent for menthol vs.

10.0 percent for non-menthol smokers. Unfortunately, in this study, the number of blacks was quite low (n=91 total, and lower when examining the effects of menthol).

Muscat et al. (2002) examined adult smokers (19,545 current and ex- smokers, 16,540 non-menthol smokers and 3,005 menthol smokers) enrolled in a case-control study on smoking tobacco-related cancers between 1981 and 1999. Ever smokers were defined as having smoked at least one cigarette each day for one year. Current smokers smoked at least one cigarette each day for the preceding year. Ex-smokers were smokers who did not smoke at least one cigarette each day for the preceding year. Menthol status was based on whether the subject reported the last brand smoked as menthol. The results from this cross-sectional dataset showed that a higher percentage of former smokers among African American non-menthol smokers vs. menthol smokers (35.7 percent vs. 29.4 percent, $p < 0.01$) and white non-menthol smokers vs. menthol smokers (52.9 percent vs. 43.7 percent, $< 0.01$). Unconditioned logistic regression analysis was used to estimate the prevalence odds ratio (POR) of current vs. ex-smoker by menthol status. The models adjusted for sex, education, case-control status, years of smoking and cigarettes per day. Menthol was not associated with continued smoking. The POR was not significant among African American (POR: 1.1; 95% CI: 0.8-1.4) or white (POR: 1.1, 95% CI: 1.0-1.3) smokers. The main weakness of this study was the use of a convenience sample rather than a random population based sample. In addition, the sample was mostly older adults. Furthermore, the criterion for ex-smokers was quite unusual (not smoking each day for the past year).

In an in-press article, Blot et al.(Blot et al., in press) analyzed data from the Southern Community Cohort Study (SCCS), a prospective study of 85,806 racially diverse adults to examine racial disparities in cancer and other chronic diseases. Adults ages 40–70 years residing in 12 southern states were predominantly recruited through mailings to stratified random samples of the general population and at a community health center. Subjects were followed from March 2002 to September 2009. Subjects were classified as smokers (defined as those who smoked 100 cigarettes in their lifetime) or former smokers. Menthol status was determined by whether or not they usually smoked menthol cigarettes. During follow-up, subjects were classified as quitting or continuing to smoke. Results from data collected at the time of enrollment showed that African American, menthol and non-menthol cigarette smokers had equal odds of quitting after adjustments for age, income, education, recruitment source, pack years smoked, BMI) (OR=1.03; 95% CI: 0.96 to 1.11). White menthol cigarette smokers were statistically significantly more likely to quit than non-menthol cigarette smokers (OR=1.55, 95% CI: 1.41 to 1.70). Among smokers who were followed for an average of 4.3 years (7,886 and 4,487 current smokers of menthol and non-menthol during baseline, respectively), the odds (adjusted for the same variables above plus race) of quitting were similar among menthol and non-menthol smokers (OR=1.02, 95% CI: 0.89 to 1.16). This is a large study, but one of the weaknesses is that older age of this population, which may limit the generalizability of results.

<u>Treatment studies</u>

Cropsey et al. (2009) examined differences in treatment outcome among white and African American female prisoners (N=233; white=109, 38.1 percent menthol while in prison; African American=124, 81.3 percent menthol while in prison) who underwent a 10-week nicotine replacement and group psychotherapy intervention. Some were randomized to a wait list for six months before entering the cessation component. Smoking cessation was assessed across the 12-month follow-up period (weeks 1-10 and 1 week and 3, 6 and 12 months post-treatment). Seven-day point prevalence abstinence (not smoking in the past seven days) was determined at each assessment period. Although whites had statistically significantly higher overall smoking cessation rates across time compared to African American women, menthol cigarettes were not associated with these differences in quit rates.

Interaction between race and smoking menthol was not significant. This study was limited by the relatively young age of participants (mean age was early to mid-thirties) and the select population of smokers.

Fu et al. (2008) examined the effects of menthol cigarette smoking on cessation among a multi-ethnic sample of smokers (N=1,343, white=76%, African American=14%, other=10%, 342 menthol users, 19 years and older) enrolled in a multi-site, randomized controlled trial of an intervention designed to facilitate repeat tobacco cessation treatment. Subjects who had received a prescription for NRT or bupropion for smoking cessation from one of five Veterans Administration Medical Centers were assigned to usual care or intervention. The intervention consisted of phone calls to patients with the aid of a computerized provider prompt to assess smoking status, interest in making another quit attempt and in preferences for tobacco treatment. The primary outcome was seven-day point prevalence abstinence at six months post-randomization. Menthol status was assessed with a follow-up survey by inquiring if subjects smoked menthol cigarettes two years ago (one year prior to the index quit attempt). Analysis on the effect of menthol was adjusted for covariates including predictors of abstinence as well as ethnicity, gender, site and time to first cigarettes. No significant effects of menthol on smoking cessation rates were observed, using multivariate analysis (OR: 1.31, 95% CI: 0.95-1.82) and unadjusted logistic regression analysis (OR: 1.14, 95% CI:0.85-1.53). Although a significant interaction between the intervention and menthol cigarettes was observed (p=0.02), with greater success among menthol smokers in the treatment condition (OR: 1.80, 95% CI: 1.18-2.76), this interaction was no longer statistically significant after Bonferroni correction for multiple comparisons. Therefore, this study found menthol did not decrease smoking cessation among older smokers during a quit attempt aided by pharmacotherapy. No differences were found in number of 24-hour quit attempts in the past month. The primary weaknesses of this study was the two-year recall for the assessment of menthol cigarettes with no brand switching information during this period, and the older age of the smoking population (mean age=56 years old).

Harris et al. (2004) examined predictors for successful quitting among 600 African Americans participating in a smoking cessation trial. This cessation study involved a double-blind, placebo-control randomized trial examining bupropion vs. placebo prescribed for seven weeks. Outcome variable was seven-day biochemically confirmed abstinence among 535 participants who completed the seven-week medication phase. Although the univariate analysis showed that not smoking menthol cigarettes was a predictor of cessation success (p=0.0062; 41.53 percent vs. 28.3 percent), menthol cigarette use was not a predictor in the logistic regression analysis. It should be noted that this is the same population of smokers used in the Okuyemi et al. (2003) study described below.

In a non-peer-reviewed secondary analysis of data, Reitzel (2010 a, 2010 b; 2010 c November) examined the menthol cigarette effects in three treatment studies, two of which found no differences in treatment outcome. One study (Reitzel, 2010 a), Project CARE, was a longitudinal cohort study designed to examine the social determinants of smoking cessation and included 424 adult (21 years or older) treatment-seeking smokers (34 percent non-Latino African Americans, 33 percent Latino, and 33 percent non-Latino white) recruited from the Houston, TX area and enrolled from 2005–2007. Menthol status was determined by asking participants if their regular brand of cigarettes was menthol or non-menthol. All subjects received six weeks of nicotine patch treatment, six brief smoking cessation counseling sessions and self-help materials. Treatment success was defined as biochemically verified continuous abstinence from smoking since the quit date through week 26 post-quit. Both unadjusted and adjusted analyses were conducted. Menthol cigarette users had lower rates of continuous abstinence than non-menthol cigarette users at all follow-up points. However, menthol cigarette use did not statistically significantly predict continuous abstinence from smoking in analyses adjusted for time (*p*

=0 .73; *n* =680), or in analyses adjusted for age, sex, race/ethnicity, partner status, income, employment status, educational achievement, time, cigarettes smoked per day, and time to the first cigarette of the day (*p* = 0.84; *n* = 607). Continuous abstinence rates within each racial/ethnic group did not differ by menthol cigarette use status in unadjusted or adjusted analysis.

In the other non-peer-reviewed paper, Reitzel (2010 b November) conducted a secondary analysis of Project BREAK FREE, a randomized clinical trial that examined the efficacy of smoking cessation treatment delivered on palmtop computers. This trial recruited 399 treatment seeking, African American smokers from 2005–2007 from the Houston, TX area. Menthol status was determined by asking participants if their regular brand of cigarettes was menthol or non-menthol. Outcome variable and analysis was similar to the previously described study (Reitzel, 2010 a November). Menthol users had higher rates of continuous abstinence than non-menthol users at all follow-up points. However, menthol cigarette use did not significantly predict continuous abstinence from smoking in analyses adjusted for time and treatment group (*p* = .40; *n* = 573), or in analyses adjusted for age, sex, partner status, income, employment status, educational achievement, time, treatment group, cigarettes smoked per day, and time to the first cigarette of the day (*p* = .30; *n* = 457).

***Studies showing a better rate of cessation among menthol smokers***

<u>Population surveys</u>

Cubbin et al. (2010) conducted a secondary data analysis using 2005 NHIS and Cancer Control Supplement of current smokers (those who smoked at least 100 cigarettes and currently smoke some days or everyday) and former smokers (those who smoked at least 100 cigarettes but did not smoke right now) (n=31,428, ages 25-65). Menthol status was determined by asking whether the usual cigarette brand was menthol (in the 12 months before quitting for former smokers). All analyses were weighted for income and education. No statistically significant differences were observed for quit attempts in the past year by cigarette type among current everyday smokers by gender and racial/ethnicity. There was, however, a trend for menthol smokers for both genders and all racial/ethnic groups to have higher levels of quit attempts than similar subgroups of non-menthol smokers (e.g., as great as 10–20 percent difference). When examining quit duration among former smokers, statistical significance was observed only in white female menthol smokers. They had abstained about 2.5 years longer than white female non-menthol smokers (15.0 vs.12.5 years, p<0.01).

In a non-peer-reviewed study, Hyland and Kasza et al. (November 2010 submission) conducted a secondary analysis of a nationally representative sample of adult smokers (N=7532) who were interviewed as part of the International Tobacco Control Four Country Survey (ITC-4) between 2002 and 2008. ITC-4 is an ongoing prospective cohort survey conducted with nationally representative respondents from four countries, including the United States. Current smokers were defined as persons who reported having smoked at least 100 cigarettes in their lifetime and who currently smoked on at least a monthly basis. Menthol cigarette use status was determined by the brand of cigarettes smoked. Cessation behaviors were defined as:

> (a) Making a quit attempt. Respondents were asked: *Have you made any attempts to stop smoking since we last talked with you?*
>
> b) Successful smoking cessation, defined as no longer smoking on at least a monthly basis; and
>
> c) Successful cessation among those making a quit attempt.

Adjusted association between menthol cigarette use and cessation behaviors were estimated for respondents overall, as well as for separate racial/ethnic groups and genders. The menthol x race/ethnicity and menthol x gender interaction terms were specifically tested in the overall models. Multivariate analyses included an adjustment for respondent gender and race/ethnicity (unless stratified on these variables), age, education, income, ever made a quit attempt before baseline, and intention to quit. Additionally, outcomes were also adjusted for the heaviness of smoking index. Results showed white respondents (particularly women) who smoked menthols were less likely than those who smoked non-menthols to report making quit attempts (OR: 0.84, 33.5 percent vs. 38.4 percent in both sexes and OR: 0.81, 34.3 percent vs. 40.1 percent in females, $p<0.05$), while African American women who smoked menthols were more likely to report successful cessation (OR:3.58, 12.8 percent vs. 8.5 percent, $p<0.05$) and successful cessation among those who attempt to quit (OR:3.96, 24.6 percent vs. 15.8 percent, $p <0.05$) than non-menthol cigarette smokers.

***Poorer cessation among menthol vs. non menthol cigarette smokers***

Population surveys

Gundersen, Delnevo and Wackowski (2009) analyzed data from the 2005 U.S. National Health Interview Survey (NHIS) to determine the relationship between race/ethnicity, menthol smoking and cessation in a nationally representative sample. The sample included 7,815 white, African American and Hispanic current and former cigarette smokers who did not use other tobacco products and who had made a quit attempt. Menthol status was determined by whether or not the usual brand of cigarettes in the past 12 months or the 12 months prior to quitting were menthols. Outcome variables were current smokers (having smoked 100 cigarettes in a lifetime and now smoking everyday or some days) vs. former smokers (having smoked 100 cigarettes in a lifetime but not currently smoking). Multiple logistic regression analysis was used to test the relationship of menthol smoking with cessation, controlling for various demographic, smoking behavior and risk perception factors (e.g., sex, age, cigarettes per day, education, perceived likelihood of getting cancer). Overall, menthol smokers were less likely than non-menthol smokers to be former smokers (56.9 percent vs. 61.5 percent, $p < 0.01$). This relationship was statistically significant among African Americans (43.7 percent vs. 62.1 percent, $p < 0.01$) and Hispanics (48.5 percent vs. 61.2 percent, $p < 0.01$), but not among whites (62.8 percent vs. 61.6 percent, $p=0.44$). In the multiple logistic regression analysis, when African Americans and Hispanics were collapsed into non-whites, non-white menthol smokers were statistically significantly less likely to have quit smoking compared to non- menthol smokers (AOR: 0.55, 95% CI: 0.43-0.71, $p<0.01$). This result was largely driven by the Hispanic group (AOR; 0.61, 95% CI: 0.39-0.97, $p=0.04$) and not by African Americans (AOR; 0.78, 95% CI: 9.56-1.00, $p=0.15$). Among white smokers, menthol cigarette smokers were more likely to be former smokers than non-menthol smokers (AOR; 1.17, 95% CI: 1.00-1.36, $p<0.05$).

Similarly, Stahre et al. (2010) conducted a secondary analysis of cross-sectional data from the 2005 National Health Interview Survey Cancer Control Supplement examining current smokers (n=6511, 1,700 menthol; 4,355 non-menthol) and former smokers (n=6774, 1,515 menthol smokers; 4,434 non-menthol smokers). Univariate analysis of the data was conducted to determine variables that differed significantly by menthol status. Menthol status was determined by whether or not the respondent's usual brand of cigarettes was menthol. Multiple logistic regression analysis modeled the relationship between menthol smoking status, demographic characteristics and smoking-related characteristics on the population quit ratio and utilization of quit aids. In the univariate analysis, the quit ratio was significantly higher among non-menthol vs. menthol smokers (50 percent vs. 47 percent, $p=0.014$). When examining quit ratios within races, no significant differences in quit ratios for menthol vs. non-menthol smokers were observed for whites (52 percent vs. 50 percent), Asian Americans (38 percent vs.

42 percent), American Indian/Alaska Native (52 percent vs. 35 percent) or Hispanics (40 percent vs. 45 percent). However, quit ratios were significantly lower for African American menthol vs. non-menthol smokers (34 percent vs. 49 percent, $p < 0.001$). In multiple logistic regression analysis, there was a significant interaction between race and menthol smoking status. African American menthol smokers were significantly less likely to quit smoking than white non-menthol smokers (OR: 0.72, 95% CI: 0.53-0.97). No analysis was done with menthol status alone. No differences were found in utilization of quit aids.

Trinidad et al. (2010) conducted a secondary data analysis of the 2003 and 2006-07 TUS-CPS that examined current smokers and their interest in seriously quitting in the next six months and former smokers (ever smokers) who had successfully quit for at least 6 months at the time of the survey. In a multiple logistic regression analysis, African American menthol smokers were significantly less likely than white non-menthol smokers to have quit smoking (AOR: 0.72, 95 percent CI: 0.53-0.97, p=0.031). Among African Americans (OR: 1.62, 95% CI: 1.35-1.95) and Hispanics/Latinos (OR: 1.21, 95% CI: 1.00-1.47), those who currently smoked menthol cigarettes were more likely to be seriously considering quitting in the next six months than non-menthol smokers, after adjusting for socio-demographic variables. Among former smokers, those who smoked menthol compared to non-menthol cigarettes were less likely to have successfully quit for at least six months within various racial/ethnic groups: African Americans (AOR: 0.23, 95% CI: 0.17-0.13); Asian Americans/PI (AOR:0.22, 95% CI: 0.11-0.45); Hispanics/Latinos (AOR:0.48, 95% CI: 0.34-0.69) and non-Hispanic Whites (AOR:0.28, 95% CI: 0.25-0.33).

In a non-peer-reviewed submission, Delnevo et al. (November 2010) conducted a secondary analysis of the 2003 and 2006/7 TUS-CPS. In this analysis, they attempted to address the limitations of Gundersen et al. (2009), that is, the inadequate control of socioeconomic variables, and the potential lack of statistical power among the African American population. The sample consisted of white, African American and Hispanic current smokers and former smokers who quit in the past five years. In addition this study examined two subpopulations of Hispanics: Mexican vs. Puerto Rican in origin. Current smoker was defined as meeting two conditions: having smoked 100 cigarettes in a lifetime and now smoking "everyday" or "some days." Former smoker was defined as meeting two conditions: having smoked 100 cigarettes in a lifetime and now smoking not at all. With regard to assessing menthol status, current smokers self-reported whether or not their usual brand of cigarettes in the past 12 months was menthol. Former smokers, who quit in the past five years, reported whether or not their usual brand 12 months prior to quitting was menthol. Because the relationship between menthol and cessation may be impacted by sample restriction decisions, the authors examined five samplerestrictions:

1. Current and former smokers who quit within the past 5 years, regardless of past quit attempts or current other tobacco product (OTP) use;

2. Current and former smokers who quit within the past 5 years who did not report current OTP use;

3. Current and former smokers who quit within the past 5 years who reported ever having made a quit attempt;

4. Current and former smokers who quit within the past 5 years who did not report current OTP use and have ever made a quit attempt (replicates Gundersen, et al., 2009)**;** and

5. Past 12-month cigarette smokers who made a quit attempt or had quit.

Multiple logistic regression was used to estimate the odds ratio of being a former smoker for menthol smokers relative to non-menthol smokers while controlling for other independent variables (education, household income, gender, age, seasonality and for restriction 5, exposure in the past 12 months to cigarette excise tax increase. Using sample restriction 1, menthol smokers were less likely to be former smokers than were non-menthol smokers (AOR=0.914, 95% CI: 0.868-0.961) overall. This relationship held among whites (AOR: 0.928, 95% CI: 0.877-0.982) and African Americans (AOR: 0.810, 95% CI: 0.670-0.979). The magnitude of the relationship among Hispanics was similar to whites, but was not statistically significant (AOR=0.936, 95% CI:0.793-1.105). Statistically significant findings were observed across various sample restrictions, with overall AOR ranging from 0.902 for sample restriction 3 to 0.932 for sample restriction 2. Only in sample restriction 5 was the finding not statistically significant. Similarly, the relationship between menthol smoking and cessation was statistically significant across sample restrictions among whites except in sample restriction 5. Among African Americans, the relationship was statistically significant across all restrictions, with an AOR ranging from 0.684 in sample restriction 4 to 0.810 in sample restriction 1. Among Hispanics, the relationship was statistically significant in sample restriction 5 only. However, when examining Hispanics by origin, menthol smokers of Mexican origin are substantially more likely to have quit smoking, though this was statistically significant only in sample restrictions 2 (AOR=1.338, 95% CI: 1.039-1.722) and 4 (1.349, 95% CI: 1.016-1.790). In contrast, menthol smokers of Puerto Rican origin were substantially *less* likely to have quit relative to non-menthol smokers across all categories, with adjusted odds ratios ranging from 0.421 in sample restriction 5 to 0.63 in sample restriction 2. Because of the number analyses, the data is provided in the Appendix. This study offers evidence that smoking menthol cigarettes leads to less cessation among smokers, in particular among African Americans and Puerto Rican Hispanics.

(b) (4)

<u>Longitudinal cohort studies</u>

Pletcher et al. (2006) used the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a longitudinal study of risk factors for coronary artery disease, to determine the effects of menthol cigarettes on smoking cessation and health outcome measures. Using this dataset, 1,535 smokers (952 menthol and 563 non-menthol) ages 18–30 and healthy were identified in 1985. Participants underwent baseline examination and then follow-up at years 2, 5, 7, 10 and 15 with 74 percent retention at year 15. At each examination, participants were questioned on four items: recent quit attempts, success in recent quit attempts, no current smoking since the past two times they were examined, and any relapses. After adjusting for ethnicity, sex, age, demographic and social factors, a trend toward menthol smokers experiencing lower cessation (OR: 0.71, 95% CI 0.49-1.02, p=0.06) and a lower likelihood of recent quit attempts (p=0.11) compared to non-menthol smokers was found. The results were not statistically significant. However, a statistically significant increase in the risk of relapse, that is, non-sustained quitting, was observed in menthol vs. non-menthol cigarette smokers (OR: 1.89, 95% CI, 1.17-3.05, p=0.009). Results were similar among African Americans and whites, after additional adjustment for cigarettes smoked daily at baseline. Baseline menthol cigarette smokers were more likely to still be smoking during follow-up examinations compared to baseline non-menthol cigarette smokers (69 percent vs. 54 percent, p <0.001), but stratification by ethnicity attenuated this association. The main weakness of this study was that it was difficult to tease apart the effects of ethnicity and menthol preference due to the limited number of white menthol smokers (N=189) and African American non-menthol smokers (N=95). The authors pointed out that differences in nicotine levels in cigarettes may confound results.

Treatment studies

Foulds et al. (2006) conducted a retrospective cohort analysis of 1,021 patients (670 white, 219 African American, 80 Hispanics, 52 other) who attempted to quit tobacco at a specialist tobacco dependence treatment outpatient clinic in New Jersey during 2001–2003. Treatment was comprehensive and multidisciplinary; it included assessment of the smoker, an individualized treatment plan that recommended medication and group treatment (six weekly 90-min. sessions), and establishment of a target quit date. A four-week follow-up was conducted in person (39 percent) or on the telephone (61 percent). Biochemical verification was obtained among those who attended in-person follow-up. Six-month follow-up was collected by telephone contact or by mail. Outcome measure was tobacco abstinence over the past seven days. Although univariate analysis demonstrated that menthol compared to non-menthol cigarette smoking had a significant effect on abstinence success (lower rates at four weeks, 35.4 percent vs. 42.3 percent and at 26 weeks, 24.9 percent vs. 35.8 percent), multivariate analysis (which took into account various demographic and tobacco history variables) showed trend toward significant menthol affects, p=0.053). Similarly, Gandhi et al. (2009) conducted a retrospective cohort analysis of 1,688 participants (778 smoked menthol cigarette smokers: 302 African American, 348 white, 99 Latino, 20 other; and 910 non-menthol cigarette smokers: 72 African American, 499 white, 50 Latino, 59 other) who attended the same specialist smoking cessation service in New Jersey during 2001–2005 and who set a quit date and attempted to quit smoking. This study extended the sample size of the Foulds et al. (2006) study. Outcome measure was self-reported seven-day point prevalence abstinence from tobacco products. Biochemical verification was available on some people, but accuracy of self-reported abstinence ranged from 99.4 percent to 100 percent. Average age was late 30s to early 40s. Unadjusted abstinence rates were lower with menthol vs. non-menthol cigarette smokers at the four-week follow-up overall (no values given) and among whites (43 percent vs. 50 percent, p=0.031), African Americans (30 percent vs. 54 percent, p <0.001) and Latinos (23 percent vs. 50 percent, p=0.001). At the six-month follow-up, similar observations were made overall (no values given), and among African Americans (18 percent vs. 36 percent, p=0.001) and Latinos (11 percent vs. 28

percent, p=0.009), but not whites. At four-week follow up, African Americans, Latino and white non-menthol smokers had similar quit rates (54 percent, 50 percent and 50 percent, respectively). In contrast, among menthol smokers African Americans and Latinos (30 percent and 23 percent, respectively) had lower quit rates compared to whites (43 percent p< 0.001). Logistic regression analyses resulted in a significant two-way interaction between race/ethnicity and menthol (p=0.04) at four weeks. African American and Latino menthol smokers had significantly lower unadjusted (OR: 0.34, 95% CI: 0.17-0.69 and OR: 0.30, 95% CI: 0.14-0.62, respectively) and adjusted odds (OR: 0.32, 95% CI: 0.16-0.62 and OR: 0.43 95% CI: 0.1-0.9, respectively) of quitting than their non- menthol counterparts. For whites this finding was evident only for the unadjusted analysis (OR: 0.75, 95% CI: 0.58-0.97). At six months follow-up, African American menthol smokers had half the odds of being abstinent compared to non-menthol smokers, for unadjusted (OR: 0.40, 95% CI: 0.23-0.07) and adjusted (OR: 0.48, 95% CI: 0.25 0.9) analysis which controlled for specific covariates (e.g., gender, education and employment status). Statistically significant differences were observed in Latinos only for unadjusted analysis (OR: 0.32, 95 percent CI0.13-0.77). The difference between four-week quit rates among menthol and non-menthol cigarette smokers was greater among those who were unemployed vs. employed, especially among African Americans (16 percent vs. 43 percent, p=0.03) whereas no differences were observed among the employed African Americans (42 percent vs. 56 percent, p=0.20).

Two treatment studies were conducted only among African American smokers. Okuyemi et al. (2007) examined 615 menthol and 138 non-menthol light smokers (10 cigarettes a day or less) in a 2 x 2 treatment study (nicotine replacement vs. placebo for eight weeks; motivational interviewing vs. health education for six sessions). Participants self-reported menthol or non-menthol cigarette use. Using logistic regression, no significant differences were observed for seven-day verified abstinence rates at eight weeks for non-menthol vs. menthol (26.8 percent vs. 22.6 percent). However, at 26 weeks post-randomization, seven-day verified abstinence rates were significantly lower for menthol smokers (11.2 percent vs. 18.8 percent, p=0.015). Using logistic regression, at 26 weeks non-menthol cigarette smokers who received nicotine gum had statistically significantly higher abstinence rates than menthol cigarette smokers who had received nicotine gum (p=0.013). There were no statistically significant differences in abstinence rates between menthol vs. non-menthol cigarette smokers who were assigned placebo. Similar findings were observed for those who received Health Education: menthol smokers had lower abstinent rate compared to non-menthol smokers (p=0.037).

In another study, Okuyemi et al. (2003) recruited African American smokers from an inner-city health center for a double-blind, placebo-controlled randomized trial examining bupropion vs. placebo prescribed for seven weeks. Subjects were 471 menthol and 129 non-menthol African American cigarette smokers who smoked at least 10 cigarettes per day. Menthol cigarette use was ascertained by the question, *Do you usually smoke menthol cigarettes?* Outcome variable was seven-day biochemically confirmed abstinence among 535 participants who completed the seven-week medication phase. Logistic regression was used to determine the effects of menthol cigarettes on smoking cessation. Seven-day point prevalence abstinence from smoking at six weeks was statistically significantly lower for menthol vs. non-menthol cigarette smokers (28.3 percent vs. 41.5 percent, p=0.006), but no differences were found at the six-month follow-up (21.4 percent vs. 27.0 percent). When separated by treatment, among those who received bupropion, the seven-day point-prevalence abstinence rate at six weeks was higher for non-menthol compared to menthol cigarette smokers (60.3 percent vs. 36.2 percent, p < 0.01), but no there were no differences within the placebo group (23.3 percent vs.20.5 percent). Statistically significant menthol effects were observed for those under the age of 50 at six-week follow-up, with lower cessation rates among menthol vs. non-menthol smokers (24.9 percent vs. 44.4 percent, p<0.01). No differences were observed among smokers 50 and older. In a stepwise logistic regression analysis, among smokers < 50 years old, non-menthol cigarette smokers were twice as likely to quit smoking at the end of six weeks compared to menthol smokers (OR: 2.12, 95% CI: 1.32-3.39).

In non-peer-reviewed submission, King et al. (November 2010) conducted a secondary analysis of data collected from a double-blind, randomized placebo-controlled trial of the efficacy of the oral opioid antagonist, naltrexone, in combination with nicotine patch and individual behavioral counseling. Participants were equally randomized to one of two medication groups: patch + counseling (PC) or patch + counseling + naltrexone (PCN). Study participants included 110 African Americans and 181 whites. Among whites, 45 were menthol cigarette users, and 136 were non-menthol cigarette users, but among African Americans, 91 were menthol cigarette users and 19 were non-menthol cigarette users. Subjects were recruited from 2006 to 2009. In a univariate analysis on baseline smoking characteristics, menthol and non-menthol cigarette smokers were comparables in terms of number of prior quit attempts and longest time quit in the past. For week four quitting, the multivariate analysis (controlling for sex, socioeconomic status, and education) indicated a statistically significant three-way interaction [medication x race x menthol, OR(se) = 22.80 (34.47), *p = 0.039*]. Separate analysis indicated a statistically significant interaction between medication and menthol use only in African Americans [OR(se) = 16.19(21.90), p = 0.039]. For week 12 quitting, the multivariate analysis revealed the three-way interaction had a p-value of 0.10 [medication x race x menthol, OR(se) = 16.84 (28.92), *p = 0.10*]. A further examination indicated a statistically significant medication x menthol interaction in African Americans [OR(se) = 31.22(49.16), *p = 0.029*], but not in whites. It appears that naltrexone may mitigate the poorer treatment response among African American menthol cigarette smokers to nicotine replacement treatment. The major weakness of this study is the small sample size, particularly the African American non-menthol group.

In another non-peer-reviewed article, Reitzel (November 2010 c) conducted a secondary analysis of a randomized clinical trial to test the efficacy of motivationally based treatment for smoking relapse prevention among pregnant mothers who were in their 30$^{th}$-33$^{rd}$ week of pregnancy at the time of enrollment. Participants (n=251, 32 percent African American, 30 percent Latina, 36 percent white, 2 percent other) who had quit smoking and were interesting in remaining quit postpartum were recruited into the study from 2005–2007. Menthol status was determined by asking participants if their usual brand of cigarettes was menthol or non-menthol. The outcome was continuous abstinence from smoking, defined as self-report of no smoking (not even a puff) since the delivery date and biochemical verification at eight and 26 weeks. Unadjusted continuous abstinence rates by menthol cigarette use status showed that menthol users had lower rates of continuous abstinence than non-menthol users at both follow-up points. However, menthol cigarette use did not significantly predict continuous abstinence from smoking in analyses adjusted for time and treatment group (*p* = .46; *n* = 338), or in analyses adjusted for age, race/ethnicity, partner status, income, and educational achievement, time, treatment group, cigarettes smoked per day, and time to the first cigarette of the day (*p* = .52; *n* = 304). In a post-hoc racial/ethnic group subgroup analyses, menthol cigarette use predicted continuous smoking abstinence among white women in unadjusted analyses [*p* = .01; *n* = 120, OR = .15 (.05 - .40)] and in analyses adjusted for age, partner status, income, and educational achievement, time, treatment group, cigarettes smoked per day, and time to the first cigarette of the day [*p* = .03; *n* = 108, OR = .19 (.04 - .89)]. White menthol users were less likely to maintain continuous abstinence through post-quit week 26 than white non-menthol users. In this analysis, the sample size of white menthol cigarette smokers was quite low (n=20).

See Table 6 for summary on population survey studies and Table 7 for summary on longitudinal cohort and treatment studies.

*Summary:* Delnevo et al. (November 2010) astutely points out that many cessation studies rely on convenience samples, secondary analysis of clinical trial data or case control studies. Some study samples are unrepresentative of the general population of smokers who quit. Other studies fail to examine subpopulations of smokers, which is critical in determining the public health effects of menthol. The characterization of cessation outcomes is inconsistent across studies. As a result, TPSAC used specific criteria to select studies that would be considered to be of sufficient quality to make an informative decision on the effects of menthol cigarettes compared to non-menthol cigarettes on cessation.

First, the most weight was placed on population survey studies. Population studies were weighed more heavily because most smokers quit on their own, rather than through cessation programs (Chapman and MacKenzie, 2010), the large sample size and the representativeness of the sample. We also believed that studies that focus on comparing cessation rates between menthol and non-menthol smokers among racial/ethnic groups are important because of potential racial/ethnic differences in response to menthol. Furthermore, the charge for TPSAC was to examine the effects of menthol on specific racial/ethnic groups. We also selected studies that focused on broad age ranges. Limitations of these population surveys include the cross-sectional nature of the study and for some studies, the uncertainty of duration of the quitting attempt.

Using these selection criteria two studies were eliminated because they did not focus on examining cessation rates among racial/ethnic groups (Alexander, et al., 2010; Fagan, et al., 2010). Five of the seven studies that met our criteria for inclusion by specifically examining the effects of menthol status on quit ratios and quit success among different racial/ethnic groups showed lower cessation success among menthol cigarette smokers. Two of these studies used the 2005 NHIS (Gundersen, et al., 2009; Stahre, et al., 2010) and the other three used the 2003/2006-7 TUS-CPS (Delnevo, et al., 2010; Trinidad, Gilpin, Lee, & Pierce, 2004)(Levy et al., in press). The type of analysis differed, but the results were consistent across the studies using similar surveys, that is, less quitting with menthol use in African American populations when analyzing data in the NHIS and less quitting with menthol use among almost all racial/ethnic groups when analyzing data in the TUS-CPS. The Delnevo et al., (2010) study was particularly strong because different subject inclusion criteria were used to examine quitting.

Four national/international surveys (two of which are listed above) found greater quitting success among subgroups of menthol smokers. Two of the studies analyzed the 2005 NHIS (Cubbin, et al., 2010; Gundersen, et al., 2009) in which white smokers were observed to have higher quit rates or duration of quitting. Another study analyzed the ITC-4 (Hyland & Kasza, 2010 a) had found African American women menthol smokers were more likely to succeed in quitting than African American non-menthol smokers. The fourth study (Delnevo, et al., 2010) found that although most other racial/ethnic menthol smokers experienced lower quitting than non-menthol smokers, Mexican American Hispanic menthol smokers as compared to Puerto Rican Hispanic menthol smokers experienced greater success than the respective non-menthol smokers.

To summarize, when focusing on population survey studies that examined difference by menthol status within racial/ethnic groups, in general, most studies support the finding that non-whites, particularly African Americans, who smoke menthol cigarettes have lower quit rates than non-whites who smoke non-menthol cigarettes, but the results for whites is mixed. A few studies showed that white menthol smokers may possibly have higher quit rates compared with non-menthol smokers.

With regards to longitudinal, cohort populations and studies, TPSAC also focused on studies that examined ethnic/racial groups, had sufficient samples sizes at least among whites and blacks (number of subjects that is at least 100 subjects), was broadly representative of a general population of smokers, and had appropriate criteria for cessation (not smoking even a puff on a cigarette). TPSAC also considered studies that focused primarily on African Americans. Of the six longitudinal cohort studies, two studies used the same COMMIT database and found consistent no menthol effect results (Hyland, et al., 2002; Hyland & Rivard, 2010 b). Although the data analyses in both these studies were well-executed, one of the studies examined smokers prior to the 1990s (Hyland, et al., 2002) and the other study had a very small sample size of black smokers who had attempted to quit, which may have reduced the power to detect any differences (Hyland & Rivard, 2010 b). Two other studies also found no effects (Murray, et al., 2007; Muscat, et al., 2002). One of these studies had an unusual definition of cessation (e.g., not smoking each day for the past year), undertook cross-sectional analysis, enrolled a convenience sample, and enrolled an older population of adults, thereby limiting generalizability (Muscat, et al., 2002). The other study did not examine potential racial ethnic differences, had few racial ethnic subjects to see a menthol effect and also enrolled subjects with mild to moderate chronic airflow obstruction (Murray, et al., 2007). The fifth study that found no affect focused on a diverse group of smokers and included a large sample size; however it primarily recruited older adults (Blot, in press). One study found a greater risk of relapse or non-sustained quitting among both African American and European American menthol smokers (Pletcher, et al., 2006). This study had a small sample size of African American non-menthol smokers. The major limitations of all these studies include the secondary analysis of studies not intended to primarily focus on menthol, but more importantly, the limited number of racial/ethnic groups that allow an examination of racial/ethnic effects. Because of their limitations, none of these studies were considered to be sufficiently informative to be considered in TPSAC's evidence review.

With regards to clinical trials, TPSAC used the criteria that was used to evaluate longitudinal, cohort populations and studies, with the additional requirement that follow-up had to be at least six months. TPSAC also considered studies that focused primarily on African Americans. Five of the eleven clinical trials did not find a menthol effect and three were not considered to meet criteria. Some of these studies tended to have a non-representative population of treatment seekers, were not focused on effects of menthol per se or only observed significant menthol effects in the unadjusted analysis. One of these trials examined female prisoners (Cropsey, et al., 2009), which is a very selective population. Another trial recruited from the VA Medical Center, therefore enrolling smokers who were older, and based on the study by Okuyemi et al. (2003), menthol effects may be found predominantly a younger population of treatment seekers. Harris et al. (2004) analyzed the same sample of African Americans as Okuyemi et al., (2003) and this study was mostly focused on examining ethnic racial differences. It should be noted that univariate analysis of the data did show poorer abstinence among menthol smokers, which is concordant with Okuyemi and associates (2003) findings. Reitzel (November 2010b) examined a more broadly representative ethnic/racial population of smokers (Reitzel, 2010 a) or an African American smokers (Reitzel, 2010 b) that showed no menthol effect . One of these studies conducted by Reitzel (2010a) observed lower cessation rate using unadjusted analysis but not adjusted analysis. Both these studies were considered to be of sufficient quality to be considered as part of TPSAC's evidence review.

With regards to the six clinical trial studies that showed poorer treatment outcomes among menthol smokers, four did not meet criteria. Two studies studies did not meet criteria because they examined pregnant women (Rietzel et. al. 2010c) or had small sample sizes in subgroups of smokers (King et al. 2010). Another study found effects at the end of treatment, but not at sixth-month follow-up (Okuyemi et al. 2003). Two other studies used a similar population of treatment seekers (Foulds, et al., 2006; Gandhi, et al., 2009). If we eliminate the Foulds et al. (2006) study with a smaller population of treatment seekers, then treatment outcomes is poorer in menthol compared to non-menthol smokers particularly among a non-White population (Gandhi, et al., 2009), which is concordant with the NHIS data results (Gundersen, et al., 2009; Stahre, et al., 2010). The other study that was considered to meet criteria included Okuyemi et al. 2007, where they found African American menthol cigarette smokers experienced a lower cessation rate than non-menthol smokers.

After eliminating clinical studies with low sample sizes, no six month follow-up and no analysis of racial/ethnic minorities, the evidence from clinical trials (Ganhdi et al., 2009; Okuyemi et al., 2007 vs. Rietzel 2101a, b) was mixed.

Studies also show that menthol effects are particularly observed among smokers who are prescribed medications (Okuyemi, et al., 2003). In the Okuyemi et al. (2003; 2007) studies, menthol status is only evident in the active treatment conditions (NRT and bupropion) and not the placebo condition. Similarly, King et al., (November 2010) conducted a study using NRT vs. NRT + Naltrexone. They observed that menthol effects were only found among the NRT only group, leading to the hypothesis that naltrexone, an opioid antagonist, has a mitigating effect. The King et al. (2010) study had very small sample size of African American smokers. Finally, it should be noted that in the Gandhi et al. (2009) and Foulds et al., (2006) study, treatment seekers were recommended to use medications. Thus, the evidence points toward negative effects of menthol cigarettes on the efficacy of medications. It is possible that the lack of response to treatment may be most evident for NRT. In the study that examined bupropion SR (Okuyemi, et al., 2003), menthol effects were only observed at the end of treatment and not at follow-up.

In conclusion, based on the various studies, the evidence is sufficient to indicate that menthol is associated with lower level of cessation among a non-white population, specifically among African Americans, and the evidence in white is mixed. Menthol cigarette smoking may also affect response to medications.

**Adolescents**

No studies have been conducted in adolescent smokers that examine the effects of menthol cigarettes on cessation. Moolchan (2004) examined adolescents living in the Baltimore area who responded via telephone to advertisements or community outreach for an outpatient teenage smoking cessation study. Moolchan (2004) observed that about 90 percent of the 622 adolescents who responded and for whom they had data were smoking menthol cigarettes.

**Mediators of cessation attempts among menthol smokers**

To date, no studies have systematically examined factors that may or may not make it difficult for menthol cigarette smokers to quit smoking. A potentially informative report by Anderson et al. (2010) was commissioned by the FDA. The report examined internal tobacco industry documents to assess menthol's potential role in quit attempts and success in quit attempts. In this qualitative research study of the digitized repository of previously internal tobacco industry documents, a snowball sampling design was used to search the Legacy Tobacco Documents Library. Based on this search and analysis of these documents, Anderson et al. (2010 November submission) came to the following conclusions.

> "Menthol smokers perceive the ….soothing, cooling, anesthetic sensations with menthol cigarettes. These perceptions appear to discourage quitting in menthol smokers (Anderson, November submission, page 9)."
>
> "Two main motivations for smokers to quit are health concerns and the social unacceptability of smoking. Menthol's cooling, soothing, and anesthetic effects mask superficial health effects such as throat irritation and cough in menthol smokers, which lessen their concern about health effects [and provide an alternative to giving up smoking altogether (page 14, Anderson, in press)]. Menthol smokers also believe menthol smoke to smell better and be less offensive to others, which lessens menthol smokers' sense of the social unacceptability of smoking. These aspects of menthol appear to discourage motivation or desire to quit among menthol smokers."
>
> "Menthol appeals to some socio-demographic groups who are also known to have difficulty initiating quitting or staying quit, including women, lower income smokers, and African Americans. Although it is not clear why there is substantial overlap between the overall menthol profile (younger, non-white, female, and low income) and socio-demographic variables that predict difficulty in quitting or staying quit, it appears that tobacco companies took an interest in this overlap (Anderson, November submission, page 10)."
>
> "The evidence demonstrating smokers' switching fro non-menthol to menthol cigarettes when they have a cold or sore throat points to a presumption of therapeutic or health protective effects of menthol, effects that lead smokers to believe it is unnecessary to quit smoking in order to protect one's health. Tobacco industry executives acknowledged the health reassurances such beliefs about menthol imply and have marketed menthol with both explicit and implicit health messages (Anderson in press, page 22)."

Philip Morris observed that African Americans, females and younger smokers were more likely to smoke menthol cigarettes than whites, males and older smokers, according to an analysis of internal company documents by Klausner (2011 in press). A Philip Morris document dated 1978 said: "These differences could have a profound effect on the future growth of the menthol share of the market. We know, for example, that males, whites, and older smokers are more likely to quit smoking than females, blacks and younger smokers."

**EVIDENCE SYNTHESIS**

The goal of chapter 6 was to gather and review evidence on the effects of menthol cigarettes on smoking experimentation and initiation, the transition to regular smoking and addiction, and the success of smoking cessation. The evidence in these areas is summarized below. TPSAC considered this information, along with other evidence gathered, reviewed and synthesized in this report, to assess the overall public health impact of menthol cigarettes and to make its recommendations to the FDA.

**Initiation and Experimentation**

*Is there evidence to indicate that the availability of menthol cigarettes increases the likelihood of experimentation and initiation?*

- The evidence is sufficient to conclude that there is a higher prevalence of menthol cigarette use is observed among younger population of smokers compared to an older population (except in African Americans among whom high rates were observed in both adolescents and adults). Within the population of youth, the evidence is sufficient to conclude that the rate of menthol cigarette use is highest among the youngest users then decreases with age.

- The evidence is sufficient to conclude that there is an increasing trend of menthol cigarette smoking and a decreasing trend of non-menthol cigarette smoking among adolescent smokers, including novice smokers (those who have smoked less than 100 cigarettes). Although cigarette smoking is becoming less prevalent, the evidence is sufficient to conclude that menthol cigarette smoking is declining at slower rate than non-menthol cigarette smoking.

- The evidence is sufficient to conclude that less established smokers (less than one year smoking) are more likely to smoke menthol cigarettes than more established smokers (greater than one year smoking).

- Although most studies showed that the age of initiation was similar comparing menthol and non-menthol cigarette smokers, one national survey of adolescents showed that menthol smokers experienced an earlier age of initiation. This finding was observed even after controlling for age, race and gender.

- The evidence shows based on concordant findings of the studies of internal tobacco industry documents, that tobacco companies were aware of the appeal of menthol cigarettes to younger, novice smokers because these cigarettes are easier to smoke. Chapter 3 documents the biological plausibility of an increased appeal of menthol cigarettes because of their pharmacological effects of menthol.

**Addiction**

*Does the availability of menthol cigarettes increase the likelihood of becoming addicted?*

- To date, one unpublished secondary analysis has addressed this issue in sample of adolescent students who were assessed in different regions in the U.S. This study strongly suggests that menthol cigarettes are associated with increased transition to greater or established smoking and dependence.

*Does inclusion of menthol in cigarettes increase the degree of addiction to the smoker compared to non-menthol cigarettes?*

- Among adults there is little evidence to support the conclusion that menthol cigarettes increase addiction to smoking based on the mixed results on differences between menthol and non-menthol for pharmacokinetics of nicotine, cigarettes smoked per day, exposure to nicotine in general and per cigarette (although little is known about differences in those who smoke less than 10 cigarettes per day or those who are in the early stages of smoking acquisition), and subjective measures of dependence.

- Among youth, there is sufficient evidence to indicate that those who smoke menthol tend to be more dependent than those who smoke non-menthol cigarettes as reflected by the number of cigarettes smoked and dependence measures.  Thus, this population seems to be particularly vulnerable to the effects of menthol cigarette smoking.

**Cessation**

*Is there evidence to indicate that smokers of menthol cigarettes are less likely to quit successfully than smokers of non-menthol cigarettes?*

- Although the number of studies that are considered to be of sufficient quality is limited, there is sufficient evidence based on national surveys to show that the non-white smokers, particularly African American, of menthol cigarettes compared to non-menthol cigarettes experience more difficulty with cessation. The data in whites is mixed.

- The results also suggest that menthol cigarette smoking leads to less responsiveness to medications.  This is an area that requires further exploration.

- No studies have been conducted with adolescent smokers.

- Menthol cigarettes are marketed toward (see Chapter 5) toward African American and the young.  These groups are at high risk for poor cessation outcomes.

**References**


Ahijevych, K., Dai, G., & Chan, K. (2002, May 17-22). *Menthol pharmacokinetics in African American women following menthol cigarette smoking.* Paper presented at the American Thoracic Society International Conference, Atlanta, GA.

Ahijevych, K., & Ford, J. (2010). The relationships between menthol cigarette preference and state tobacco control policies on smoking behaviors of young adult smokers in the 2006-07 Tobacco Use Supplements to the Current Population Surveys (TUS CPS). *Addiction, 105 Suppl 1*, 46-54. doi: 10.1111/j.1360-0443.2010.03201.x

Ahijevych, K., Gillespie, J., Demirci, M., & Jagadeesh, J. (1996). Menthol and nonmenthol cigarettes and smoke exposure in black and white women. *Pharmacol Biochem Behav, 53*(2), 355-360. doi: 0091-3057(95)02034-9 [pii]

Ahijevych, K., & Parsley, L. A. (1999). Smoke constituent exposure and stage of change in black and white women cigarette smokers. *Addict Behav, 24*(1), 115-120. doi: S0306-4603(98)00031-8 [pii]

Ahijevych, K., Tyndale, R. F., Dhatt, R. K., Weed, H. G., & Browning, K. K. (2002). Factors influencing cotinine half-life during smoking abstinence in African American and Caucasian women. *Nicotine Tob Res, 4*(4), 423-431.

Alexander, L. A., Crawford, T., & Mendiondo, M. S. (2010). Occupational status, work-site cessation programs and policies and menthol smoking on quitting behaviors of US smokers. *Addiction, 105 Suppl 1*, 95-104. doi: 10.1111/j.1360-0443.2010.03227.x

Allen, B., Jr., & Unger, J. B. (2007). Sociocultural correlates of menthol cigarette smoking among adult African Americans in Los Angeles. *Nicotine Tob Res, 9*(4), 447-451. doi: 776187489 [pii]10.1080/14622200701239647

Altria Client Services on behalf of Philip Morris USA. (2010). Menthol discussion. Background information to the Tobacco Products Scientific Advisory Committee.

Anderson, S. J. (2010). Menthol cigarettes and smoking cessation behavior.

Appleyard, J., Messeri, P., & Haviland, M. L. (2001). Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. *Asian Am Pac Isl J Health, 9*(1), 5-14.

Barker, D. (1994). Changes in the cigarette brand preferences of adolescent smokers -- United States, 1989-1993. *MMWR. Morbidity and Mortality Weekly Report, 43*(32), 577-579.

Benowitz, N. L., Herrera, B., & Jacob, P., III. (2004). Mentholated cigarette smoking inhibits nicotine metabolism. *J Pharmacol Exp Ther, 310*(3), 1208-1215.

Blot, W. J., Cohen, S. S., Aldrich, M., McLaughlin, J. K., Hargreaves, M. K., & Signorello, L. B. (in press). Lung cancer risk among smokers of menthol cigarettes. *Journal of the National Cancer Institute*.

Bover, M. T., Foulds, J., Steinberg, M. B., Richardson, D., & Marcella, S. W. (2008). Waking at night to smoke as a marker for tobacco dependence: patient characteristics and relationship to treatment outcome. *International Journal of Clinical Practice, 62*(2), 182-190. doi: IJCP1653 [pii]10.1111/j.1742-1241.2007.01653.x

Caraballo, R. S., & Asman, K. (in submission). Epidemiology of menthol cigarette use in the United States.

Caraballo, R. S., Giovino, G. A., Pechacek, T. F., Mowery, P. D., Richter, P. A., Strauss, W. J., . . . Maurer, K. R. (1998). Racial and ethnic differences in serum cotinine levels of cigarette smokers: Third National Health and Nutrition Examination Survey, 1988-1991. *JAMA, 280*(2), 135-139.

Clark, P. I., Gautam, S., & Gerson, L. W. (1996). Effect of menthol cigarettes on biochemical markers of smoke exposure among black and white smokers. *Chest, 110*(5), 1194-1198.

Collins, C. C., & Moolchan, E. T. (2006). Shorter time to first cigarette of the day in menthol adolescent cigarette smokers. *Addictive Behaviors, 31*(8), 1460-1464. doi: S0306-4603(05)00259-5 [pii]10.1016/j.addbeh.2005.10.001

Croghan, E., Aveyard, P., Griffin, C., & Cheng, K. K. (2003). The importance of social sources of cigarettes to school students. *Tob Control, 12*(1), 67-73.

Cropsey, K. L., Weaver, M. F., Eldridge, G. D., Villalobos, G. C., Best, A. M., & Stitzer, M. L. (2009). Differential success rates in racial groups: results of a clinical trial of smoking cessation among female prisoners. *Nicotine Tob Res, 11*(6), 690-697. doi: ntp051 [pii]10.1093/ntr/ntp051

Cubbin, C., Soobader, M. J., & LeClere, F. B. (2010). The intersection of gender and race/ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. *Addiction, 105 Suppl 1*, 32-38. doi: 10.1111/j.1360-0443.2010.03191.x

Curtin, G. M., Sulsky, S. I., Fuller, W. G., Van Landingham, C., Ogden, M. W., & Swauger, J. E. (2010a). Descriptive epidemiological analysis of menthol use from four national US surveys: I. Demographics. *International Journal of Environmental Research and Public Health*.

Curtin, G. M., Sulsky, S. I., Fuller, W. G., Van Landingham, C., Ogden, M. W., & Swauger, J. E. (2010b). Descriptive epidemiological analysis of menthol use from four national US surveys: II. Smoking initiation age. *International Journal of Environmental and Public Health*.

Curtin, G. M., Sulsky, S. I., Fuller, W. G., Van Landingham, C., Ogden, M. W., & Swauger, J. E. (2010c). Descriptive epidemiological analysis of menthol use from four national US surveys: III. Smoking dependence. *International Journal of Environmental Research and Public Health*.

Delnevo, C. D., Gundersen, D. A., & Hrwyna, M. (2010). Examining the relationship between menthol smoking and cessation using data from the 2003 and 2006/7 Tobacco use Supplement: U S Food and Drug Administration commissioned secondary analysis.

DiFranza, J. R., Savageau, J. A., Fletcher, K., Ockene, J. K., Rigotti, N. A., McNeill, A. D., . . . Wood, C. (2004). Recollections and repercussions of the first inhaled cigarette. *Addict Behav, 29*(2), 261-272. doi: S0306460303001151 [pii]

Emery, S., Gilpin, E. A., White, M. M., & Pierce, J. P. (1999). How adolescents get their cigarettes: implications for policies on access and price. *J Natl Cancer Inst, 91*(2), 184-186.

Fagan, P., Moolchan, E. T., Hart, A., Jr., Rose, A., Lawrence, D., Shavers, V. L., & Gibson, J. T. (2010). Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. *Addiction, 105 Suppl 1*, 55-74. doi: 10.1111/j.1360-0443.2010.03190.x

Farrelly, M. C., Loomis, B. R., & Mann, N. H. (2007). Do increases in cigarette prices lead to increases in sales of cigarettes with high tar and nicotine yields? *Nicotine Tob Res, 9*(10), 1015-1020. doi: 781561713 [pii]10.1080/14622200701491289

Fernander, A., Rayens, M. K., Zhang, M., & Adkins, S. (2010). Are age of smoking initiation and purchasing patterns associated with menthol smoking? *Addiction, 105 Suppl 1*, 39-45. doi: 10.1111/j.1360-0443.2010.03188.x

Forster, J., Chen, V., Blaine, T., Perry, C., & Toomey, T. (2003). Social exchange of cigarettes by youth. *Tob Control, 12*(2), 148-154.

Foulds, J., Gandhi, K. K., Steinberg, M. B., Richardson, D. L., Williams, J. M., Burke, M. V., & Rhoads, G. G. (2006). Factors associated with quitting smoking at a tobacco dependence treatment clinic. *Am J Health Behav, 30*(4), 400-412. doi: 10.5555/ajhb.2006.30.4.400

Fu, S. S., Okuyemi, K. S., Partin, M. R., Ahluwalia, J. S., Nelson, D. B., Clothier, B. A., & Joseph, A. M. (2008). Menthol cigarettes and smoking cessation during an aided quit attempt. *Nicotine Tob Res, 10*(3), 457-462. doi: 791308364 [pii]10.1080/14622200801901914

Gandhi, K. K., Foulds, J., Steinberg, M. B., Lu, S. E., & Williams, J. M. (2009). Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic.

*International Journal of Clinical Practice, 63*(3), 360-367. doi: IJCP1969 [pii]10.1111/j.1742-1241.2008.01969.x
Giovino, G. A. (2010). Patterns and recent trends in the use of mentholated cigarettes in the United States *Submission to the Food and Drug Administration's Tobacco Products Scientific Advisory Committee*.
Giovino, G. A., Sidney, S., Gfroerer, J. C., O'Malley, P. M., Allen, J. A., Richter, P. A., & Cummings, K. M. (2004). Epidemiology of menthol cigarette use. *Nicotine Tob Res, 6 Suppl 1*, S67-81. doi: 10.1080/14622203710001649696 14AH8W576MJQ7MCN [pii]
Gundersen, D. A., Delnevo, C. D., & Wackowski, O. (2009). Exploring the relationship between race/ethnicity, menthol smoking, and cessation, in a nationally representative sample of adults. *Prev Med, 49*(6), 553-557. doi: S0091-7435(09)00478-2 [pii]10.1016/j.ypmed.2009.10.003
Harris, K. J., Okuyemi, K. S., Catley, D., Mayo, M. S., Ge, B., & Ahluwalia, J. S. (2004). Predictors of smoking cessation among African-Americans enrolled in a randomized controlled trial of bupropion. *Prev Med, 38*(4), 498-502. doi: 10.1016/j.ypmed.2003.12.008S0091743503003517 [pii]
Harrison, P. A., Fulkerson, J. A., & Park, E. (2000). The relative importance of social versus commercial sources in youth access to tobacco, alcohol, and other drugs. *Prev Med, 31*(1), 39-48. doi: 10.1006/pmed.2000.0691S0091-7435(00)90691-1 [pii]
Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerstrom, K. O. (1991). The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict, 86*(9), 1119-1127.
Heck, J. D. (2009). Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. *Cancer Epidemiol Biomarkers Prev, 18*(2), 622-629. doi: 1055-9965.EPI-08-0550 [pii]10.1158/1055-9965.EPI-08-0550
Henningfield, J. E., Benowitz, N. L., Ahijevych, K., Garrett, B. E., Connolly, G. N., & Wayne, G. F. (2003). Does menthol enhance the addictiveness of cigarettes? An agenda for research. [THYNJTCEQA87K1NR pii]. *Nicotine Tob Res, 5*(1), 9-11.
Hersey, J. C., Ng, S. W., Nonnemaker, J. M., Mowery, P., Thomas, K. Y., Vilsaint, M. C., . . . Haviland, M. L. (2006). Are menthol cigarettes a starter product for youth? *Nicotine Tob Res, 8*(3), 403-413. doi: R32206802V873N68 [pii]10.1080/14622200600670389
Hersey, J. C., Nonnemaker, J., Homsi, G., & Allen, J. (2010). Menthol cigarettes, saliva cotinine, and nicotine dependence in adolescents. Report for the Food and Drug Administration Center for Tobacco Products.
Hersey, J. C., Nonnemaker, J. M., & Homsi, G. (2010). Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. *Nicotine Tob Res, 12 Suppl 2*, S136-146. doi: ntq173 [pii]10.1093/ntr/ntq173
Hooper, M. W., Zhao, W., Byrne, M. M., Davila, E., Caban-Martinez, A., Dietz, N. A., . . . Lee, D. J. (2011). Menthol Cigarette Smoking and Health, Florida 2007 BRFSS. *Am J Health Behav, 35*(1), 3-14. doi: 10.5555/ajhb.2011.35.1.3 [pii]
Hyland, A., Garten, S., Giovino, G. A., & Cummings, K. M. (2002). Mentholated cigarettes and smoking cessation: findings from COMMIT. Community Intervention Trial for Smoking Cessation. *Tob Control, 11*(2), 135-139.
Hyland, A., & Kasza, K. (2010 a). A longitudinal study of the association between menthol cigarettes and indicators of dependence: Findings from the International Tobacco Control Project: U S Food and Drug Administration commissioned secondary analysis.
Hyland, A., & Rivard, C. (2010 b). Analysis of mentholated cigarettes using the COMMIT data - summary report: U S Food and Drug Administration commissioned secondary analysis.

Hymowitz, N., Corle, D., Royce, J., Hartwell, T., Corbett, K., Orlandi, M., & Piland, N. (1995). Smokers' baseline characteristics in the COMMIT trial. *Prev Med, 24*(5), 503-508. doi: S0091-7435(85)71080-8 [pii]10.1006/pmed.1995.1080

Institute of Medicine. (1994). *Growing up tobacco free. Preventing nicotine addiction in children and youths*. Washington, D.C.: National Academy Press.

Johnston, L. D., O'Malley, P. M., Backhan, J. G., & Schulenberg, J. E. (1999). Cigarette brand preferences among adolescents *Monitoring the Future Occasional Paper* Ann Arbor, MI: Institute for Social Research.

Kaufman, N. J., Castrucci, B. C., Mowery, P., Gerlach, K. K., Emont, S., & Orleans, C. T. (2004). Changes in adolescent cigarette-brand preference, 1989 to 1996. *Am J Health Behav, 28*(1), 54-62.

King, A., Cao, D., & Matthews, A. (2010). Influence of menthol use on smoking cessation outcomes in a smoking cessation treatment program: U S Food and Drug Administration commissioned secondary analysis.

Klausner, K. (2011 in press). Menthol cigarettes and smoking initiation: a tobacco industry perspective. *Tobacco Control*.

Lawrence, D., Rose, A., Fagan, P., Moolchan, E. T., Gibson, J. T., & Backinger, C. L. (2010). National patterns and correlates of mentholated cigarette use in the United States. *Addiction, 105 Suppl 1*, 13-31. doi: 10.1111/j.1360-0443.2010.03203.x

Levin, E. D., Behm, F., & Rose, J. E. (1990). The use of flavor in cigarette substitutes. *Drug Alcohol Depend, 26*(2), 155-160. doi: 0376-8716(90)90122-U [pii]

Lorillard Tobacco Company. (2010). The science relating to menthol cigarettes for the meeting of the Tobacco Products Scientific Advisory Committee.

Ma, G. X., Shive, S., Legos, P., & Tan, Y. (2003). Ethnic differences in adolescent smoking behaviors, sources of tobacco, knowledge and attitudes toward restriction policies. *Addict Behav, 28*(2), 249-268. doi: S0306460301002258 [pii]

Moolchan, E. T. (2004). Adolescent menthol smokers: will they be a harder target for cessation? *Nicotine Tob Res, 6 Suppl 1*, S93-95. doi: 10.1080/146222033100016495221HHRW3F8K70QEL2H [pii]

Muilenburg, J. L., & Legge, J. S., Jr. (2008). African American adolescents and menthol cigarettes: smoking behavior among secondary school students. *J Adolesc Health, 43*(6), 570-575. doi: S1054-139X(08)00408-4 [pii]10.1016/j.jadohealth.2008.08.017

Murray, R. P., Connett, J. E., Skeans, M. A., & Tashkin, D. P. (2007). Menthol cigarettes and health risks in Lung Health Study data. *Nicotine Tob Res, 9*(1), 101-107. doi: 770436176 [pii]10.1080/14622200601078418

Muscat, J. E., Chen, G., Knipe, A., Stellman, S. D., Lazarus, P., & Richie, J. P., Jr. (2009). Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation. *Cancer Epidemiol Biomarkers Prev, 18*(1), 35-41. doi: 18/1/35 [pii]10.1158/1055-9965.EPI-08-0744

Muscat, J. E., Richie, J. P., Jr., & Stellman, S. D. (2002). Mentholated cigarettes and smoking habits in whites and blacks. *Tob Control, 11*(4), 368-371.

Mustonen, T. K., Spencer, S. M., Hoskinson, R. A., Sachs, D. P., & Garvey, A. J. (2005). The influence of gender, race, and menthol content on tobacco exposure measures. *Nicotine Tob Res, 7*(4), 581-590. doi: Q78290J1V1726638 [pii]10.1080/14622200500185199

Nonnemaker, J., Hersey, J., Homsi, G., Busey, A., & Vallone, D. (2010). Menthol cigarettes and youth smoking uptake *Submission to the Food and Drug Administration's Tobacco Products Scientific Advisory Committee*.

Okuyemi, K. S., Ahluwalia, J. S., Ebersole-Robinson, M., Catley, D., Mayo, M. S., & Resnicow, K. (2003). Does menthol attenuate the effect of bupropion among African American smokers? *Addiction, 98*(10), 1387-1393. doi: 443 [pii]

Okuyemi, K. S., Ebersole-Robinson, M., Nazir, N., & Ahluwalia, J. S. (2004). African-American menthol and nonmenthol smokers: differences in smoking and cessation experiences. *Journal of the National Medical Association, 96*(9), 1208-1211.

Okuyemi, K. S., Faseru, B., Sanderson Cox, L., Bronars, C. A., & Ahluwalia, J. S. (2007). Relationship between menthol cigarettes and smoking cessation among African American light smokers. *Addiction, 102*(12), 1979-1986. doi: ADD2010 [pii]10.1111/j.1360-0443.2007.02010.x

Pickworth, W. B., Moolchan, E. T., Berlin, I., & Murty, R. (2002). Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery. *Pharmacol Biochem Behav, 71*(1-2), 55-61. doi: S0091305701006232 [pii]

Piper, M. E., McCarthy, D. E., Bolt, D. M., Smith, S. S., Lerman, C., Benowitz, N., . . . Baker, T. B. (2008). Assessing dimensions of nicotine dependence: an evaluation of the Nicotine Dependence Syndrome Scale (NDSS) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM). *Nicotine Tob Res, 10*(6), 1009-1020.

Piper, M. E., Piasecki, T. M., Federman, E. B., Bolt, D. M., Smith, S. S., Fiore, M. C., & Baker, T. B. (2004). A multiple motives approach to tobacco dependence: the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68). *J Consult Clin Psychol, 72*(2), 139-154.

Pletcher, M. J., Hulley, B. J., Houston, T., Kiefe, C. I., Benowitz, N., & Sidney, S. (2006). Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Arch Intern Med, 166*(17), 1915-1922. doi: 166/17/1915 [pii]10.1001/archinte.166.17.1915

Pritchard, W. S., Houlihan, M. E., Guy, T. D., & Robinson, J. H. (1999). Little evidence that "denicotinized" menthol cigarettes have pharmacological effects: an EEG/heart-rate/sujective-response study. *Psychopharmacology (Berl), 143*(3), 273-279.

Reitzel, L. R. (2010 a). Menthol cigarettes, tobacco dependence, and smoking cessation: Project CARE final report: U S Food and Drug Administration commissioned secondary analysis.

Reitzel, L. R. (2010 b). Menthol cigarettes, tobacco dependence, and smoking cessation: Project BREAK FREE final report: U S Food and Drug Administration commissioned secondary analysis.

Reitzel, L. R. (2010 c). Menthol cigarettes, tobacco dependence, and smoking cessation: Project MOM final report: U S Food and Drug Administration commissioned secondary analysis.

Rock, V. J., Davis, S. P., Thorne, S. L., Asman, K. J., & Caraballo, R. S. (2010). Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. *Nicotine Tob Res, 12 Suppl 2*, S117-124. doi: ntq204 [pii]10.1093/ntr/ntq204

Shiffman, S., Waters, A., & Hickcox, M. (2004). The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. *Nicotine Tob Res, 6*(2), 327-348. doi: 10.1080/1462220042000202481VBH32VQ8399VPHFL [pii]

Sidney, S., Tekawa, I., & Friedman, G. D. (1989). Mentholated cigarette use among multiphasic examinees, 1979-86. *Am J Public Health, 79*(10), 1415-1416.

Signorello, L. B., Cai, Q., Tarone, R. E., McLaughlin, J. K., & Blot, W. J. (2009). Racial differences in serum cotinine levels of smokers. *Disease Markers, 27*(5), 187-192. doi: W37L72G804611241 [pii]10.3233/DMA-2009-0661

Stahre, M., Okuyemi, K. S., Joseph, A. M., & Fu, S. S. (2010). Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. *Addiction, 105 Suppl 1*, 75-83. doi: 10.1111/j.1360-0443.2010.03200.x

Substance Abuse and Mental Health Services Administration. (2007). Cigarette brand preferences in 2005. Rockville, MD: Office of Applied Studies.

Substance Abuse and Mental Health Services Administration. (2009). The NSDUH Report: Use of menthol cigarettes. Rockville, MD: SAMHSA, Office of Applied Studies.

Tauras, J. A., Levy, D., Chaloupka, F. J., Villanti, A., Niaura, R. S., Vallone, D., & Abrams, D. B. (2010). Menthol and non-menthol smoking: the impact of prices and smoke-free air laws. *Addiction, 105 Suppl 1*, 115-123. doi: 10.1111/j.1360-0443.2010.03206.x

Trinidad, D. R., Gilpin, E. A., Lee, L., & Pierce, J. P. (2004). Do the majority of Asian-American and African-American smokers start as adults? *Am J Prev Med, 26*(2), 156-158. doi: S0749379703003180 [pii]

Trinidad, D. R., Perez-Stable, E. J., Messer, K., White, M. M., & Pierce, J. P. (2010). Menthol cigarettes and smoking cessation among racial/ethnic groups in the United States. *Addiction, 105 Suppl 1*, 84-94. doi: 10.1111/j.1360-0443.2010.03187.x

U. S. Department of Health and Human Services. (1988). The health consequences of smoking: nicotine and addiction. A report of the Surgeon General. *DHHS Publication No. (CDC) 88-8406*.

U. S. Department of Health and Human Services. (1994). Preventing tobacco use among young people. A report of the Surgeon General. Atlanta, Georgia: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. (Reprinted from: NOT IN FILE).

U. S. Department of Health and Human Services. (2010). How tobacco smoke causes disease: The biology and behavioral basis for smoking - attributable disease: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

Wackowski, O., & Delnevo, C. D. (2007). Menthol cigarettes and indicators of tobacco dependence among adolescents. *Addict Behav, 32*(9), 1964-1969. doi: S0306-4603(06)00403-5 [pii]10.1016/j.addbeh.2006.12.023

Wang, J., Roethig, H. J., Appleton, S., Werley, M., Muhammad-Kah, R., & Mendes, P. (2010). The effect of menthol containing cigarettes on adult smokers' exposure to nicotine and carbon monoxide. *Regul Toxicol Pharmacol, 57*(1), 24-30. doi: S0273-2300(09)00242-6 [pii]10.1016/j.yrtph.2009.12.003

Williams, J. M., Gandhi, K. K., Steinberg, M. L., Foulds, J., Ziedonis, D. M., & Benowitz, N. L. (2007). Higher nicotine and carbon monoxide levels in menthol cigarette smokers with and without schizophrenia. *Nicotine Tob Res, 9*(8), 873-881. doi: 780760571 [pii]10.1080/14622200701484995

Williams, S. S., & Mulhall, P. F. (2005). Where public school students in Illinois get cigarettes and alcohol: characteristics of minors who use different sources. *Prev Sci, 6*(1), 47-57.

Yerger, V. B. (in press). Menthol's potential effects on nicotine dependence: A tobacco industry perspective. *Tobacco Control*.

# Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Appleyard. Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. 2001 American Legacy Foundation and CDC | Cross-sectional survey, secondary analysis of the 2000 National Youth Tobacco Survey | N=35,828 US middle school (MS) and high school (HS) students<br><br>Overall response rate was 84%.<br><br>Number of subjects:<br>Asian-American: 1742<br>Hawaiian/Pacific Islander: 487<br>African-American: 5913<br>Hispanic: 6565<br>White: 19,884<br>American Indian/Alaskan Native: 666 | Independent Variables:<br>MS and HS by Race/ethnicity<br><br>Outcome variable.<br>Menthol smoking initiation—grade smoked first cigarette among ever smokers<br><br>Current smokers defined as reported smoking a cig on ≥1 day of last 30 days<br><br>Menthol use defined as usually smoking menthol brand | Percentage of youth who usually smoke menthol brand of cigarettes by Middle and High School<br><br>Middle School / High School<br>Asian American 50.9% / 59.9%<br>Hawaiian/PI 38.9% / 51.2%<br>African American 70.9% / 75.0%<br>Hispanics 56.9% / 48.7%<br>Whites 42.4% / 29.6% | |
| Barker D. Changes in the Cigarette Brand Preferences of Adolescent Smokers — United States, 1989–1993. 1994. Centers for Disease Control and Prevention | Cross-sectional national survey; secondary analysis 1989 and 1993 Teen Age Attitudes and Practices Survey (TAPS): national household sample of adolescents (aged 12–18 years) | Of the 9135 respondents to the 1989 TAPS, 7960 (87.1%) participated in TAPS-II (age 15-22)<br><br>In addition, 4992 (89.3%) persons from a new probability sample participated in TAPS-II.<br><br>Data for the 12–18-year-olds in each survey were analyzed (n=9135 for TAPS; n=7311 for TAPS-II). | Independent variable:<br>Age group of adolescent<br><br>Outcome Variable:<br>Adolescent current smokers were asked if they usually bought their own cigarettes, and if so, which brand they usually bought.<br><br>Current smoking defined as smoking on 1 or more of the 30 days preceding the survey<br><br>Menthol cigarettes defined as brand usually bought | Younger smokers (aged 12–15 years) were more likely than older smokers (aged 16–18 years) to buy Newport (19.4% vs. 10.6%) and less likely to buy Marlboro (49.5% vs. 63.1%) | • Small number of Black and Hispanic respondents in TAPS II,<br>• Study conducted in early 90s. |
| Caraballo, Asman. Epidemiology of menthol cigarette use in the United States. 2010. | Literature review and data analyses using the National Survey on Drug Use and Health, the National Youth | NYTS: US students grades 6-12; n=1,978 middle school students and 6,163 hs from years '04, '06, '09 who smoked in past 30 days and | Independent Variables:<br>Middle School vs. High School<br><br>Outcome variable:<br>Percent current adolescent | Almost half of smokers age 12-17 reported smoking menthol (~ n=1 million) (NSUDH). | |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Funding source not explicitly stated | Tobacco Survey, the Monitoring the Future Survey, and the National Health and Nutrition Examination Survey | have a usual brand. N=2,580 adol. smokers from 35 states | menthol smokers<br><br>Current smoking defined as smoking at least 1 day of past 30 days<br><br>NYTS: Menthol use defined as usually smoking menthol cigarettes | Proportion of menthol use among Middle and High School students (NYTS)<br>Middle School: 49.4%<br>High School: 44.9% | |
| Curtin et al. Descriptive Epidemiological Analysis of Menthol Use from Four National US Surveys: I. Demographics. 2010 (FDA Submission) RJReynolds | Cross-sectional survey; secondary analyses of 2006 NYTS | N=27,038 students enrolled in US public and private schools, grades 6 through12 (aged 9-21 years)<br><br>Response rate information not provided in the article<br><br>N in analysis:<br>Menthol smokers=745<br>Non-menthol smokers =758 | Independent Variables:<br>Age group of smoker<br><br>Outcome variable:<br>Percent current menthol smoker<br><br>Current smokers defined as smoking any cigarettes on 10 or more of the last 30 days<br><br>Menthol use defined by usual cigarettes being menthol | Proportion of menthol use by age group<br>9-13 year olds: 59.3%<br>14-16 years old: 45.8%<br>17-18 years old: 38.3% | |
| Fernander, A., Rayens, M.K., Zhang, M., Adkins, S. Are age of smoking initiation and purchasing patterns associated with menthol smoking? 2010 Funding source not explicitly stated | Cross-sectional survey data; secondary analysis of in 2003 and 2006/2007 TUS-CPS | N=66,145 current smokers<br>Menthol smokers = 16, 294<br>Non-menthol smokers = 46,899<br>[2,952 smokers were unresponsive] | Independent variable<br>Before 18 years old vs. after 18 years old<br><br>Outcome variable:<br>Age at which first started smoking cigarettes fairly regularly<br><br>Current smoking defined as smoking at least 100 cigarettes in life-time and currently smoking every day or some days (including at least once in the last 30 days)<br><br>Menthol smoking status was | Current smokers who were younger were more likely to smoke menthol cigarettes (e.g., OR: 1.66, 95% CI: 1.47-1.88 for 18-24 y/o relative to those aged 65 and above).<br><br>Of the menthol smokers: 53.2% (95% CI +/-.9) started smoking before age 18 and 46.8% (95% CI +/-.9) started smoking at age 18 or older.<br><br>Of non-menthol smokers: 56.2% (95% CI +/-.6) started smoking before age 18 and 43.8% (95% CI +/-.6) started smoking at age 18 or older. | • Reference group was those aged 65 and above |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | | determined with the item: 'Is your usual cigarette band menthol or non-menthol?' with responses of 'menthol', 'nonmenthol' and 'no usual type'. Those who stated that they had no usual type were treated as missing values for the cigarette type variable. | | |
| Giovino 2010, Patterns of and Recent Trends in the Use of Mentholated Cigarettes in the United States<br>American Legacy Foundation | Cross-sectional survey; secondary analysis of 2004-2008 NSDUH | 179,242 respondents in the U.S. population who were 12-25 years old. Also used data on 69,322 smokers who were >=12 years old to report on patterns of methol use.<br><br>Response rate – 66.2% (2008 survey) | Independent variable:<br>Age<br><br>Outcome variable:<br>Percent menthol use among all smokers<br><br>Current cigarette smoking defined as smoking cigarettes in the past month<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol | Use of mentholated cigarettes by age<br>- 12-17 years old: 49.3%<br>- 18-25 years old: 37.5%<br>- 26-34 years old: 29.9%<br><br>A statistically significant age gradient in these age categories also was observed among males, females, whites, and Hispanics. Among African Americans, a ceiling effect likely occurred, with menthol use rates of at least 91.9% observed in all of the 12-34 year old age categories examined.<br><br>Use of mentholated cigarettes by age and race/ethnicity<br>12-15 y/o / 16-17 y/o / 18-21 y/o / 22-25 y/o<br>Total 53.5% 47.0% 40.5% 34.6%<br>White 47.6% 40.1% 32.6% 25.7%<br>Black 95.6% 93.9% 94.1% 92.5%<br>Hispanic 56.2% 50.5% 44.7% 34.9%<br>Asian 70.7% 50.7% 32.8% 39.6% | • Data were weighted to produce estimates that were representative of the population being sampled. |
| Giovino GA, Sidney S, Gfroerer JC, O'Malley PM, Allen JA, Richter PA, Cummings KM. Epidemiology of menthol cigarette use. | Cross-section national survey, secondary analysis of 2000 National Household Survey on Drug Abuse (NHSDA) | N in analysis=18,359 current smokers | Independent variable:<br>Age of smoker by race/ethnicity<br><br>Outcome variable:<br>Percent current smoker smoking menthol cigarettes | Percentage of current smokers who most often smoked menthol by age and race/ethnicity: 2000 NHSDA<br><br>12-17 y/o / 18-25 y/o / 26 + y/o<br>Total 31.6% 25.8% 28.6%<br>White 28.4% 20.1% 22.5%<br>Black 55.7% 68.6% 69.5%<br>Hispanic 35.7% 25.9% 29.7% | • All data were weighted to provide nationally representative estimates, and standard errors for 95% confidence intervals were |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| 2004 National Institute on Drug Abuse | | | Current smoking defined as smoking during the past 30 days<br><br>Menthol status defined as response to: "During the past 30 days, what brand of cigarettes did you smoke most often?" and "During the past 30 days, did you smoke (name of brand) menthol or regular cigarettes most often?" | Newport cigarettes use by race/ethnicity and age<br><br>12-17 y/o — 18-25 y/o — 26 + y/o<br>White 18.0% 9.3% 2.9%<br>Black 79.2% 76.7% 31.5%<br>Hispanic 31.4% 16.7% 7.1%<br><br>Marlboro cigarette use by race/ethnicity and age<br><br>12-17 y/o — 18-25 y/o — 26 + y/o<br>White 58.8% 61.4% 37.9%<br>Black 5.3% 7.3% 6.6%<br>Hispanic 52.5% 67.7% 54.0% | calculated in a way that reflected the complex survey design.<br><br>Potential Weakness:<br>• Misclassification of self reported menthol status in NHSDA |
| Hersey JC, Ng SW, et al: Are menthol cigarettes a starter product for youth? 2006 American Legacy Foundation | Cross-sectional survey; secondary analysis of 2000 and 2002 NYTS | 2000 NYTS: 35,828 students in grades 6 through 12 in spring 2000 and to 26,149 students in spring 2002. Response rate: 84% in 2000, 75% in 2002.<br><br>N in analysis=5,512 youth (2000 NYTS) and 3,202 youth (2002 NYTS). | Independent variable: School grade by race/ethnicity<br><br>Outcome variable: Prevalence of smoking menthol cigarettes among youth smokers<br><br>Current smoking defined as 'smoking cigarettes on one or more of the past 30 days'<br><br>Menthol use: defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol ("During the past 30 days, what brand of cigarettes did you usually smoke?" and "Is the brand of cigarettes that you usually smoked during the past 30 days mentholated?") | Menthol Use<br><br>Middle School — High School<br>Total 59.6% 43.6%<br>White 53.1% 37.4%<br>Black 87.5% 86.8%<br>Hispanic 62.9% 52.4% | • Controlled for demographic background and the length, frequency, and level of smoking;<br>• Takes into account misclassification; standardized scale to measure dependence.<br><br>Weaknesses:<br>• Possible misclassification in the reporting of menthol; |
| Hersey et al., 2010 Menthol cigarettes contribute to the | Cross-sectional survey; secondary analysis of 2006 NYTS | 2006 NYTS: Administered to 27,038 students enrolled in US public and private | Independent variable: School grade by racial/ethnic groups | Percent menthol smokers among past 30 day smokers<br><br>Middle School — High School | |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| appeal and addiction potential of smoking for youth,<br>NTR Dec 2010 supplement | | schools, grades 6 through 12 (aged 9-21 years)<br><br>Response rate – 80.2%<br><br>N in analysis=4,738 youth who smoked in the past 30 days, had a regular brand and could identify whether the brand was menthol or non-menthol | Outcome variable: Prevalence of smoking menthol cigarettes among youth smokers<br><br>Current smoking defined as 'smoking cigarettes on one or more of the past 30 days' and smoking 100 plus cigaettes in a lifetime<br><br>Menthol use defined as usual brand of cigarette smoked ("usual brand is menthol or nonmenthol") | White 43.1% 37.6%<br>Black 80.6% 84.8%<br>Hispanic 57.9% 56.4%<br><br>Percent menthol smokers among smokers who smoked 100 plus cigarettes in a lifetime<br><br>High School<br>White 38.1%<br>Black 84.4%<br>Hispanic 66.1% | |
| Hymowitz N, Corle D, Royce J, Hartwell T, Corbett K, Orlandi M, Piland N. Smokers' Baseline Characteristics in the COMMIT Trial 1995. National Cancer Institute | Baseline telephone survey data from 10 of 22 COMMIT sites,<br><br>COMMIT is a collaborative prospective clinical trial of community-based intervention. It is a community-level, multi-channel, 4-year intervention designed to increase quit rates among cigarette smokers. | Smokers ages 25-64 years from intervention and matched comparison communities in CA, NJ, NY, NM, and NC.<br>N=16,857<br><br>White: 11,128<br>Black: 3,322<br>Puerto Rican: 537<br>Mexican: 1,870 | Independent Variables:<br>Age<br><br>Outcome Variables:<br>Menthol cigarette use<br><br>Current smoking defined as smoking cigarettes now<br><br>Menthol use definition not provided in the article | Preference for menthol was greatest among the youngest smokers (OR: 0.71 (0.68-0.74). | • Studies conducted in 90s |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

## Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Rock V.J., Davis S.P., Thorne S.L., Asman K.J., Caraballo R.S. Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. 2010 Funding source not explicitly stated | Cross-sectional data: secondary analysis of 2004–2008 NSDUH | 2004-2008 NSDUH: Menthol smokers: 25,579<br>Non-menthol smokers: 46,026<br><br>See Table 1 and 2 (p S119 and S120) for more details. | Independent Variables:<br>Age by race/ethnicity.<br><br>Outcome Variables:<br>Prevalence of menthol use<br><br>A current cigarette smoker defined as anyone who answered "yes" to the question, "During the past 30 days, have you smoked part or all of a cigarette?"<br><br>Menthol use defined by response to "Were the cigarettes you smoked during the past 30 days menthol?" | Higher prevalence of menthol smokers vs. non-menthol smokers among those aged 12-17 years old (5.8% [5.5,6.1] vs. 3.4% [3.3,3.5])<br><br>Proportion of cig smokers smoked menthol among adolescents than young or older adults<br>12-17 y/o: 44.7%<br>18-25 y/o: 36.1%<br>26+: 30.2%<br><br>Prevalence of menthol cigarette use among current smokers aged 12 years or older by race/ethnicity<br><br>  12-17 y/o / 18-25 y/o / 26+ y/o<br>Total 44.7% 36.1% 30.2%<br>White 41.0% 28.8% 21.9%<br>Black 71.9% 85.0% 82.2%<br>Hispanic 47.0% 38.2% 29.5%<br>Asian 51.5% 35.8% 28.6%<br>AI/AN 34.7% 27.4% 23.0%<br><br>. | .<br>• The precision of smoking prevalence estimates for certain racial/ethnic populations was low due to small sample size (i.e., Asians and Native Americans/Alaska Natives), especially when stratified by age. |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 1: Age Gradient for Menthol Cigarette Use

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Sidney S., Tekawa I., Friedman G. Mentholated cigarette use among multiphasic examinees, 1979–86. 1989 NCI | Prospective cohort | Starting in July 1979, patients at Kaiser Permanente Medical Care Program medical centers in Oakland and San Francisco were asked to complete a supplementary questionnaire that explored their smoking habits in detail. Between 1979 – 1986, the questionnaire had been completed by 114,934 examinees (approximately 86 percent of the examinees), of whom 31,428 (27.3 percent) were current smokers.<br><br>Mentholated cigarette use habits were examined in the 29,037 current smokers ages 15-79 years of Black, White, or Asian race. | Independent variable: age<br><br>Outcome variable: percent menthol users<br><br>No definition provided for current smoking or menthol use | There was a marked inverse relationship between age and mentholated cigarette use in Blacks and in Asians, while there was relatively little difference in mentholated cigarette use with age in Whites (see Figure 1, page 1416).. | • |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

## Table 2: Trends in menthol use over time among youth

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Barker D. Changes in the Cigarette Brand Preferences of Adolescent Smokers — United States, 1989–1993. 1994. Centers for Disease Control and Prevention | Cross-sectional national survey; secondary analysis of 1989 and 1993 Teen Age Attitudes and Practices Survey (TAPS): national household sample of adolescents (aged 12–18 years) | Of the 9135 respondents to the 1989 TAPS, 7960 (87.1%) participated in 1993 TAPS-II (age 15-22)<br><br>In addition, 4992 (89.3%) persons from a new probability sample participated in TAPS-II.<br><br>Data for the 12–18-year-olds in each survey were analyzed (n=9135 for TAPS; n=7311 for TAPS-II).<br><br>N for analysis=702 smokers who usually bought their own cigarettes | Independent variable: Brand of cigarettes<br><br>Outcome Variables: Changes in brand preferences of teenage smokers over time<br>Current smoking defined as smoking cigarettes on 1 or more of the past 30 days<br><br>Menthol cigarettes defined as brand usually bought | Between 1989 and 1993, the percentage of adolescents purchasing Newport cigarettes increased 4.5 percentage points (55% increase). Increases for Newport cigarettes were greatest among younger smokers and adolescents residing in the Northeast.<br><br>Change in self-reported cigarette brand preference among adolescents aged 12-18 years<br>TAPS 1989 / TAPS 1993 / Change<br>Newport 8.2% / 12.7% / +4.5<br>Marlboro 68.7% / 60.0 / -8.7<br>Camel 8.1% / 13.3% / +5.2<br><br>Increase in Newport cigarette preference in youth exceed market share increase of +0.1 | Weaknesses:<br>• Small number of Black and Hispanic respondents in TAPS II,<br>• Study conducted in early 90s, but provide historical perspective |
| Caraballo, Asman. Epidemiology of menthol cigarette use in the United States. 2010. Funding source not explicitly stated | Literature review and data analyses using the National Survey on Drug Use and Health, the National Youth Tobacco Survey, the Monitoring the Future Survey, and the National Health and Nutrition Examination Survey | NSDUH: ages 12-17 who smoked in past month (9,595) and 18+ who smoked in past month (62,010) from surveys conducted 2004-2008<br><br>NYTS: US students grades 6-12; n=1,978 middle school students and 6,163 high school from years '04, '06, '09 who smoked in past 30 days and have a usual brand. Analysis on 2,580 adol. smokers from 35 states | Independent Variables: Menthol status; brand of cigarettes<br><br>Outcome variable: Percent current adolescent menthol smokers over time<br><br>Current smoking defined: smoking at least 1 day of past 30 days | According to NSDUH, menthol cig use increased from 04-08 (see below, Rock et al. 2010)<br><br>According to the MTFS data from 1998 to 2008, no consistent or significant change was observed during the period for Newport among 8th, 10th and 12th graders, however, a significant increase was observed for Kool.<br><br>According to the data from the 2004, 2006, and 2009 NYTS survey, a slight non-significant decrease in smoking Newport was observed among middle school smokers and no change among high school smokers. | |

1



* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

## Table 2: Trends in menthol use over time among youth

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | MTFS: US Students in 8th (n=20,863), 10th (n=30,722), 12th (n=40,914) grades for years '98-'08 | | | |
| Giovino GA, Sidney S, Gfroerer JC, O'Malley PM, Allen JA, Richter PA, Cummings KM. Epidemiology of menthol cigarette use. 2004 National Institute on Drug Abuse | Cross-section national survey, secondary analysis of 1998, 1999, 2000 Monitoring the Future | 136,000 participants surveyed<br>16,313 students analyzed | Independent variable:<br>Brand of cigarettes<br><br>Outcome measure:<br>Percent current smoker who smoked Newport, Kool or Salem between 1998 and 2000 by grade<br><br>Current and menthol status defined as response to what brand usually smoked in the past 30 days. | No significant change was observed in percent smoking menthol cigarettes (Newlport, Kool or Salem) across time within each grade. | Weakness<br>Brands not examined separately. For example, Kool cigarette smoking may have decreased but Newport smoking may have increased. |
| Giovino 2010, Patterns of and Recent Trends in the Use of Mentholated Cigarettes in the United States American Legacy Foundation | Cross-sectional survey; analysis of 2004-2008 NSDUH | 2004-2008 NSDUH: 179,242 respondents in the U.S. population who were 12-25 years old. Also used data on 69,322 smokers who were >12 years old<br>I<br>Response rate for 2008 survey was 66.2% | Independent variable:<br>Menthol status<br><br>Outcome variable:<br>Prevalence of menthol smokers in all youth over time<br><br>Current smoker defined as smoking cigarettes in the past month<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol | Trends in prevalence of menthol and non-menthol cigarettes among all youth<br>2004 2008<br>12-17 y/o<br>Menthol 5.3% 4.6%<br>Non-menthol 6.0% 3.9%<br><br>Slopes of regression liens are -0.14 for menthol and -0.53 for non-menthol and statistically different (p=0.003).<br><br>18-25 y/o<br>Menthol 14.0% 14.5%<br>Non-menthol 25.7% 20.4%<br><br>Slopes of regression liens are 0.17 for menthol and -1.49 non-menthol and statistically different (p=0.0002). | Strengths:<br>Data were weighted to produce estimates that were representative of the population being sampled. |

1



* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 2: Trends in menthol use over time among youth

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | | | | |

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Hersey JC, Ng SW, et al: Are menthol cigarettes a starter product for youth? 2006 American Legacy Foundation | Cross-sectional survey; secondary analysis of 2000 and 2002 NYTS | 2000 NYTS: 35,828 students in grades 6 through 12 in spring 2000 and to 26,149 students in spring 2002.<br><br>Response rate: 84% in 2000, 75% in 2002.<br><br>Data analyzed on 5,512 youth (2000 NYTS) and 3,202 youth (2002 NYTS). | Independent variable: Menthol use<br><br>Outcome variable: Rate of smoking menthol cigarettes among MS and HS by year<br><br>Current smoking defined as smoking cigarettes on one or more of the past 30 days'<br><br>Menthol use defined as the brand of cigarettes usually smoked and if the brand of cigarettes usually smoked during the past 30 days is menthol | Menthol cigarette use among youth between 2000 and 2002<br><br>2000 / 2002<br>Total * 40.0% / 47.4%<br>Middle School* 51.6% / 59.6%<br>High School 36.9% / 43.6%<br><br>*Significant difference $p < 0.05$ | Strengths:<br>• Controlled for demographic background and the length, frequency, and level of smoking;<br>• Takes into account misclassification; standardized scale to measure dependence.<br><br>Weaknesses:<br>• Possible misclassification in the reporting of menthol; |
| Hersey et al., 2011 Trends in brand and type of cigarette smoking by 12-17 year olds from 2004 to 2008, presentation to TPSAC, February | Cross-sectional survey; secondary analysis of 2004 to 2008 NSDUH | NSDUH samples of 12-17 year olds range from 17,727 to 18,678 for each of the years; number of smokers range from 1,759 to 2,255 | Independent variable: Brand of cigarettes<br><br>Outcome variable: Rate of smoking menthol cigarettes among youth smokers over time | Percentage of brand use among 12-17 year old smokers in the NSDUH: 2004 to 2008<br><br>2004 / 2008<br>Marlboro Menthol 12.7% / 18.2%<br>Marlboro Non-menthol 37.1% / 28.5%<br>Camel Menthol 1.7% / 6.4% | |

1



* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 2: Trends in menthol use over time among youth

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| 2011 | | | Current cigarette defined as smoking menthol cigarettes in the past month<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol | Camel Non-menthol 7.7% 9.0%<br>Newport 24.2% 23.5% | |
| Kaufman, N.J., Castrucci, B.C., Mowrey, P., Gerlach, K.K., Emont, S., Orlean, T. Changes in Adolescent Cigarette-Brand Preference, 1989 to 1996. 2004<br>Funding source not explicitly stated | Cross-sectional national survey; secondary analysis of The Robert Wood Johnson Foundation 1996 National Survey of Tobacco Price Sensitivity, Behavior, and Attitudes Among Teenagers and Young Adults (RWJF survey) was used to make national estimates of brand preference in 1996. These estimates were compared with similar estimates derived from the Centers for Disease Control and Prevention (CDC) Teenage Attitudes and Practices Surveys (TAPS) conducted in 1989 (TAPS I) and 1993 (TAPS II) surveys | RWJ survey N=17,287<br>TAPS-I N=9,315<br>TAPS-II N=12,952 (7,960 from TAPS-I plus 4,992 new respondents) | Independent variable:<br>Brand preference<br><br>Outcome variable:<br>Trends over time<br><br>Current smoking and menthol use defined as: In TAPS, adolescents who had smoked on at least one day during the past 30 and who usually bought their own cigarettes were asked, "What brand do you usually buy?" RWJF survey respondents who had smoked on at least one day during the past 30 and who had ever bought cigarettes were asked, "When you buy cigarettes, what brand do you usually buy?" The possible cigarette brand choices differed slightly among the 3 surveys. More brands were listed in the RWJF survey than in TAPS. Both the RWJF survey and TAPS-II included "no usual brand" as a | Between 1989 and 1996, Marlboro, Camel, and Newport were the brands respondents most often reported as the "brand usually bought." These 3 brands combined accounted for slightly over 84% in 1989 and 1993 and over 90% in 1996 of all brands respondents reported that they usually bought.<br><br>Of the 3 brands, Newport was the only one to increase significantly in each of 3 age-groups from 1989 to 1996. The percent reporting usually buying Newport increased 347% among 13 to 14 year olds, 189% among 15 year olds, and 69% among 16 to 18 year olds.<br><br>Percentage distribution of cigarette brand usually bought by adolescents by age<br>1989 1996<br>Marlboro<br>13-14 y/o 69.6% 66.9%<br>15 y/o 77.4% 64.1%<br>16-18 66.9% 68.1%<br>Total 68.5% 67.2%<br>Camel<br>13-14 y/o 13.7% 3.3%<br>15 y/o 13.9% 7.6%<br>16-18 3.6% 8.4%<br>Total 8.1% 8.1%<br>Newport<br>13-14 y/o 4.8% 19.2%<br>15 y/o 7.4% 21.4%<br>16-18 8.8% 14.9 % | Weaknesses:<br>• This is not generalizable to children who obtained cigarettes from nonretail sources or who had not smoked during the 30 days prior to survey.<br>• Old data set , but provides historical perspective |

1



* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 2: Trends in menthol use over time among youth

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study and Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | | possible response.<br><br>On the RWJF survey, respondents were queried as to the brand they usually smoked. Respondents were asked, "What *one* brand of cigarettes do you *usually* smoke?" | Total 8.3% 16.4%<br><br>When brand preferences by race and ethnicity are examined, only slight fluctuations were found in market share for Marlboro and Camel when comparing 1989 to 1996. However, the percentage of white and Hispanic adolescents who reported Newport as the brand they usually buy doubled (for whites, 5.3% to 10.4%, for Hispanics, 12.8% vs. 25.9%). No significant change was observed in Blacks. Kool also had a significant portion of the African American adolescent market, ranging from 9.4% in 1989 to 7.7% in 1996. Although almost 6% of Hispanic adolescents usually bought Kool in 1989, by 1996 Kool had less than a one-percent preference among any ethnic group or race other than African American. | |
| Rock V.J., Davis S.P., Thorne S.L., Asman K.J., Caraballo R.S. Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. 2010 Funding source not explicitly stated | Cross-sectional data; secondary analysis of 2004–2008 NSDUH | 2004-2008 NSDUH: Menthol smokers: 25,579<br>Non-menthol smokers: 46,026<br><br>See Table 1 and 2 (p S119 and S120) for more details. | Independent variable: Menthol smoking<br><br>Outcome Variables: Prevalence of menthol smoking from 2004 to 2008 by age and race/ethnicity<br><br>A current cigarette smoker was defined as anyone who answered "yes" to the question, "During the past 30 days, have you smoked part or all of a cigarette?"<br><br>To estimate menthol cigarette use, current smokers (*n* = 71,605) were asked, "Were the cigarettes you smoked during the past 30 days menthol?" Anyone who answered "yes" was considered to be a current menthol cigarette smoker. | **Trends is prevalence of menthol cigarette use among current smokers of different ages**<br><br>2004 2008<br><br>12- 17 y/o<br>--White* 40.3% 46.0%<br>--Black 72.5% 66.6%<br>--Hispanic 40.4% 46.7%<br>18-25 y/o<br>--White* 26.7% 32.5%<br>--Black 86.6% 87.4%<br>--Hispanic* 33.9% 42.4%<br><br>Significant changes from 2004 to 2008 in white 12-17 y/o smokers<br><br>Significant changes from 2004 to 2008 in white and Hispanic 18-25 y/o smokers<br><br>No significant changes from 2004 to 2008 among 26 plus year old among all ethnic/racial groups. | Weakness<br>.<br>• The precision of smoking prevalence estimates for certain racial/ethnic populations was low due to small sample size (i.e., Asians and Native Americans/Alaska Natives), especially when stratified by age. |

1

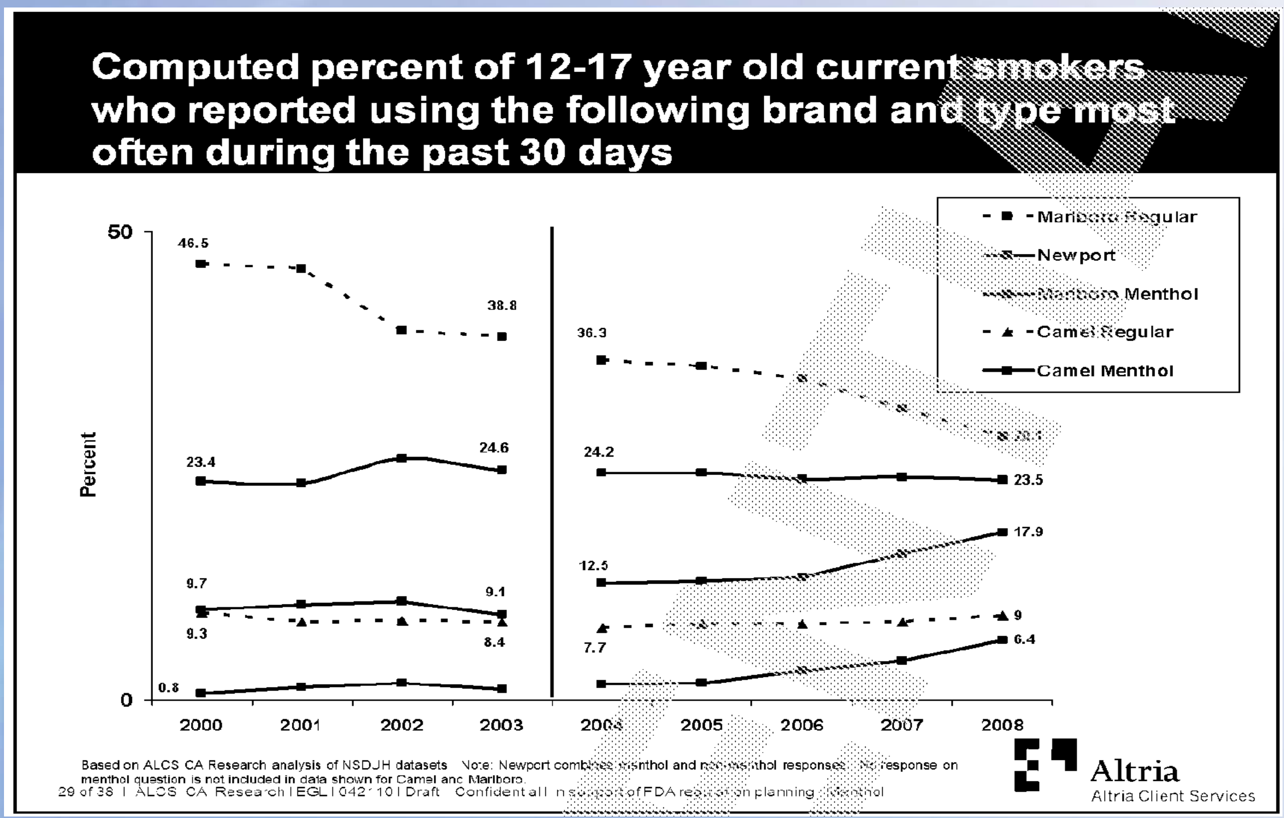


* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

Table 2: Trends in menthol use over time among youth
Version Date: 3-12-11

*RTI International*

# Percent of 12–17 Year-Old Smokers Smoking Menthol Cigarettes: 2000–2008 Industry analysis of National Survey on Drug Use and Health (NSDUH)




10 Source: *Industry Document.*

1



* Note: Some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

## Table 3: Rate of menthol smoking in recent vs. established smokers

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study/Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Results/Conclusion(s) related to Menthol* | Comments |
|---|---|---|---|---|---|
| Caraballo, Asman. Epidemiology of menthol cigarette use in the United States. 2010. Funding source not explicitly stated | Literature review and data analyses using the 2004, 2006 and 2009 National Survey on National Youth Tobacco Survey (NYTS) | NYTS: US students grades 6-12; n=1,978 middle school students and 6,163 hs from years '04, '06, '09 who had information on smoking history<br><br>Data analyzed on 2,580 adol. smokers from 35 states | Independent Variables: Amount of cigarette smoking<br><br>Outcome variable: Percent current adolescent menthol smokers in adolescents who started smoking less than 2 years ago<br><br>Current smoking defined as smoking at least 1 day of past 30 days<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol ("During the past 30 days, what brand of cigarettes did you smoke most often?" and "During the past 30 days, did you smoke (name of brand) menthol or regular cigarettes most often?") | # cigarettes by days smoking in the past 30 days — % menthol smoker<br>≤ 1 cigarette on 1-5 days — 39.9%<br>1-5 cigs on 1-5 days — 45.3%<br>1-5 cigs on 6-9 days — 47.5%<br>1-5 cigs on 10-19 days — 44.2%<br>1-5 cigs on 20-29 days — 49.7%<br>1-5 cigs on all 30 days — 46.6% | |
| Giovino 2010, Patterns of and Recent Trends in the Use of Mentholated Cigarettes in the United States American Legacy Foundation | Cross-sectional survey; secondary analysis of 2004-2008 NSDUH | 2004-2008 NSDUH: 179,242 respondents in the U.S. population who were 12-25 years old. Also used data on 69,322 smokers who were >12 years old<br><br>Response rate for 2008 survey was 66.2% | Independent variable: Amount of cigarette smoking<br><br>Outcome variable: Prevalence of menthol smokers in all youth based on amount of smoking<br><br>Current smoker described as smoking menthol cigarettes in | Percent menthol smoking by number of days per month<br>(1-5 days / 6-9 days / ≥10 days)<br>>12 y/o: 36.1% / 38.3% / 31.9%<br>12-17 y/o: 52.8% / 54.5% / 46.3% | Strengths:<br>• Data were weighted to produce estimates that were representative of the population being sampled. |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 3: Rate of menthol smoking in recent vs. established smokers

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study/Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Results/Conclusion(s) related to Menthol* | Comments |
|---|---|---|---|---|---|
| | | | the past month<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol | | |
| Hersey JC, Ng SW, et al: Are menthol cigarettes a starter product for youth? 2006<br>American Legacy Foundation | Cross-sectional survey; secondary analysis of 2000 and 2002 NYTS | 2000 NYTS: 35,828 students in grades 6 through 12 in spring 2000 and to 26,149 students in spring 2002.<br><br>Response rate: 84% in 2000, 75% in 2002.<br><br>Data analyzed on N=5,512 youth (2000 NYTS) and 3,202 youth (2002 NYTS). | Independent variable: Duration of smoking<br><br>Outcome variable: Rate of smoking menthol cigarettes among MS and HS smokers<br><br>Current smoking defined as smoking cigarettes on one or more of the past 30 days'<br><br>Menthol use defined as the brand of cigarettes usually smoked and if the brand of cigarettes usually smoked during the past 30 days is menthol | Menthol use and length of smoking by grade level, 2002 NYTS<br><br>(Less than year / More than a year)<br>Middle school *: 62.4% / 53.3%<br>High School: 45.9% / 41.9%<br>* $p < 0.002$ | • Takes into account misclassification; standardized scale to measure dependence.<br><br>Weaknesses:<br>• Possible misclassification in the reporting of menthol. |
| Hersey et al., 2010 Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth,<br>NTR Dec 2010 supplement | Cross-sectional survey; secondary analysis of 2006 NYTS | 2006 NYTS: 27,038 students enrolled in US public and private schools, grades 6 through 12<br><br>Response rate: 80.2%<br><br>Data analyzed on 4,738 youth who smoked in the past 30 days, had a regular brand and could identify whether the brand was menthol or non-menthol | Independent variable: Duration of smoking<br><br>Outcome variable: Rate of smoking menthol cigarettes among MS and HS smokers<br><br>Current smoking defined as 'smoking cigarettes on one or more of the past 30 days' and smoking 100 plus cigaettes in a lifetime<br><br>Menthol use defined as | Menthol use and length of smoking by grade level, 2006 NYTS<br><br>(Less than year / More than a year)<br>Middle school: 42.2% / 54.7%<br>High School: 42.8%% / 43.1%%<br><br>No significant differences in rate of menthol smoking among less established vs. more established smokers<br><br>No differences were foundi in rate of menthol smoking across different amounts of smoking | |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

# Table 3: Rate of menthol smoking in recent vs. established smokers

Version Date: 3-12-11

| Author Name(s), Article Title and year | Type of Study/Study Design | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Results/Conclusion(s) related to Menthol* | Comments |
|---|---|---|---|---|---|
| | | | usual brand of cigarette smoked ("usual brand is menthol or nonmenthol") | | |
| Footnote<br>Rising & Blader 2010<br><br>RJR June 2010 submission | | | | In a white paper written by the FDA, unpublished data from 2004 to 2008 NSDUH of menthol cigarette use among young smokes (aged 12-21 years) was presented. The data showed that rate of menthol smoking was higher among new smokers (smoking fore less than 1 year) than among experienced smokers (smoking for more than a year). The pattern, however, was reversed in 2008.<br><br>Using the same data, in the June 2010 submission by RJR, an analysis was presented in which menthol smokers were divided into smoking less than 100 cigarettes in a lifetime and smoking 100 cigarettes or more in a lifetime. The results again showed greater menthol cigarette smoking among the initiates as opposed to the more established smokers with the rates converging in 2008. | Data beyond 2008 should be examined to determine whether this data point is unusual. |
| Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *The NSDUH Report: Use of Menthol Cigarettes*. 2009<br>SAMHSA | Cross-sectional survey; secondary analysis of 2004 to 2008 National Survey on Drug Use and Health (NSDUH) survey includes individuals ages 12 and older. | 2004 to 2008 NSDUH survey of subjects 12 or older | Independent variable: Duration of smoking by age and race/ethnicity<br><br>Outcome Variable: Percent menthol smoker<br><br>Current smoker defined as smoking menthol cigarettes in the past month<br><br>Menthol use defined by most often smoked usual brand and whether this brand smoked in past 30 days was menthol | Past month use of menthol cigarettes among past month cigarette smokers 12 and older, by recency of cigarette initiation and demographic characteristics<br><br>Past year initiate / > 1 year use<br>Age 12 and older: 44.6% / 31.8%<br>12 to 17 y/o: 49.2% / 43.8%<br>18-25 y/o: 40.2% / 36.4%<br><br>Black: 73.9% / 82.8%<br>Hispanic: 42.9% / 32.1%<br>White: 39.9% / 23.6%<br><br>. | |



* Note: some of these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

**Table 4. Rates of Switching***

| Author | Survey/Study | Menthol to Non-menthol | Non-menthol to menthol |
|---|---|---|---|
| Pletcher 2006 | CARDIA<br><br>1535 current smokers | Among menthol smokers:12% | Among non-menthol smokers: 11% |
| Hyland 2010 | COMMIT<br><br>Smokers defined as<br><br>N=2095 completing 3 waves of surveys | Among all smokers: 6.4% | Among all smokers: 4.2% |
| Hyland & Karza2010 | ITC-4<br><br>Smokers defined as smoking at least 100 cigarettes in a lifetime and currently smoking monthly<br><br>N=7532 | Among menthol smokers<br><br>Total: 8.11%<br><br>Whites: 7.6%<br><br>Blacks: 7.8%<br><br>Hispanics: 17.4% | Among non-menthol smokers<br><br>Total: 2.2%<br><br>Whites: 1.74%<br><br>Blacks: 14.8%<br><br>Hispanics: 6.7% |
| Switching Book. 1991, Phillip Morris | | Among all past year switchers: 6.9% | Among all past year switchers: 5.7% |

| | | | |
|---|---|---|---|
| Eric Johnson presentation January 10, 2010<br><br>Switching Book | % among 34,117 cigarette smokers 18 year of age and older participating in a national telephone survey (1990-1991). | Among all current smokers:<br><br>0.6%<br><br>Among past year menthol smokers: 26.1% | Among all current smoker's<br><br>0.5%<br><br>Among past year non-menthol smokers: 7.7% |
| Giovino (2010) | 2003 Youth Smoking Cessation Survey<br><br>16-24 y/o<br><br>N=1045 | Among menthol smokers: 15% | Among non-menthol smokers: 6.9% |

**Table 5. Studies of Menthol Smoking and Dependence Among Youth (updated Table from Hersey et al., 2010)**

| Study | Population | Operational definition of menthol | Findings |
|---|---|---|---|
| Initial smokers | | | |
| DiFranza et al. (2004) | 267 seventh-grade students in two small Massachusetts cities who had inhaled a cigarette sometime during the study (68% White and 20% Hispanic) followed every 4 months for 30 months | Analysis based on the 50.6% of smokers (n=121) who recalled that their first cigarette was menthol (42%) or nonmenthol | 10-item Hooked on Nicotine Checklist scores not related to reported menthol of first cigarette<br>Menthol / Nonmenthol<br>Median 6.5 / 7.0<br>Mean 6.0 / 6.0<br>*SD* 3.3 / 3.4 |
| Nonemaker et al., 2010 | 1,100 out of 47,237 middle and high school youth in the 2000 through 2003 American Legacy Longitudinal Tobacco Use Reduction Study | First cigarette smoked is reported to be menthol | Menthol initiates higher than nonmenthol initiates on the following:<br><br>Smoking daily *OR*: 1.99<br>Established (smoking 20 or more days in past 30 days) *OR*: 1.94<br>Lifetime smoking (100+ cigs In lifetime) *OR*: 1.94<br>Nicotine dependence *OR*: 1.04 |
| Earlier smoker | | | |
| Hersey et al. (2006) | 26,149 6th - to 12th-grade students in the 2002 NYTS (for the subset who smoked in last month and had a usual brand of cigarettes) | Youth who identified their usual brand as menthol (excluding nonmenthol brands) | Menthol higher than nonmenthol smokers on a six-item Nicotine Dependence Scale for Adolescents: *OR*: 1.45** (*p*=.006) |
| Hersey et al., (2010) | 3,281 out of 27,038 6th-to-12th grade students in the 2006 NYTS who smoked in the last month and had a usual brand of cigarettes | Youth who identified their usual brand as menthol (excluding nonmenthol brands) | Menthol higher than nonmenthol on reduced time for needing a cigarette among smokers with regular brand: OR: 1.86** |
| Hersey et al., (November 2010 submision) | 5,511 youth in 48 schools around the country in a national biochemical validation survey; 1,215 students smoked in the past 30 days, 441 reported usual brand of cigarettes was menthol, 587 smoked in the prior 3 days and had positive cotinine ($\geq$ 5 ng/ml) | Youth who identified their usual brand as menthol | No main effect for menthol on cotinine levels<br><br>Menthol higher than nonmenthol on levels of dependence among smokers who smoked less than one year (P< 0.05). No differences in those who smoked 1 year or longer. |

| | | | |
|---|---|---|---|
| Muilenburg and Legge (2008) | 2,061 9th- to 12th-grade students in six southern schools (48% male; 73% Black) | Answered “yes” to usually smoking menthol cigarettes | Menthol higher than nonmenthol smokers on the following:<br>Shorter time since last smoke *OR*: 3.22***<br>Total cigarettes/lifetime *OR*: 4.35***<br>Smoke more days per month *OR*: 5.35**<br>Ever a daily smoker *OR*: 3.41*** |
| Established youth smokers | | | |
| Collins and Moolchan (2006) | 572 adolescent smokers recruited for a cessation study (55% female, 45% Black; mean age: 15.1 years) | Usual brand was menthol | Menthol Nonmenthol<br>Smoke within <5 min after waking 45%* 29% |
| Hersey et al., (2010) | 1,457 out of 27,038 6th-to-12th grade students in the 2006 NYTS who smoked in the last month and had a usual brand of cigarettes and smoked at least a 100 times in their lifetime | Youth who identified their usual brand as menthol (excluding nonmenthol brands) | Menthol higher than nonmenthol on reduced time for needing a cigarette among smokers with regular brand: OR: 2.06** |
| Wackowski and Delnevo (2007) | 1,345 current established smokers (30 days smoking and 100 cigarettes lifetime) in Grades 9 to 12 in the 2004 NYTS | Answered “yes” to usually smoking menthol cigarettes | Menthol vs. nonmenthol smokers more likely to need a cigarette within 1 hr after smoking: 16.3% vs. 7.4%; *AOR*: 2.6*<br>Menthol vs. nonmenthol smokers more likely to experience cravings after not smoking for a few hours: 35.9% vs. 25.4%; *AOR*: 1.6* |

*Note*. *AOR* = adjusted odds ratio; *OR* = odds ratio; NYTS = National Youth Tobacco Survey.
*$p$<.05; **$p$<.01; ***$p$<.001.

## Table 6: Quitting Success in National Surveys

Version Date: 3-12-11

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Alexander et al. Occupational status, work-site cessation programs and policies and menthol smoking on quitting behaviors of US smokers. 2010 Funding source not explicitly stated | Cross-sectional study; analysis of 2006/07 TUS CPS | In the 2006/07 TUS CPS data set, there was a total of 172 023 self-respondents. Respondents eligible for inclusion in this analysis were TUS CPS current smokers (every day or some days) aged 18 years or older. There was a total of 31 501 eligible self-respondents. Of these, 1325 were excluded due to missing information on cigarette brand type (non-menthol or menthol).<br><br>Total sample size for current study = 30,176 (Menthol=7718; Non-menthol=22,458)<br><br>Percent in each ethnic group: Menthol smokers--30.2% Black, 69.8% white/other<br>Non-menthol smokers--Black: 4.4%, white/other: 95.6% | Independent variable: Menthol status<br><br>Outcome Variable: Ever stopped smoking for one day or longer because trying to quit smoking | Controlling for occupational status and work-place policies and demographics, there were no differences for menthol versus non-menthol smokers on quitting behaviors OR = 0.98 (95% CI: 0.83-1.15) | Weaknesses:<br>• Menthol use, whether or not survey participants switched brands during or after any quit attempts, and exposure to menthol content in cigs cannot be validated<br>• Measure of quitting (measure is same for quit attempts no matter length of time without smoking) |
| Cubbin C, Mah-Jabeen S, LeClere FB. The intersection of gender and race/ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. 2010 Funding source not explicitly stated | Cross-sectional survey; analysis of 2005 NHIS and Cancer Control Supplement | Total sample= 31 428; analytical sample = 21,196 (included women and men 25–64); sample analyzed for quitting = 3902 - 3786<br>The final analytical sample size was 21 196, including all current, former and never smokers. Among those, 3902 were current every day smokers and 3786 were former smokers.<br><br>Response rate: 90% of eligible | Independent variable: Menthol status<br><br>Outcome Variables: (i)proportion of quit attempt in the past year (ii) time since quitting<br><br>Current smokers: smoked at least 100 cigs and smoke some or every day<br><br>Former smokers: smoked at least 100 cigs and currently do not smoke | Menthol smokers had higher levels of quit attempts compared with non-menthol smokers; differences were as great as 10–20%<br><br>Among white women menthol smokers had abstained about 2.5 years longer than non-menthol smokers ($p < 0.01$) | • No data if respondents started and remained smoking menthol or non-menthol cigarettes |



* Note: some these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | households.<br>Percent cigarette type and each racial/ethnic group: See attachment A | | | |
| Delnevo et al. Examining the relationship between menthol smoking and cessation using data from the 2003 and 2006/7 Tobacco Use Supplement 2010 submission. NCI and CDC | Cross-sectional survey; analysis of 2003 and 2006/07 Tobacco Use Supplements to the Current Population Survey: multistage clustered probability sampling | Sample size ranged from 71,193 to 24,465 (depending on criteria used for inclusion)<br><br>Response rate: The individual level self response rates for the 2003 TUSCS were 65.8%, 63.6%, and 61.4% for February, June, and November, respectively, and for the 2006/07 TUS the response rates were 60.7%, 61%, and 64.3% for May, August, and January respectively<br><br>N in each ethnic/racial group: See attachment B | Independent Variables:<br>Menthol status<br><br>Outcome Variables:<br>Cessation operationalized as current and former smokes who quit within the past 5 years who did not report current other tobacco products.<br><br>Former smoker deified as having smoked 100+ cigs in lifetime and now smokes 'not at all.'<br><br>Current smoker defined as having smoked 100+ cigs in lifetime and now smoke 'everyday' or 'some days'<br><br>Menthol use defined as self-report if usual brand in past 12 months (or 12 months prior to quitting) was mentholated | Current smokers who quit in the past 5 years, menthol vs. non-menthol cigarettes<br>AOR (95% CI)<br>Total 0.92 (0.88-0.97)<br>White 0.94 (0.89-0.999)<br>Black 0.78 (0.64-0.95)<br>Hispanics 0.96 (0.81-1.13)<br><br>If Hispanics are divided by country of origin, AORs are 1.34 (1.04- 1.73) for Mexicans and 0.63 (0.40-098) for Puerto Ricans.<br><br>Additional details on the covariates and AORs by the 5 sample restrictions available in Appendix X. | • Replication of Gundersen et al while addressing limitations of that paper. |
| Fagan P, Augustson E, Backinger CL, O'Connell ME, Vollinger RE Jr, Kaufman A, Gibson JT. Quit attempts and intention to quit cigarette smoking among young adults in the United States. 2007 National Cancer Institute | Cross-sectional survey; analysis of 2003 Tobacco Use Special Cessation Supplement (TUSCS) to the Current Population | Total N=33983 smokers and nonsmokers (Table 1 in article).<br><br>Analysis included young adult current smokers aged 18 to 30 years old: N=7912<br><br>Response rate: 82.8%:, 76% were self-respondents and were eligible for the entire TUSCS<br><br>Percent ethnic in each group<br>Hispanic: 19% | Independent variable:<br>Menthol status<br><br>Outcome Variables:<br>Number of quit attempts and a serious intention to quit<br><br>- *Quitting behaviors.* Quit attempts were assessed by asking current smokers, "How many times during the past 12 months have you stopped smoking for 1 day or longer because you were trying to quit smoking?" Responses were | Multivariate logistic regression of 1 or more quit attempts during the past 12 months among menthol vs. non-menthol smokers showed OR (95% CI) was 1.00 (0.89-1.16) for current smokers, 1.00 (0.85-1.18) for daily smokers and 0.99 (0.62-1.41) for nondaily smokers.<br><br>Multivariate logistic regression of 1 or more quit attempts during the past 12 months among smokers who reported serious intention to quit within the next 6 months showed non-significant effects of metnol among current smokers and daily smokers. However among non-daily smokers, the OR (95% CI) was 1.35 (0.60-3.03) | • Small sample sizes for racial/ethnic among nondaily smokers |



* Note: some these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | 2 or more races: 2%<br>Non-Hispanic White: 61%<br>Non-Hispanic Black: 13%<br>Non-Hispanic Asian/ Pacific Islander: 5%<br>Non-Hispanic American Indian/Alaska Native: 0.7% | categorized into 1 or more quit attempts and zero quit attempts. The intention to quit was assessed by asking smokers, "Are you seriously considering quitting smoking within the next 6 months?" and included the responses yes or no.<br><br>Current smokers defined as smoked every day (daily smokers) or some days (nondaily smokers).<br><br>Menthol status defined as menthol or non-menthol as usual cigarette type or no usual type. | but non-significant.. | |
| Fagan et al. Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. 2010 National Cancer Institute. | Cross-sectional survey; analysis of 2003 and 2006/07 Tobacco Use Supplements to the Current Population Surveys | Daily current smokers aged 18+ (*n* = 46 273)<br><br>Response rate: 82.9% and 82.6%<br><br>Menthol=11,671; NM=33, 644<br><br>For the number of individuals in each ethnic group by usual cigarette brand smoked, refer to Attachment C. | Independent Variable:<br>Menthol status<br><br>Outcome Variable:<br>--Number of times during the past 12 months quit for one day or longer because trying to quit<br>--Longest period of abstinence in last 12 months because trying to quit smoking<br>--Intention to quit (planning to quit in next 30 days)<br><br>Current daily smoking defined as smoked at least 100 cigarettes and smoking every day<br><br>Menthol status defined as usuabrand of cigarettes as being menthol or non-menthol | Multivariate models did not show sig. associations between usual brand of cigs and quit attempts 1 day or longer in past 12 months: OR (95% CI) ranged from 0.92 (0.83-1.02) to1.10 (0.91-1.34) depending upon cigarettes smoked per day<br><br>Multivariate models did not show sig. associations between usual cig brand duration of smoking abstinence 2 weeks vs. $\leq$ 2 weeks in the past 12 months: OR (95% CI) ranged from 0.93 (0.79-1.12) to1.05 (0.82-1.36) depending upon cigarettes smoked per day | |
| Gundersen DA, Delnevo CD, | Cross-sectional survey; analysis of 2005 U.S. | N=7815 white, black, and Hispanic current and former | Independent Variable: Menthol status | Menthol smokers were less likely than nonmenthol smokers to be former smokers | • Who quit long ago may be more |

# Table 6: Quitting Success in National Surveys

Version Date: 3-12-11

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Wackowski O. Exploring the relationship between race/ethnicity, menthol smoking, and cessation, in a nationally representative sample of adults. 2009 Funding source not explicitly stated | National Health Interview Survey —Cancer Control Supplement (NHIS-CCS). | cigarette smokers who indicated that they do not currently use other tobacco products and have made a quit attempt.<br><br>Response rate: NA<br><br>Menthol smokers : 26.5%<br>Non-menthol smokers: 73.5%<br><br>Percent ethnic in each group<br>White: 82.7%<br>Black: 8.9%<br>Hispanic: 8.4% | Outcome Variable: Cessation operationalized as current vs. former smoker<br><br>Former smoker is defined as having smoked 100 cigarettes in a lifetime and now smoking "not at all."<br><br>Current smoker is defined as having smoked 100 cigarettes in a lifetime and now smoking "everyday" or "some days."<br><br>Menthol use defined as whether or not their usual brand of cigarettes in the past 12 months or in the 12 months prior to quitting was mentholated. | (56.9% vs. 61.5%; p<0.01). This relationship was found among blacks (43.7% vs. 62.1%; p<0.01) and Hispanics (48.5% vs. 61.2%; p<0.001), but was not statistically significant among whites (62.8% vs. 61.6%, p=0.44).<br><br>The odds of being a former smoker does not differ statistically or substantially relative to nonmenthol smokers (AOR=1.05, p=.47; Model 1) after controlling for demographics, smoking behavior, and perceived risk of cancer. White menthol smokers are more likely to be former smokers than their nonmenthol smoking counterparts, while black and Hispanic menthol smokers are less likely to have quit relative to black and Hispanic nonmenthol smokers respectively. Among non-whites (i.e. blacks and Hispanics collapsed) menthol smokers are less likely to have quit relative to nonmenthol smokers (AOR=0.55, p<0.01).<br>AOR (95% CI)<br>White: 1.17 (1.00-1.36)<br>Blacks: 0.78 (0.56-1.09)<br>Hispanic: 0.61 (0.39-0.97)<br>Non-white: 0.55 (0.43-0.71) | subject to recall bias on variables such as number and type of cigarettes smoked compared to more recent quitters or current smokers |
| Hyland & Kasza. A Longitudinal Study of the Association Between Menthol Cigarettes and Indicators of Dependence: Findings from the International Tobacco Control Project 2010. National Cancer Institute Canadian Institutes for Health | Cohort survey; analysis of International Tobacco Control Four Country Survey ITC-4, which is an ongoing prospective cohort survey conducted with nationally representative respondents from four countries, including the United States. | Data were collected from 7532 adult smokers (18 years +) between 2002 and 2008. Random digit dialing was initially used to recruit current smokers within strata defined by geographic region and community size. Respondents who agreed to participate (cooperation rate ~80%) were typically contacted and completed a 35-minute survey designed to evaluate the | Independent variable:<br>Menthol status<br><br>Outcome variables:<br>-Making a quit attempt – respondents were asked: "Have you made any attempts to stop smoking since we last talked with you?"<br>-Successful smoking cessation defined as no longer smoking on at least a monthly basis<br>-Successful cessation among those making a quit attempt | In terms of quit attempts and quit outcomes, white respondents who smoked menthol cigarettes were significantly less likely to report making a quit attempt compared to white respondents who smoked non-menthol brands (0.84). No differences were seen in African Americans and Hispanics.<br><br>No significant differences were observed in successful smoking cessation across all races, except African American women who smoked menthols were more likely to report successful cessation (3.58) and cessation among attempters | • Sample sizes were relatively small among minority racial/ethnic groups. |



* Note: some these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| Research, Australian National Health and Medical Research Council, Australian Commonwealth Department of Health and Aging<br>Cancer Research UK, Canadian Tobacco Control Research Initiative, Centre for Behavioural Research and Program Evaluation of the National Cancer Institute of Canada/Canadian Cancer Society | | psychosocial and behavioral impact of various national-level tobacco control policies.<br><br>Menthol smokers: 27%<br>Non-menthol smokers: 73%<br><br>Percent/number in each ethnic group<br>White: 79%<br>African-American: 11%<br>Hispanic 5%<br>Asian: 1%<br>Native American:4% | | at quitting (OR 3.96) than African American non-menthol smokers. | |
| Stahre M., Okuyemi K.S., Joseph A.M., Fu S.S. Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. 2010<br>Funding source not explicitly stated | Cross-sectional survey; analysis of 2005 National Health Interview Survey (NHIS). | 6055 current adult smokers. Of these; 3068 male, 4932 White, 861 African American, 54 AI/AN, 119 Asian, average # cpd = 16.8, 1700 menthol smokers, 4355 non-menthol smokers<br><br>5949 former smokers. Of these; 3058 male, 5147 White, 573 African American, 45 AI/AN, 98 Asian, average # cpd = 18.6, 1515 menthol smokers, 4434 non-menthol smokers | Independent variable:<br>Menthol status by racial/ethnic groups<br><br>Outcome Variables:<br>Population quit ratio: dividing the total number of former smokers by the total number of individuals who had reported smoking during their life-time (i.e. both former and current smokers).<br><br>Current smokers not defined<br><br>Former smokers defined as individuals who had reported quitting smoking within the previous 12 months.<br><br>Current smokers were also asked whether they had attempted to quit smoking within the past year.<br><br>Menthol cigarette status defined as | Of current menthol smokers, 49% reported a quit attempt in the past year, while 41% of non-menthol smokers reported a quit attempt. In addition, the quit ratios were significantly higher for non-menthol versus menthol smokers (50% versus 47%, *P* = 0.014).<br><br>No significant difference in the quit ratios for menthol versus non-menthol smokers for whites (52% versus 50%), Asian Americans (38% versus 42%), AI/AN (52% versus 35%) or Hispanics (40% versus 45%). However, significant differences in the quit ratio for menthol versus non-menthol among African American smokers (34% versus 49%, *P* < 0.001). African American menthol smokers were significantly less likely than white nonmenthol smokers to have quit smoking (AOR: 0.72, 95% CI: 0.53, 0.97, *P*-value 0.031) after controlling for age group, sex, region, marital status and average number of cigarettes smoked per day | : |

# Table 6: Quitting Success in National Surveys

Version Date: 3-12-11

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | | whether or not respondent's usual brand of cigarettes was mentholated. | | |
| Trinidad D, Perez-Stable EJ, Messer K, White M, Pierce JP. Menthol cigarettes and smoking cessation among racial/ethnic groups in the United States. 2010 Funding source not specified | Cross-sectional survey; analysis of 2003 and 2006-2007 Tobacco Use Supplements to the Current Population Survey (TUS CPS). | Respondents ages 20-65 years at the time of the survey.<br><br>Total N=283,441; 25,758 (Af-Am), 10,853 (Asian), 28,720 (Hispanic), 2,616 (Native American), 212,693 (White)<br><br>Among current smokers – 14,791 were menthol smokers vs 42,352 non-menthol smokers.<br><br>Among former smokers who had quit less than 6 months ago; 2,876 were menthol smokers, 9707 were non-menthol smokers<br><br>Among smokers who had quit smoking for 6+ months prior to the survey; 950 were menthol smokers, 3015 were non-menthol smokers<br><br>Response rate: CPS response rate 92%. Survey includes proxy and self-response data. Response rate for self-response data (only self-response data was used in this article) – 61% | Independent Variables:<br>Menthol status by racial/ethnic group<br><br>Outcome Variables:<br>-Quit attempts: Current smokers were asked if they made an attempt to quit in the past 12 months, and, if so, the length of their longest quit attempt and the length of their last quit attempt.<br>-Quitting intentions: Current smokers were asked if they were seriously considering quitting smoking within the next 6months (yes/ no). Current smokers were also asked to assess how likely they thought they would succeed in quitting smoking altogether in the next 6 months.<br>-Quitting success: Among former smokers, successful smoking cessation/ long-term quitting was defined as being quit for at least 6 months at the time of the survey.<br><br>Menthol status defined as response to question on their brand preferences (menthol, non-menthol or no usual brand). Former smokers were asked to think to the year before they quit and identify their brand preference. Those who reported having no usual brand were excluded from statistical modeling analyses. | African Americans and Hispanics/Latinos who smoked mentholated cigarettes were significantly more likely to be seriously considering quitting in the next 6 months compared to those who smoked nonmentholated cigarettes [African Americans: odds ratio (OR) = 1.62, 95% CI: 1.35–1.95; Hispanics/Latinos: OR = 1.21, 95% CI: 1.00–1.47]. No suggestion of a similar relationship was found among Asian Americans/ Pacific Islanders, Native Americans/Alaska Natives or non-Hispanic whutes,<br><br>African Americans and Hispanics/Latinos who smoked mentholated cigarettes were significantly more likely to have a positive estimation of quitting successfully in the next 6 months compared to those who smoked nonmentholated cigarettes (African Americans: OR = 1.87, 95% CI: 1.60–2.19; Hispanics/Latinos: OR = 1.34, 95% CI: 1.11–1.62). This was not found among Asian Americans/Pacific Islanders, Native Americans/Alaska Natives and non-Hispanic whites.<br><br>Those who smoked mentholated cigarettes were significantly less likely to have quit successfully for at least 6months, for all racial/ethnic groups except Native Americans/Alaska Natives (African Americans: OR = 0.23, 95% CI: 0.17–0.31; Asian Americans/ Pacific Islanders: OR = 0.22, 95% CI: 0.11–0.45; Hispanics/Latinos: OR = 0.48, 95% CI: 0.34–0.69; Native Americans/Alaska Natives: OR = 0.49, 95% CI: 0.14–1.71; non-Hispanic whites: OR = 0.28, 95% CI: 0.25–0.33). | .<br>Pure copy paste from the cited paper |



* Note: some these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

## Table 6: Quitting Success in National Surveys

Version Date: 3-12-11

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Independent & Outcome Variables | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) | Comments |
|---|---|---|---|---|---|
| | | | Current and former smoker defined as lifetime cigarette use (Have you ever smoked 100 cigarettes?') Current cig use defined as smoking every day or some days; former smoker as not smoking at all. | | |

Note: Please see text for information on embargoed study by Levy et al., in press



* Note: some these statements are taken directly from articles and may not include all relevant results/conclusions. Please read the entire article.

**Table 7** Main Characteristics and Findings of Longitudinal Cohort and Clinical Trial Studies Comparing Smoking Cessation Outcomes in Menthol and Nonmenthol Cigarette Smokers (additional information added to Table in Foulds et al., 2010)

| Author (publication year) / study years | Location | N M / NM | *N*—W / AA / Hisp / Other | Cigarettes / day (M / NM) | Design | Intervention? | Definition (of a quitter) | Evidence of M effect? | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Fu et al. (2008)/2006 | United States— VA pharmacy databases | Total = 1,343<br>M = 342 (25%)/<br>NM = 1,001 (75%)<br>*M* age = 56 (10.3) | All smokers:<br>Caucasian: 76%<br>AA: 14%<br>Other: 10% | Total: 25<br>M: 20<br>NM: 30 | Cross-sectional analysis at end of interventional trial | Intervention aimed to stimulate repeat quit attempts<br>All participants had previously failed using NRT or bupropion | Seven-day point prevalence, self-reported | No overall effect of M on abstinence. Some evidence of increased quitting among menthol smokers, restricted to intervention group, with lower menthol quitting in controls. | Older sample. One significant interaction between menthol status and treatment group only, not significant after Bonferroni correction |
| Cropsey et al. (2009)/ 2004–2006 | Women's prison in Virginia | N=233<br>M=159<br>NM=74<br>*M* age = 34 | W = 109 (49% M)<br>AA = 124 (95% M)<br>(all female) | W = 20<br>AA = 14 | Retrospective analysis of trial cohort. | Randomized trial of NRT plus group, versus wait list control | Seven-day point prevalence by self-report (and exhaled CO < 3 ppm) at 6 weeks and 12 months. | No effect of menthol | Relatively small sample of incarcerated women (only six AA nonmenthol smokers) |
| Gandhi et al. (2009)/ 2001–2005 | Outpatient Smokers' Clinic Central New Jersey | Total = 1688<br>M = 778 (46%)/<br>NM = 910 (54%)<br>*M* age = 42 (13.3) | 1086/374/149/79<br>64%/22%/9%/5% | Total sample: 21<br>M: 19<br>NM: 23 | Clinic cohort, followed up at 4 weeks and 6 months. | Tailored Smoking cessation treatment with meds and counseling | Self-report of not smoking in previous 7 days at 4 weeks and 6 -month follow-up. Biochemical verification in those attending at 4 weeks. | Yes, but restricted to non-whites. Also related to *SES*. For AAs at 6 months, Adj. OR = 0.48 (0.25–0.9) | Cigarettes/day lower in AA and H menthol smokers. Follow-up rate= 74% at 4 weeks and 58% at 6 months. |
| Okuyemi et al. (2007)/ 2003–2004 | Kansas | 755 light smokers (<11 cigarettes/day) *M* age = 45.1 (*SD* = 10.7) | 0/755/0/0 | M: 7.5<br>NM: 7.8 | Clinical trial cohort followed up at 6m. | Nicotine gum × motivational interviewing trial (factorial) | Seven-day point prevalence, verified by CO/salivary cotinine at 6-month follow-up | Yes, unadjusted: 11.2% vs. 18.8% | M not significant in fully adjusted model (overadjusted by using number of appointments attended?) (Nollen et al. 2006); M effect stronger in age < 50 |
| Okuyemi et al. (2003)/ | Kansas | 600 smokers (471/129) | 0/600/0/0 | M: 18<br>NM: 18 | Clinical trial cohort followed up at 6m. | Bupropion versus placebo | Seven-day point | Yes, in subgroup. At 6 weeks in | No significant effect at 6 months or in age |

| **Author (publication year) / study years** | **Location** | **N M / NM** | ***N*—W / AA / Hisp / Other** | **Cigarettes / day (M / NM)** | **Design** | **Intervention?** | **Definition (of a quitter)** | **Evidence of M effect?** | **Comments** |
|---|---|---|---|---|---|---|---|---|---|
| 1999–2000 | | *M* age = 44 | | | | randomized controlled trial | prevalence, verified by CO/salivary cotinine | age < 50: OR (NM) 2.02 (1.03–3.95) | > 50 |
| Murray et al. (2007)/ 1986–2001 | United States | Total = 5,883 M = 1,216 (21%)/ NM = 4,671 (79%) *M* age = 48.4 (*SD* = 6.8) | White:95.2% AA: 3.8% H: 0.6% | Overall average 26 cigarettes/ day Pack-years: M: 38.18 NM: 40.1 | Clinical trial cohort followed up 5 and 14 years after enrollment | 12-week group intervention plus nicotine gum (repeatable for 5 years) or usual care | Smoking at all in past 12 months | Three categories: sustained quitter, intermittent smoker, continuing smokers; no menthol effect | Only 114 AA menthol smokers in the study. |
| Pletcher et al. (2006)/ 1985–2000 | Birmingham, Chicago, Minneapolis, and Oakland | 1535 smokers (972/563) *M* age= 25.1 (3.6) | 657/878/0/0 | M: 10 NM: 15 | Prospective cohort study | No | *Sustained cessation*: not current smoker at last 2 visits *Relapse*: smoker → nonsmoke → smoker at last exam | Yes *Sustained cessation*: Adj. OR = 0.71(0.49-1.02) *Relapse*: Adj. OR = 1.89 (1.17–3.05) | Long-term study, not in context of a quit attempt |
| Muscat et al. (2002)/ 1981–1999 | Hospitals in New York, Washington DC, and Pennsylvania | Total = 19545 NM = 16540 (85%) M = 3005 (11%) 56%–72% aged > 54 | W = 17,637 (89%) AA = 1906 (11%) | W: NM = 29 M = 28 AA NM = 21 M = 18 | Cross-sectional case-control study based on convenience sample of cases (lung cancer) and controls (other medical patients) | No intervention | Ever smoked daily for a year and not smoked daily in past year. | No effect on quitting OR = 1.1 | Older and relatively affluent sample, with unusually low menthol rate in AAs (34%). Definition of abstinence relatively lenient. Possible effect of illness on quitting. |

| Author (publication year) / study years | Location | N M / NM | *N*—W / AA / Hisp / Other | Cigarettes / day (M / NM) | Design | Intervention? | Definition (of a quitter) | Evidence of M effect? | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Hyland et al. (2002) / 1988–1993 | 22 communities in North America | *N* = 13,268 (age 25–64) M = 3,184 (24%) / NM = 10,084 (76%) 23% Whites smoke M, 57% AAs smoke M. 51% ages < 45 | All smokers: Caucasian: 10,004 (75%) AA: 878 (7%) Hispanic: 693 (5%) Other: 294 (2%) Canadian: 1,382 (10%) | Total sample: 23.2/day | Prospective population cohort survey, followed up after 5 years. | Randomized community intervention trial | Self-report of no cigarette use in past 6 months at 5-year follow-up. | No. (e.g., adjusted RR for quitting by AA menthol smokers = 1.04.) | M smokers more likely to have 2+ prior quit attempts. No data on whether participants tried to quit. |
| **Unpublished November 2010 submissions to FDA** | | | | | | | | | |
| Hyland, Rivard et al. (2010a) | 22 communities in North America | N=2095 M=400 NM=1464 Other=222 | W=866 AA=91 | | Prospective population cohort survey, assessed in 2005; Menthol status 1988-2001. | Randomized community intervention trial | Self-report of no cigarette use in past 6 months in 2005 | No effect on quitting OR: 0.84 | Sample size too small for AA |
| King et al. | Outpatient smokers clinic Chicago | N=291 M=126 NM=155 | W=181 B=110 | | Clinical trial cohort followed up at 4 and 12 weeks | NRT vs. NRT plus naltrexone | CO verified prolonged abstinence | Significant med x menthol interaction in AA (OR=31.22, p=0.029) | AA menthol vs. nonmenthol smokers who used NRT only did worse |
| Rietzel a | Outpatient clinic Houston TX | N=420 M=175 NM=245 | W=138 B=143 Latino=139 | M=20.7 NM=21.5 | Clinical trial cohort followed up to 26 weeks | NRT plus counseling | CO verified no smoking since quit date | Menthol did not predict abstinence | |
| Rietzel b | Outpatient clinic | N=391 M=321 | B=391 | M=20.6 NM=21.0 | Clinical trial cohort | Treatment with palm pilot | CO verified no | Menthol did not predict | |

| Author (publication year) / study years | Location | N M / NM | *N*—W / AA / Hisp / Other | Cigarettes / day (M / NM) | Design | Intervention? | Definition (of a quitter) | Evidence of M effect? | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | Houston, TX | NM=70 | | | followed up to 26 weeks | computers | smoking since quit date | abstinence | |
| Rietzel c | Outpatient clinic Houston, TX | N=249 M=125 NM=124 | W=88 B=81 Latina=75 Other=5 | M=9.2 NM=11.1 | Clinical trial cohort followed up to 26 weeks | Motivation based treatment for pregnant women | CO verified no smoking since quit date | Menthol did not predict abstinence | Post-hoc analysis showed White menthol vs. non-menthol smokers did worse (small n) |

- *Note.* M = menthol; NM = nonmenthol; OR= odds ratio; RR= relative risk; adj. = adjusted for other baseline variables; CO = exhaled carbon monoxide concentration; AA= African American; W = white (non-Hispanic); H = Hispanic/Latino; *M* age = mean age of sample; SES = Socioeconomic status; NRT = Nicotine Replacement Therapy.
- ***Note:* Please see text for embargoed study by Blot et al., in press.**

# CHAPTER 7: EFFECTS OF MENTHOL ON THE DISEASE RISKS OF SMOKING

## INTRODUCTION

This chapter addresses the question: Do smokers of menthol cigarettes have increased risk for diseases caused by smoking in comparison with smokers of non-menthol cigarettes? In the TPSAC conceptual framework, this question is directed at the relative risks for development of the various diseases caused by smoking with the comparison being between users of non-menthol cigarettes as the reference. Risks could be greater or lesser for smokers of menthol cigarettes if the various toxins and carcinogens in smoke differ by type of cigarette; if smoking patterns differ by type of cigarettes in ways that affect the doses of disease causing-agents reaching target sites; if menthol affects the kinetics and metabolism of disease-causing tobacco smoke components; and if menthol itself contributes to disease risk.

Multiple lines of research are relevant to the overall question that is the focus of this chapter. These include: (1) studies directed at the topography of smoking; (2) studies comparing levels of biomarkers of tobacco smoke in smokers of menthol and non-menthol cigarettes; (3) studies on the toxicology of menthol; and (4) epidemiological studies that directly compare disease risks in smokers of menthol compared with non-menthol cigarettes.

## STUDIES OF SMOKING TOPOGRAPHY

An important question in assessing risks of smoking menthol cigarettes is whether menthol cigarette smokers inhale more smoke and are exposed to more tobacco smoke toxins than smokers of non-menthol cigarettes. This question has been examined in two types of studies. The first type involves laboratory studies that compare puffing behaviors (called topography studies) or the increase (boost) of nicotine and/or carbon monoxide levels from smoking a cigarette in individual menthol and non-menthol smokers. This section reviews such studies. The second consists of cross-sectional studies in which tobacco smoke exposure biomarkers are measured in people smoking cigarettes, typically their usual brand of cigarette, and menthol and non-menthol smokers are compared. A subsequent section considers these studies.

Before describing the various studies, it is important to mention important potential confounding factors and other methodologic problems that are relevant to a number of studies. Since most African American smokers smoke menthol cigarettes and most whites smoke non-menthol cigarettes, any comparison of menthol vs. non-menthol without considering race is problematic. African American and white smokers differ in several relevant ways. On average African Americans smoke fewer cigarettes per day, take in more smoke per cigarette and metabolize nicotine and cotinine differently than white smokers (Perez-Stable et al. 1998). Some studies statistically control for race, but "control" may not be possible, given the high proportion of African Americans who smoke menthol cigarettes. The optimal study design compares menthol vs. non-menthol smokers within a racial group, but few studies have adequate numbers to do this. Also, a number of the published studies, particularly the topography studies, are quite small and predominantly include adult heavy smokers recruited by advertisements for experimental studies. This approach to identifying participants limits the generalizability of findings. Furthermore, topography studies generally measure puffing behavior while smoking one cigarette via a cigarette holder, to which monitoring equipment is attached. Smoking a single cigarette through a cigarette holder is not representative of how a person normally smokes their cigarettes throughout the day. Several studies have involved rapid smoking of cigarettes or smoking with fixed puff sizes or fixed numbers of puffs, also experimental scenarios that are not representative of usual smoking.

Eleven laboratory studies of topography were identified (table 1). These studies varied considerably in design, but included at least some measurement of smoking behavior: number of puffs per cigarette, average puff volume, total puff volume, time to smoke the cigarette and/or biomarker measurements: increase in nicotine and/or carbon monoxide levels before and after smoking a cigarette.

Nine studies reported effects of menthol smoking on number of puffs or puff volume (Nil and Battig 1989; Caskey et al. 1993; Miller et al. 1994; Ahijevych et al. 1996; Jarvik et al. 1994; McCarthy et al. 1995; Ahijevych and Parsley 1999; Pickworth et al. 2002; Strasser et al. 2007). Some studies compared smokers smoking their preferred type of cigarette while some were crossover studies. Some studies reported a decrease, one reported an increase, and others saw no change in puffing behavior comparing menthol to non-menthol cigarette smoking. Jarvik et al. (1994) also compared inhaled volume and lung retention time and found no effect of menthol cigarettes. St Charles et al. (2009) similarly reported no effect of smoking menthol cigarettes on inhalation volume or total lung exposure times, although the inhalational tidal ratio (the inhalation volume as a proportion of resting tidal volume) was borderline lower in menthol (1.52, SD 0.47) compared to non-menthol (1.79, 0.60) smokers ($p = 0.054$).

Six studies reported CO boost in relation to type of cigarette smoked (Nil and Battig, 1989; Miller et al. 1994; McCarthy et al. 1995; Jarvik et al. 1994; Ahijecych et al. 1996; and Pickworth et al. 2002). In general there were small or no differences between the CO boost by type of cigarette. Miller et al. (1994) found that CO boost was higher from smoking cigarettes into which 8 mg menthol had been injected compared to lower levels, despite no change in puff volume. Two other studies also found that the increase in CO in relation to puff volume or number of puffs was higher in smokers of menthol cigarettes compared with non-menthol cigarettes.

Patterson et al. 2003 measured the plasma nicotine boost in treatment-seeking smokers and in a multivariate analysis found no effect of menthol cigarette smoking.

Overall, there is little evidence from laboratory studies that the presence of menthol in a menthol cigarette increases the extent of inhalation of smoke from a cigarette. Some studies suggest that menthol might selectively enhance absorption of CO. However, the generalizability of this finding is uncertain since the subjects in these studies were all experienced adult daily smokers. There are no data on the effect of menthol cigarettes on inhalation parameters in novice smokers, and or in light and intermittent smokers. The latter group is important because there is strong evidence that people who smoke fewer cigarettes per day inhale more smoke per cigarette. Additionally, African Americans are more likely to be light smokers. Since African Americans predominantly smoke menthol cigarettes, it is important to determine whether menthol facilitates inhalation of large volumes of smoke in those who are smoking few cigarettes per day.

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description<br><br>(Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| 1. Ahijevych, K., Gillespie, J., Demirci, M., Jagadeesh, J., 1996. Menthol and nonmenthol cigarettes and smoke exposure in African American and white women. Pharmacology Biochemistry and Behavior 53, 355–360. | Two-factorial design | N = 37 women stratified by race and menthol or nonmenthol cigarettes<br><br>18 AA/8 menthol<br><br>19 white/10 menthol | Blood nicotine and cotinine and expired air carbon monoxide was measured before and after smoking one of her usual cigarettes. Subjects' smoking and respiratory topography were measured. | Nicotine and expired CO boost; number of puffs, puff volume and total puff duration. | There were significant main and interaction effects of race and menthol/nonmenthol cigarette use on CO boost. African American women had a mean CO boost of 10.1 ppm vs. 7.2 ppm for white women, while women using nonmenthol cigarettes had a higher CO boost (mean = 10.6 ppm) compared to those regularly using menthol cigarettes (mean = 6.5 ppm). African American women had nonsignificantly higher puff volumes compared to white women (mean – 48.4 vs. 43.5 ml), while nonmenthol smokers had nosignificantly higher puff volumes than menthol smokers (mean = 48.5 vs. 42.7 ml). Lower CO boost with mentholated cigarettes suggests factors beyond mentholation may affect elevated smoke constituent exposure among African American women. | Strengths include groups balanced race and mentho<br><br>Weaknesses include small N, research volunte all heavy smoker women only, limi generalizability. |
| 2. Ahijevych, K., Parsley, L.A., 1999. Smoke constituent exposure and stage of change | Two-factorial design | N = 95 women stratified by ethnicity and menthol/nonmenthol preference | Respiratory and puffing topography were measured during the cigarette smoking | Puff volume | Menthol smokers had significantly larger puff volumes compared to nonmenthol smokers | Strengths include groups fairly well balanced by race and menthol. Weaknesses |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| in African American and white women cigarette smokers. Addictive Behaviors 24, 115–120. | | 48 AA/27 menthol<br>47 White/22 menthol | bout. | | | include women o |
| 3. Caskey, N.H., Jarvik, M.E., McCarthy, W.J., Rosenblatt, M.R., Gross, T.M., Carpenter, C.L., 1993. Rapid smoking of menthol and non-menthol cigarettes by African American and white smokers. Pharmacology Biochemistry and Behavior 46, 259–263. | Repeated-measures cross-over design | Two independent groups of male cigarettes smokers. One group (N = 12) characterized themselves as predominantly menthol cigarette smokers and other as non-menthol smokers (N = 16).<br>25 AA/9 menthol<br>11 white/3 menthol | Subjects participated in a modified rapid smoking procedure in two sessions, 1 week apart. In one session, subjects smoked regular cigarettes and in the other, they smoked menthol cigarettes. Subjects puffed cigarettes every 15 seconds until they were unable to continue. | Number of puffs<br>Expired CO boost | No difference was observed for the number of puffs taken or CO boost from regular compared to menthol cigarettes. | Weaknesses include small N, imbalance of rac and menthol; rap smoking differs fı usual way of smoking. |
| 4. Clark, P.I., Gautam, S., Gerson, L.W., 1996. Effect of menthol cigarettes on biochemical markers of smoke exposure among African American and white smokers. Chest 110, 1194–1198. | Cross-sectional | N = 65 AA and N = 96 white adult smokers<br>65 AA/54 menthol<br>96 white/22 menthol | Subjects were asked to smoke one cigarette and carbon monoxide levels were measured. | Expired carbon monoxide | The mean unadjusted expired-air carbon monoxide levels were not significantly higher in menthol smokers (40.3 ppm) compared to nonmenthol smokers (35.8 ppm; p=0.09). However, menthol was a significant contributor to expired-air carbon monoxide levels after adjusting for cigarettes per day and amount of each | Weaknesses include imbalanc or race and ment |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description<br><br>(Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| | | | | | cigarette smoked | |
| 5. Jarvik, M.E., Tashkin, D.P., Caskey, N.H., McCarthy, W.J., Rosenblatt, M.R., 1994. Mentholated cigarettes decrease puff volume of smoke and increase carbon monoxide absorption. Physiology and Behavior 56, 563–570. | Crossover | N = 20 smokers<br><br>10 AA/5 menthol<br><br>10 white/5 menthol | All subjects smoked both types of cigarettes, one on each of two days, through puff monitoring device.. | Carbon monoxide boost<br><br>Number of puffs<br><br>Average puff volume<br><br>Total puff volume<br><br>Mean puff flow | Compared to regular smokers, mentholated cigarettes produced a significantly greater boost in carbon monoxide measured as both blood carboxyhemoglobin and end-expired carbon monoxide, despite the fact that mentholated cigarettes decreased average and total cumulative puff volumes and increased mean puff flow rates of inhaled smoke. These chemical and topographic differences were independent of race. No significant differences in depth of inhalation of the smoke or the amount of insoluble smoke particulates delivered to or retained in the respiratory tract were noted between the two types of cigarettes. Mentholation of cigarettes may decrease volume of smoke inhaled but appears to increase exposure of smokers to toxic effects of carbon monoxide. | Strengths include balanced race ar menthol.<br><br>Weaknesses include small N a subjects randomized to smoke non-preferred cigaret |
| 6. McCarthy, W.J., Caskey, N.H., Jarvik, M.E., Gross, T.M., Rosenblatt, M.R., Carpenter, C., 1995. Menthol vs. non-menthol | Crossover | N = 29 male smokers<br><br>16 AA/ 8 menthol<br><br>13 white/3 menthol | Smokers smoked either a regular or a mentholated cigarette in two separate sessions 1 week apart. Commercial brands with comparable tar, | Number of puffs<br><br>Puff volume | When smoking the non-mentholated brand of cigarettes, participants smoked 22% more puffs and had 13% higher mean volumes per puff than they did when smoking the mentholated brand of cigarettes. The aggregate | Weaknesses: sm N, race and men imbalance, artific smoking procedu used one brand c cigarettes, poor generalizabilty because of samp |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| cigarettes: effects on smoking behavior. American Journal of Public Health 85, 67–72. | | | nicotine, and CO content were used. Smoking behavior was constrained by fixed 15-second interpuff intervals but puff volume and number of puffs were unconstrained. | | 39% excess exposure of cigarette smoke in the regular-cigarette conditions was not accompanied by commensurate excesses in expired carbon monoxide or in physiological measures normally correlated with nicotine exposure. | characteristics |
| 7. Miller, G.E., Jarvik, M.E., Caskey, N.H., Segerstrom, S.C., Rosenblatt, M.R., McCarthy, W.J., 1994. Cigarette mentholation increases smokers' exhaled carbon monoxide levels. Experimental and Clinical Psychopharmacology 2, 154–160. | Crossover | N = 12 male smokers<br><br>Recruited from drug treatment program<br><br>All were AA/6 menthol | 3 smoking sessions spaced 1 week apart. In each session, subjects inhaled cigarette through smoking apparatus, one puff every 30 sec until 1200 cc of cigarette smoke was inhaled. Menthol dosage varied across sessions, such that subjects smoked experimental cigarettes that had been injected with 0 mg, 4 mg, or 8 mg of menthol. | Exhaled carbon monoxide boost<br><br>No puffs, puff volume | No effect of menthol on number or volume of puffs. The CO boost was 5.6, 6.1 and 8.1 ppm for 0, 4 and 8 mg menthol cigarettes ($p < 0,004$). | Weaknesses include small N, of subjects with drug abuse histo artificial smoking procedure, result in poor generalizability. |
| 8. Nil R, Battig K: Separate effects of cigarette smoke yield and smoke taste on smoking behavior. *Psychopharmacology (Berl)* | Crossover | N = 15; no data on usual brand menthol preference or race | Subjects came to laboratory weekly for 7 weeks. Each week a test cigarette or own brand was smoked. The test cigarettes include 2 menthol brands, | No puffs, average puff volume, puff volume per cigarette, expired CO boost | Significantly fewer puffs and smaller total puff volume in high tar menthol vs other brands during natural smoking; smaller total puff volume for high tar menthol vs other brands for 30 second-puff smoking | Weaknesses include small N, smokers not smoking preferre cigarettes, artifici smoking procedu |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| 1989, 99(1):54–59. | | | one high and one low tar. During each session the first cigarette was smoked naturally through a cigarette holder, the second was puffed every 30 seconds. | | | |
| 9. Patterson, F., Benowitz, N., Shields, P., Kaufmann, V., Jepson, C., Wileyto, P., Kucharski, S., Lerman, C., 2003. Individual differences in nicotine intake per cigarette. Cancer Epidemiology Biomarkers and Prevention 12, 468–471. | Clinical trial of nicotine replacement therapy for smoking cessation | N = 190 treatment-seeking smokers<br><br>120 white, 47 AA and 23 other race<br><br>55 menthol (no data by race) | Plasma nicotine levels measured before and after participants smoked one of their own brand cigarettes *ad libitum*. | Plasma Nicotine boost | Nicotine boost not significantly different in menthol vs nonmenthol cigarettes smokers. | Weaknesses: sample was treatment seeker generalizability, studied nicotine boost after smok one cigarette in t middle of the day |
| 10. Pickworth, W.B., Moolchan, E.T., Berlin, I., Murty, R., 2002. Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery. Pharmacology, Biochemistry and Behavior 71, | Double blind experimental study | N = 18 menthol smokers (17 AA)<br><br>N = 18 nonmenthol smokers (3 AA) | Menthol and nonmenthol cigarette smokers participated in a single session during which three cigarettes were smoked 45 minutes apart, in random order. Cigarettes were research nicotine low yield (0.2 mg), commercial cigarettes (1.2 | Number of puffs<br><br>CO boost | No differences between menthol and nonmenthol cigarettes on number of puffs or CO boost were observed. | Weaknesses include small number of subjec race by menthol imbalance; smok smoked research cigarettes or commercial cigarettes but no their own brand. |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| 55–61. | | | mg) and research high nicotine yield (2.5 mg). Subjects smoked menthol or non-menthol on the basis of their usual brand. | | | |
| 11. St.Charles, F.K., Krautter, G.R., Dixon, M., Mariner, D.C., 2006. A comparison of nicotine dose estimates in smokers between filter analysis, salivary cotinine, and urinary excretion of nicotine metabolites. Psychopharmacology 189, 345–354. | Observational study | N = 74 smokers selected according to machine determined yield of usual cigarettes.<br>18 menthol smokers, race not specified. | A 5-day clinical study was conducted.<br>Filters were analyzed to estimate the daily mouth exposure of nicotine. Twenty-four-hour urine samples for nicotine equivalents. Saliva samples were collected daily for cotinine analysis. Respiratory pattern recording during smoking of selected cigarettes | Inhalation tidal ratio (ratio of inhalation volume / resting tidal volume) | Inhalation tidal ratio borderline higher in nonmenthol (1.79) compared to menthol (1.52) smokers ($p = 0.054$) | No Strengths or Weaknesses specifically notec authors. |
| 12. Strasser, A.A., Malaiyandi, V., Hoffmann, E., Tyndale, R.F., Lerman, C., 2007. An association of CYP2A6 genotype and smoking topography. Nicotine and Tobacco | Observational study | N = 119 participants enrolled in smoking cessation clinical | Subjects smoked a cigarette through in a cigarette holder attached to a puffing monitoring device. | Number of puffs<br>Mean puff volume<br>Total puff volume | Smoking topography variables did not differ significantly by level of nicotine dependence or cigarette mentholation (p values >0.2). | Weaknesses: subjects seeking smoking cessatic treatment, smoki a single cigarette through cigarette holder, generalizability |

| Chapter 6 Table 1: Menthol Smoking and Topography | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description<br><br>(Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| Research 9 (4), 511–518. | | | | | | |
| 13. Williams JM, Gandhi KK, Steinberg ML, Foulds J, Ziedonis DM, Benowitz, NL: Higher nicotine and carbon monoxide levels in menthol cigarette smokers with and without schizophrenia. *Nicotine and Tobacco Research* 2007, 9(8):873–881. | Observational study | N = 89 smokers with schizophrenia<br><br>N = 53 control smokers<br><br>Race…<br><br>Menthol…. | All subjects attended on the afternoon of a normal smoking day and provided a measure of exhaled CO and a blood sample approximately 2 min after smoking one of their usual cigarettes. | Expired carbon monoxide<br><br>Serum nicotine<br><br>Serum cotinine | Serum nicotine levels (27 vs. 22 ng/ml, p=.010), serum cotinine levels (294 vs. 240 ng/ml, p=.041), and expired CO (25 vs. 21 ppm, p=.029) were higher in smokers of menthol compared with nonmenthol cigarettes | Weaknesses: mi psychiatric and health study grou race by menthol imbalance,<br><br>generalizability |

**BIOMARKER STUDIES**

This section reviews studies that have compared biomarkers of exposure to tobacco smoke constituents in smokers of menthol and non-menthol cigarettes. Biomarker measurements provide a quantitative assessment of systemic exposure to cigarette constituents. Exposure biomarkers include measurement of nicotine intake (nicotine, cotinine and other nicotine metabolites), gas phase exposure (carbon monoxide and various volatile organic compounds) and particulate phase (the tobacco-specific nitrosamine NNAL and metabolites of polycyclic aromatic hydrocarbons). The biomarkers may be measured in blood, urine or saliva. Carbon monoxide (CO) is measured either as carboxyhemoglobin in blood or as CO in exhaled air. (For details about specific biomarkers of exposure to tobacco smoke, see chapter 3.)

Most biomarker studies are cross-sectional in design, involving comparisons of biomarker levels in menthol vs non-menthol cigarette smokers at a single point in time. Some studies have measured biomarkers immediately before or after smoking a cigarette in a laboratory. Some additional, general methodologic issues warrant mention. All studies included adult daily smokers and the protocols for most studies required subjects to have smoked five or more cigarettes per day. Some urine samples were collected as spot urine samples and some as 24-hour collections. The latter are more accurate reflectors of daily exposure, but it is difficult to collect a full specimen from people in naturalistic settings. Correction for urine creatinine to deal with dilutional differences is useful. Many researchers do not report time from last cigarette to time of biomarker collection. Information on this interval may be needed as some biomarkers, like nicotine, have relatively short half-lives.

As previously discussed, there is the potential for confounding or modification of results by race in studies of menthol cigarettes. Racial factors are important in relation to interpreting cotinine levels. African Americans on average metabolize cotinine more slowly than whites (Perez-Stable et al 1998). Many studies show that cotinine levels are higher when normalized for cigarettes smoked per day in African Americans vs. whites (for example, Caraballo et al. 1998; Benowitz et al. 2009). Therefore higher cotinine levels in menthol smokers overall could result from a predominance of African Americans among the menthol cigarette smokers. Urine nicotine equivalents is a term used to describe the sum of nicotine and its metabolites, nicotine glucuronide, cotinine, cotinine glucuronide, trans-3' hydroxycotinine and its glucuronide, in urine. The sum of metabolites accounts for 85–90 percent of the nicotine doses and is a useful surrogate for nicotine intake that is not affected by racial differences (Hukkanen et al. 2005).

We have identified thirteen published cross-sectional studies and one unpublished tobacco company analysis of a cross-sectional study that compared biomarker levels in smokers of menthol and non-menthol cigarettes. We also describe one experimental study in which biomarkers of exposure were measured in smokers while smoking menthol or non-menthol cigarettes. Study design and results are summarized in table 2. Brief descriptions of the studies follow.

Wagenknecht et al. (1990) measured serum cotinine in 822 African American and 602 white smokers who were participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study. In a multiple linear regression model which included race, age, sex, education, cigarettes per day, inhalation pattern, secondhand smoke exposure and machine-determined nicotine yield, African-American race was associated with substantially and highly statistically significantly greater cotinine levels compared to whites. Higher serum levels in African-Americans compared to whites were seen both in menthol and non-menthol cigarette smokers. The beta coefficient for race in the regression model was higher for menthol smokers (89.0 ng/ml) compared to non-menthol smokers (51.5 ng/ml), but no statistical comparison of these coefficients was presented by the authors.

Ahijevych et al. (1996) measured plasma cotinine in 37 women stratified by race and menthol cigarette smoking. Plasma cotinine tended to be higher in menthol (254 ng/ml) compared to non-menthol (204 ng/ml) smokers, but this difference was not significant. The ratio of plasma cotinine to cigarettes per day was higher in menthol (18.1 ng/ml/cig) compared to non-menthol (15.3 ng/ml/cig) smokers, but this difference also was not statistically significant.

Clark et al. (1996) measured serum cotininine in 65 African American and 96 white smokers who smoked at least five cigarettes per day. Serum cotinine levels overall in menthol (478 ng/ml) vs. non-menthol (349 ng/ml)smokers, and the difference (84 ng/ml) remained statistically significant in a linear regression analysis after controlling for race, cigarettes per day and amount of each cigarette smoked.

Mustonen et al. (2005) measured saliva cotinine in 51 African American and 256 white smokers of at least 10 cigarettes per day. Cotinine levels were higher overall in menthol vs. non-menthol smokers (476 ng/ml vs. 442 ng/ml), but the difference was not statistically significant. The cotinine per cigarette per day ratio was statistically significantly higher in menthol smokers, but this could be due at least in part to racial confounding. Analysis of covariance found several race x sex x menthol subgroup differences, but these cannot be readily interpreted as a general effect of menthol cigarettes.

Williams et al. (2007) measured serum nicotine and cotinine in 155 smokers, of which 89 had schizophrenia or schizoaffective disorder and 53 were healthy controls. Blood samples were collected two minutes after smoking one of their usual cigarettes. After adjustment for psychiatric diagnostic group, race and cigarettes per day, serum nicotine, serum cotinine and expired CO were statistically significantly higher in menthol cigarette smokers.

Signorello et al. (2009) reported serum cotinine levels in 130 African American and 125 white smokers. In a linear regression analysis adjusted for cigarettes per day, age, race and sex no significant effect of menthol brand was observed.

Muscat et al. (2009) measured plasma cotinine, urine cotinine, plasma thiocyanate (a biomarker of cyanide exposure) and urine NNAL (a metabolite of the tobacco-specific nitrosamine and carcinogen NNK) in 237 African American and 288 white smokers of at least 5 cigarettes per day. In a multiple regression analysis adjusted for cigarettes per day, age and sex and performed separately by race, there was no effect of smoking menthol cigarettes on these biomarkers. However, when NNAL was analyzed as the ratio of NNAL glucuronide / NNAL, the ratio was lower in menthol cigarette smokers. This finding was statistically significant, and along with the in vitro data presented in the paper, suggests that menthol may inhibit the glucuronidation of NNAL, which represents a detoxification pathway for this known carcinogen.

In a study conducted by Lorillard Tobacco Company, Heck et al. (2009) measured blood carboxyhemoglobin, urine nicotine and metabolites and urine total NNAL (24-hour urine collection) in 28 African American and 84 white smokers of at least 15 cigarettes per day. The menthol smokers appear to have been switched to a specified menthol brand for 3 weeks prior to sample collection. Statistically significant differences in biomarker levels comparing menthol and non-menthol cigarette smokers were not observed.

Ho et al. (2009) studied 755 African American light smokers (ten or fewer cigarettes per day) who were enrolled in a smoking cessation trial. This group included 569 menthol and 131 nonmenthol cigarette smokers. Menthol smokers smoked fewer cigarettes per day compared to nonmenthol smokers(7.07 vs 7.53, $p = 0.05$). However levels of expired CO and plasma cotinine were quite similar for the groups.

This suggests that the intake of CO and nicotine may be higher per cigarette for menthol compared to nonmenthol cigarettes, although that specific analysis was not presented by the authors.

In the Total Exposure Study supported by Altria Client Services, Wang et al. (2010) reported data from a large multi-center study involving 1,044 menthol cigarette smokers (448 African American and 596 white) and 2,299 non-menthol smokers (161 African American and 2,031 white). All had smoked at least one cigarette per day for a year, with a mean of 15.0 for menthol cigarette smokers and 16.8 for non-menthol smokers. Blood was collected for serum cotinine and blood carboxyhemoglobin and a 24-hour urine for nicotine equivalents was also obtained. In unadjusted analyses, urine nicotine equivalents per 24 hours and carboxyhemoglobin were significantly lower in menthol smokers. As seen in most other studies, African Americans smoked on average fewer cigarettes per day than whites, and the level of nicotine equivalents per cigarette smoked was on average higher in menthol cigarette smokers. Analysis of covariance that adjusted for race found no statistically significant difference. Smoking menthol cigarettes was not associated with serum cotinine level or carboxyhemoglobin level.

Additional unpublished data from the Wang et al. study were provided to the TPSAC by (Altria Client Services 2010). Analyses were presented on particulate phase markers, urine total NNAL and 1-hydroxypyrene, and 4-aminophenol adducts; and gaseous phase markers (metabolites of acrolein and 1,3 butadiene). No statistically significant differences in biomarker levels were found, comparing the two groups of smokers.

Benowitz et al. (2011) examined the menthol cigarette biomarker question from a different perspective. The question was asked: Does smoking menthol cigarettes increase exposure to toxins in tobacco smoke in a dose-related way? As described earlier, different brands of menthol cigarettes contain different amounts of menthol. Ben owitz et al. analyzed the relationship between urine menthol concentration (a quantitative indicator of menthol exposure) and various exposure biomarkers. In a group of 60 menthol cigarette smokers (70 percent African American) there were strong positive correlations between urine menthol concentration and plasma nicotine, plasma cotinine, urine nicotine equivalents, urine total NNAL and urine total PAH metabolites. However, in a multiple regression model, when both menthol and a measure of nicotine intake (nicotine equivalents or plasma cotinine) were included, only the nicotine intake effect remained statistically significant. Thus, while urine menthol is highly correlated with biomarkers of exposure, it is not an independent predictor of carcinogen exposure. This study also reported average levels of various biomarkers in menthol vs. regular smokers (not controlled for race) and found no differences in plasma cotinine or urine NNAL. Urine nicotine equivalents and urine PAHs were lower in menthol cigarette smokers, and although this difference was statistically significant, it may be partly due to a longer interval from last cigarette to time of urine collection for the menthol smokers.

Finally, Benowitz et al. (2004) conducted a crossover study involving 14 subjects, half regular menthol and half non-menthol cigarette smokers. All subjects smoked a non-menthol cigarette for the first week, then they were randomized to smoke a menthol or non-menthol for the second week, after which they were switched to other type of cigarette for the third week. From days 3 to 6 subjects were confined to a research ward, where they smoked 20 cigarettes per day and had frequent blood and urine sampling. Findings with respect to rates and pathways of nicotine metabolism are discussed in chapter 3. While nicotine metabolism was on average slower in menthol cigarette smokers, based on similar levels of plasma nicotine and blood carboxyhemoglobin levels through the day while smoking menthol compared to non-menthol cigarettes, there was no significant effect of menthol on nicotine or CO exposure.

In summary, some cross-sectional studies of biomarkers, particularly smaller studies, have found higher blood nicotine or cotinine levels per cigarette smoked in menthol cigarette smokers, consistent with greater inhalation. This increment persisted after controlling for race in some of the studies. Larger studies have generally not found independent effects of menthol cigarette smoking on exposure biomarkers. However, the findings of the study by Muscat et al. suggest that menthol may impair detoxification of NNAL, which is a pulmonary carcinogen. As mentioned previously, there has been no analysis of menthol effects on biomarkers of exposure at very low levels of cigarette consumption. At such levels of consumption, menthol could have its greatest effects in facilitating greater inhalation and hence exposure to tobacco smoke toxins.

Chapter 6 Table 2: Biomarkers of Exposure

| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
|---|---|---|---|---|---|---|
| 1. Ahijevych K, Gillespie J, Demirci M, Jagadeesh J. Menthol and nonmenthol cigarettes and smoke exposure in African American and white women. Pharmacol Biochem Behav. 1996 Feb;53(2):355-60. | Laboratory<br>Two-factorial design | N = 37 women stratified by race and menthol or nonmenthol cigarettes<br>18AA/8menthol<br>19 white/10menthol | A blood sample for nicotine and baseline cotinine analysis was obtained before and after smoking a cigarette. | Plasma cotinine | Plasma cotinine was Plasma cotinine was nonsignificantly higher in nonmenthol smokers compared to menthol smokers (254 ng/ml and 204 ng/ml, respectively). Cotinine per cigarette ratios were nonsignificantly higher in nonmenthol smokers as well (18.1 vs. 15.3 ng/ml cotinine/cigarette). | Strengths include groups balanced race and mentho Weaknesses include small N, heavy smokers, women only. |
| 2. Ahijevych K, Parsley LA: Smoke constituent exposure and stage of change in African American and white | Laboratory Two factorial design | N = 95 women stratified by ethnicity and menthol/nonmenthol preference | A blood sample for nicotine and cotinine analysis was obtained 1 min before | Plasma nicotine and cotinine | . Menthol smokers )had significantly, higher cotinine levels compared to nonmenthol smokers | Strengths – race and menthol balanced. Weaknesses include small N, |

| Chapter 6 Table 2: Biomarkers of Exposure | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| | women cigarette smokers. Addictive Behaviors 1999, 24(1):115–120. | | N = 48 African American/ 27M<br><br>N = 47 White / 22M | smoking. | | | women only |
| 3. | Altria Total Exposure Study (Altria 7/15/10; chapter 4) | Cross-sectional multi-center study | Total Exposure Study (TES): 3341 smokers of one or more cpd, recruited from 39 investigative sites from 31 states, selected by 4 categories of machine yields.<br><br>1044 menthol / 448 AA<br><br>2297 non-menthol / 166 AA | Blood and 24-hour urine samples. Smokers were asked to return all cigarette butts smoked over the 24 hour period. | COHb<br><br>Urine 3-HPMA<br><br>MHBMA and DHBMA<br><br>4-aminobiphenyl adducts<br><br>Nicotine<br><br>Cotinine<br><br>Trans-3'-hydroxycotinine<br><br>Total NNAL<br><br>Total 1-hydroxypyrene | No statistically significant differences in biomarkers of exposure were observed between menthol and non-menthol smokers, stratified by race. No statistically significant difference in the nicotine metabolite ratio between menthol and non-menthol smokers. | Strengths include the large study s and the multi-cer recruitment of smokers; weakne if race by menthc imbalance. |
| 4. | Benowitz N, Dains K, Dempsey D, et al. Urine menthol as a biomarker of mentholated cigarette smoking. Cancer Epidemiology Biomarkers and Prevention. 2010, 19: 3013-3019. | Cross-sectional study | N = 127 cigarette smokers<br><br>60 menthol / 42 AA<br><br>67 non-menthol / 19 AA | Concentrations of menthol glucuronide, nicotine equivalents, NE), NNAL and polycyclic aromatic hydrocarbon (PAH) metabolites were measured in the urine. | Urine menthol, nicotine equivalents, NNAL, PAH metabolites; plasma cotinine | Urine menthol was measurable in 82% of menthol and 54% in regular cigarette smokers. Among menthol smokers, urine menthol was highly correlated with NE, NNAL, and PAHs. In a multiple regression model NE but not menthol was significantly associated with NNAL and PAHs. Plasma cotinine similar in menthol and non-menthol smokers. | Strengths includ quantification of menthol exposur Weaknesses include race by menthol imbalan |
| 5. | Clark PI, GautamS, Gerson LW. Effect of menthol cigarettes on | Laboratory<br><br>cross- | N = 65 African American and N = 96 white smokers | Serum samples for cotinine analyses | Serum Cotinine | After adjusting for race, cigarettes per day, and mean amount of each cigarette smoked, menthol | Weaknesses include race and menthol imbalan |

| Chapter 6 Table 2: Biomarkers of Exposure | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| biochemical markers of smoke exposure among African American and white smokers. Chest. 1996 Nov; 110(5):1194-8. | sectional | 65 AA / 54 menthol<br>96 W / 22 menthol | | | was associated with higher cotinine levels (p=0.03) and expired carbon monoxide concentrations<br>(p=0.02). | |
| 6. Heck JD. Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. Cancer Epidemiol Biomarkers Prev. 2009 Feb; 18(2):622-9. Epub 2009 Feb. 3. Erratum in Cancer Epidemiol Biomarkers Prev. 2009 Jul;18(7):2155. | Parallel arm study | N = 112 male and female heavy smokers<br>28 AA / 23 menthol<br>84 white / 31 menthol | The study subjects were provided with specified brands of cigarettes according to their menthol or nonmenthol preference for 3 weeks. On the third week two 24-hour urine samples spaced one week apart, were collected. | Blood carboxyhemoglobin<br>Urine nicotine equivalents; urine NNAL | There were no significant differences in carboxyhemoglobin, urine nicotine equivalents or total urinary NNAL comparing the menthol and nonmenthol cigarette smokers | Weaknesses include smoking brands other thai usual brand; race menthol imbalan subjects smoked least 15 cigarette per day |
| 7. Ho MK, Mwenifumbo JC, Al Koudsi N, Okuyemi KS, Ahluwalia JS, Benowitz NL, Tyndale RF: Association of nicotine metabolite ratio and CYP2A6 genotype with smoking cessation treatment in African-American light smokers. *Clinical Pharmacology and* | Smoking cessation clinical trial | N = 755 African American smokers of 10 or fewer cigarettes per day; 569 smoked menthol cigarettes | Blood and expired CO samples obtained prior to randomization | Plasma cotinine; expired CO | Menthol cigarette smokers tended to smoke fewer cigarettes per day (7.07 vs 7.53, p = 0.05). Expired CO and plasma cotinine were not significantly different in menthol vs nonmenthol smokers (13.49 vs 14.74 ppm; 243 vs 247 ng/ml, respectively). Suggests that CO and/or nicotine intake may be higher per cigarette for menthol smokers. | Strengths include large number of African Americar smokers with considerable numbers of ment and nonmenthol smokers; include light smokers |

| Chapter 6 Table 2: Biomarkers of Exposure | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| *Therapeutics* 2009 Jun, 85(6):635-43. | | | | | | |
| 8. Muscat JE, Chen G, Knipe A, Stellman SD, Lazarus P, Richie JP Jr. Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation. Cancer Epidemiol Biomarkers Prev. 2009 Jan; 18(1):35-41. | Cross-sectional | N = 525 male and female smokers of at least 5 cpd.<br><br>237 AA / 204 menthol<br><br>288 white / 80 menthol | Plasma and urine collection. | Urinary and plasma cotinine<br><br>Plasma thiocyanate<br><br>Urinary NNAL and NNAL-Gluc | In regression models that adjusted for daily cigarette intake, no significant differences were observed in the concentration of these biomarkers by menthol status in both races. The ratio of NNAL-Gluc to NNAL, was significantly lower in menthol versus nonmenthol smokers. The NNAL Gluc/NNAL ratio was 34% lower in Whites (P < 0.01) and 22% lower in African Americans | Strengths include relatively large sample size; Weaknesses include race by menthol imbalan |
| 9. Mustonen TK, Spencer SM, Hoskinson RA, Sachs DP, Garvey AJ. The influence of gender, race, and menthol content on tobacco exposure measures. Nicotine Tob Res. 2005 Aug;7(4):581-90. | Cross-sectional study | N = 307 male and female smokers participating in cessation clinic<br><br>51 AA / 33 menthol<br><br>256 white / 54 menthol | Saliva cotinine obtained prior to cessation treatment | Salivary cotinine<br><br>Expired carbon monoxide | Cotinine and CPD correlations varied by gender and race among menthol cigarette smokers. Significant genderxracexmenthol interaction on salivary cotinine level as well as cotinine/CPD ratio. | Weaknesses included race by menthol imbalan small N for subgroup analys treatment seekin smokers of at lea 10 cigarettes per day |
| 10. Signorello LB, Cai Q, Tarone RE, McLaughlin JK, Blot WJ. Racial differences in serum cotinine levels of smokers. Dis Markers. | Cohort Study; | Southern Community Cohort Study.<br><br>130 AA and 125 white smokers; no data on number of menthol smokers | Blood samples taken at time of baseline evaluation | Serum cotinine measured by radioimmunoassay | After adjustment for race and sex and cigarettes smoked per day, no significant difference in cotinine levels comparing menthol vs non-menthol smokers | Weaknesses include race by menthol imbalan cotinine assay is non-specific with some cross-reactivity with cotinine metaboli |

| Chapter 6 Table 2: Biomarkers of Exposure | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description (Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| 2009;27(5):187-92. | | | | | | |
| 11. Wagenknecht LE, Cutter GR, Haley NJ, Sidney S, Manolio TA, Hughes GH, Jacobs DR. Racial differences in serum cotinine levels among smokers in the Coronary Artery Risk Development in (Young) Adults Study. Am J Public Health. 1990 Sept;80(9):1053-6. | Prospective cohort study | N = 142418-30 year old smokers of at least five cigarettes per week, African American and White, men and women participating in the Coronary Artery Risk Development in (Young) Adults Study<br><br>822 AA/733 menthol<br><br>602 white/ 178 menthol | Blood same at initial examination. | Serum cotinine | . Serum cotinine level was significantly higher in African American than White smokers. The race difference persisted for African Americans who smoked menthol or nonmenthol cigarettes (no details of this analysis were presented) | Strengths include the large study s and the multi-cer recruitment of smokers; weaknesses incl race by menthol imbalance |
| 12. Wang J, Roethig HJ, Appleton S, Werley M, Muhammad-Kah R, Mendes P. The effect of menthol containing cigarettes on adults smokers' exposure to nicotine and carbon monoxide. Regulatory Toxicology and Pharmacology. 2010; 57: 24-30. | Cross sectional multi-center study | Total Exposure Study<br><br>N=3341 African-American and White adult cigarette smokers<br><br>1044 menthol / 448 AA<br><br>2297 non-menthol / 166 AA | Blood and 24-hour urine samples.. Smokers were asked to return all cigarette butts smoked over the 24 hour period. | Nicotine equivalents (NE) in 24 hour urine, NE/cigarette, COHb, and serum cotinine | No statistically significant effects of mentholated cigarettes on NE/24 h, COHb, serum cotinine and NE/cigarette. On average menthol users (MS) smoked 15.0 and non-menthol users (NMS) 16.8 cigarettes/day. The unadjusted mean differences were as follows: MS had lower NE/24 h (5.4%) and COHb (3.2%), higher serum cotinine (3.0%) and NE/cigarette (5.7%) than NMS. | |
| 13. Williams JM, Gandhi KK, Steinberg ML, Foulds J, Ziedonis DM, Benowitz, NL: Higher nicotine and carbon monoxide levels in menthol cigarette smokers | Laboratory study | 89 smokers with schizophrenia<br><br>53 control smokers<br><br>Data on number of menthol smokers or | Subjects provided a measure of exhaled CO and a blood sample approximately 2 min after smoking one of their usual cigarettes. | Expired carbon monoxide<br><br>Serum nicotine, cotinine and trans-3' hydroxycotinine | Serum nicotine levels (27<br><br>vs. 22 ng/ml, p=.010), serum cotinine levels (294 vs. 240 ng/ml, p=.041), and expired CO (25 vs. 21 ppm, p5.029)<br><br>were higher in smokers of | Weaknesses include small numbers of subjects, many o whom have psychiatric disea |

| Chapter 6 Table 2: Biomarkers of Exposure | | | | | | |
|---|---|---|---|---|---|---|
| Author Name(s), Article Title and Year | Type of Study | Subject Recruitment, Description<br><br>(Including Special population(s)) and Sample Size | Study Design | Outcome Variables | Results related to Menthol | Strengths / Weaknesses |
| with and without schizophrenia. *Nicotine and Tobacco Research* 2007, 9(8):873–881. | | race not provided | | | menthol compared with nonmenthol cigarette smokers., with no differences in 3 hydroxycotinine/cotinine ratios between cigarette types with adjustment for diagnostic group and race | |

**TOXICOLOGY STUDIES**

Additional understanding of the differential risks posed by menthol versus non-menthol cigarettes comes from toxicological studies. The relevant studies include in vitro and in vivo approaches using menthol or smoke from cigarettes. As for toxicologic studies in general, there are questions about the relevance of animal and cell toxicology studies with respect to the potential toxic effects of menthol in cigarette smokers.

Various studies have addressed the toxicity of menthol using in vitro cellular assays that assess whether menthol damages or kills cells. One general issue in interpreting such studies is the relevance of the concentrations used and the endpoints investigated to toxicity in smokers. Bernson and Pettersson (1983) investigated the toxicity of menthol in four different bioassays. They summarize the findings as suggesting that menthol may lead to "...a deterioration of biological membranes." Other studies have shown that menthol affects cell membrane properties. Azzi et al. (2006) used a system that measures diffusion of carcinogens across porcine esophageal tissue to assess the effect of menthol on permeation and reservoir formation in the tissue for NNK and B[a]P. Menthol slowed the diffusion of these two carcinogens but increased the size of the tissue reservoir for NNK. In another cell system, menthol decreased the transepithelial electrical resistance, but the decrease was not different from that observed with non-menthol cigarettes (Alakayak and Knall 2008).

Several studies have addressed interactions of menthol with membrane receptors. Sidell et al. (1990) used a human neuroblastoma cell line and identified a calcium channel that was blocked by menthol. More recent studies have focused on the TRPM8 $Ca^{2+}$-permeable channel. Results from various cellular systems show that activation of the TRPM8 channel by menthol induces cell death (Yamamura et al. 2008; li et al. 2009), although one study using prostate cancer cells found that TRPM8 activation was not the mechanism of menthol-induced cell death in that system (Kim et al. 2009).

(b) (4)

Another inhalation study was reported in the peer-reviewed literature in 1997 (Gaworski et al. 1997). In this study, Fischer 344 rats were exposed to mainstream smoke from a reference cigarette and a similar cigarette containing 5000 ppm synthetic *l*-menthol. The only difference noted between the two exposure groups was a dose-response trend with level of particulate matter for nasal discharge in the reference cigarette group but not in the menthol cigarette group.

R.J. Reynolds Tobacco Co. conducted a 90-day inhalation study comparing menthol vs no menthol in heated tobacco vs. conventional cigarettes (ref 26 cited in Salgado and Glantz 2011 ). Menthol inhalation from heated tobacco produced more severe histopathological changes in the lungs compared to conventional cigarettes.

Several studies have shown that menthol increases the amount of tar and fine particles in cigarette smoke (Carmines 2002, Baker 2004, Rustemeier 2001 as cited in Lee and Glantz 2011). The mechanism of increased particle formation was speculated to be greater transfer of the additive materials to the particle phase of the smoke compared to tobacco constituents (Rustemeier 2001 as cited in Lee and Glantz 2011). Increased particulate matter in smoke is of concern because particulates are associated with greater morbidity and mortality from cardiovascular disease and are suspected to increase the risk of sudden cardiac death (Brook 2010; Pope 2009; IOM 2010; also see Lee and Glantz 2011). The smoke generated from cigarettes to which menthol was added also delivered higher levels of formaldehyde and lead, both tobacco smoke toxicants, compared to smoke from the control cigarettes (Rustemeier 2001 as cited in Lee and Glantz 2011).

Several short-term human studies also supply relevant information. A group of investigators in Turkey reported findings of a series of studies involving measurements of cardiovascular parameters after smoking menthol cigarettes versus non-menthol cigarettes (Ciftci et al. 2008a, Ciftci et al. 2008b; Ciftci et al. 2009). They describe differing patterns of short-term response using echocardiography and measures of vascular response. The participants were healthy young volunteers. These findings have uncertain implications with regard to the comparative cardiovascular disease risks of smokers of menthol cigarettes versus non-menthol cigarettes. Pritchard et al. (1999) investigated the effects of menthol in cigarettes by having volunteers smoke "denicotinized" cigarettes, with and without menthol. Using electroencephalogram and heart rate as outcome measures, they did not identify differences in response to the menthol-containing and non-menthol-containing cigarettes.

The Altria-supported Total Exposure Study mentioned above also examined biomarkers of potential harm, including markers of oxidative stress (i-epi-prostaglandin-F2 alpha, 8-isoprostaglandin F2 alpha-V1), inflammation (white blood cell count, fibrinogen, C-reactive protein, monocyte chemotactic protein and interleukin-6), endothelial function (von Willebrand factor, microalbumin, soluble intercellular adhesion molecule-1, soluble vascular cell adhesion molecule-1), coagulation (platelets, fibrinogen, von Willebrand factor, 11-dehydrothroboxane-B2), lipids (triglycerides, LDL cholesterol, HDL cholesterol, total cholesterol, oxidized LDL, lipoprotein-associated phospholipase A2) and metabolism (glucose, adiponectin, leptin) (Altria Client Services 2010). No significant effects of menthol smoking on these biomarkers were observed.

**EPIDEMIOLOGICAL STUDIES**

The comparative risks of menthol cigarette smokers versus non-menthol cigarette smokers have been assessed for several cancer sites, and selected cardiovascular and respiratory outcomes. The evidence comes primarily from case-control studies but also from three cohort studies. A variety of indicators were used for classifying the extent of exposure to menthol cigarettes. None of the studies were designed to specifically address risks of menthol cigarettes and consequently the investigators constructed indices that used the available information with acknowledgement of the potential for misclassification. For example, the cohort study of Northern California Kaiser Permanente participants used the type of cigarette smoked on enrollment to classify menthol cigarette status (Sidney et al. 1995). In the four-city case-control study of lung cancer, Kabat and Hebert (1991) determined mentholation for each brand smoked.

For cancer, the evidence is most abundant for lung cancer (table 3). Findings are available from three case-control studies and three cohort studies, the Northern California Kaiser Permanente Study, the Lung Health Study, and the Southern Community Cohort Study. The analyses took account of other smoking-related determinants of lung cancer risk, e.g., amount smoked. Most of the studies found no significant differences in risk for lung cancer in smokers of menthol compared with non-menthol cigarettes. In fact, most of the point estimates were around unity, indicating no difference in risk, and measures of the extent of menthol smoking were not associated with lung cancer risk. The most recent study, the Southern Community Cohort Study, found a statistically significantly reduced risk of lung cancer in smokers of menthol cigarettes vs. the comparison of non-menthol cigarette smokers (Blot et al., in press). Only one study, the Kaiser Permanente Study, found a statistically significantly increased risk for menthol cigarette smokers. In males, the relative risk for menthol smokers was 1.45 (95 percent confidence interval 1.03–2.02). In females, the relative risk was 0.75 (95 percent confidence interval 0.52–1.11).

More limited findings are available for other cancers, including esophageal and oral cancers and all smoking-related cancers other than lung cancer. For each of these outcomes, findings are available from only a single study (table 3). As for lung cancer, the evidence does not show a difference in risk for menthol smokers compared with non-menthol cigarette smokers.

For cardiovascular disease, two cohort studies provide findings: the Coronary Artery Risk Development in Young Adults (CARDIA) Study (Pletcher et al. 2006) and the Lung Health Study (Murray et al. 2007). In the CARDIA Study, a long-term cohort study, coronary calcification was measured in 2000, 15 years after participants were enrolled (Pletcher et al. 2006). Using the periodically collected smoking information, the numbers of pack-years of smoking menthol and non-menthol cigarettes were estimated. Risk for the prevalence of calcification increased similarly with pack-years of menthol and non-menthol cigarettes. In the Lung Health Study, participants were classified as menthol smokers based on the type of cigarette smoked at enrollment (Murray et al. 2007). Risks of death from coronary heart disease death or cardiovascular disease were not increased for menthol cigarette smokers, nor was all-cause mortality.

The same two cohort studies provide information on several respiratory outcome measures. In the Lung Health Study, the frequencies of participant reports for "...having seen or talked to a physician for the following conditions: any respiratory condition, emphysema, asthma, pneumonia, head cold, chest cold, or sore throat..." were similar in menthol and non-menthol cigarette smokers (Murray et al. 2007). In the CARDIA Study, the 10-year rates of lung function decline (the forced expiratory volume in one second or the $FEV_1$) were similar in the two groups (Pletcher et al. 2006).

Overall, the epidemiological studies indicate comparable risks for a number of cigarette-caused diseases in smokers of menthol compared to non-menthol cigarettes. The point estimates are largely centered around unity. Several limitations of these studies need to be noted in interpreting the findings. The extent of information on smoking of menthol cigarettes was variable and complete across the full smoking history only in one of the case-control studies. Random misclassification of menthol smoking would tend to bias estimates of the comparative risk of smoking menthol cigarettes towards unity, regardless of whether there was a "true" increase or decrease in risk for menthol cigarette smokers. Additionally, many of the studies, particularly those on cancer risk, were carried out several decades previously. Consequently, given historical patterns of menthol cigarette use, there would be few participants in these studies who had smoked menthol cigarettes across their full smoking history.

Finally, the studies generally have relatively small numbers of participants. However, even with the relatively modest sample sizes of some of the studies, the point estimates do not provide any consistent indication of increased risk.

**Table 3: Cancer risk for smokers of menthol versus non-menthol cigarettes**

| Author (Publication year) | Study design, study period, location | Sample size | Menthol exposure | Findings |
|---|---|---|---|---|
| **Lung cancer** | | | | |
| Kabat and Hebert (1991) | Case-control study<br>1985-1990<br>Four U.S. cities | 1044 cases<br>1324 controls | Non-menthol smokers<br>Menthol 1-14 years<br>Menthol ≥15 years | No significant difference in risk overall, or by histological type |
| Sidney et al. (1995) | Cohort study<br>1979-1991<br>Northern California Kaiser enrollees | 9761 participants<br>Current smokers<br>318 cases | Current cigarette brand<br>Menthol or non-menthol | Increased risk for males, but not for females |
| Carpenter et al. (1999) | Case-control study<br>1990-1994<br>Los Angeles county | 337 cases<br>478 controls | Proportion of cigarettes smoked that were menthol | No increase in risk with extent of menthol smoking |
| Brooks et al. (2003) | Case-control study<br>1981-2000<br>Multi-hospital, eastern U.S. | 643 cases<br>4110 controls | Years smoked menthol cigarettes based on current brand and brand smoked the longest | No indication of increased risk for ever smoking menthol or with extent of menthol smoking |
| Murray et al. (2007) | Randomized trial in observational phase<br>1986-2001<br>Multi-site | 5887 participants<br>240 deaths | Baseline cigarette type | No increase in risk for menthol smokers |
| Blot et al. (2011) | Nested case-control study<br>2002-2009<br>Twelve southern U.S. states | 440 cases<br>2213 controls | Menthol or non-menthol, adjusted for pack-years smoked | Significantly lower risk of lung cancer incidence and mortality among menthol compared to non-menthol smokers, with the deficit holding among both African Americans and whites. |
| **Oropharyngeal cancer** | | | | |
| Kabat and Hebert (1994) | Case-control study<br>1985-1990<br>Four U.S. cities | 276 cases<br>1256 controls | Ever menthol use<br>Duration of menthol use | No significant difference in risk overall, or by subsite |
| **Esophageal cancer** | | | | |
| Hebert and Kabat (1989) | Case-control study<br>1969-1984<br>Nine U.S. cities | 312 cases<br>462 controls | Menthol based on brand<br>Ever menthol use<br>Duration of menthol | No clear pattern of significantly different risk |

| | | | | |
|---|---|---|---|---|
| | | | use | |
| **Non-lung smoking-related cancers** | | | | |
| Friedman et al. (1998) | Cohort study 1979-1994 Northern California Kaiser enrollees | 11760 participants 281 cases | Current brand of mentholated cigarettes | No indication of increased risk |

**EVIDENCE SYNTHESIS**

This chapter reviews diverse lines of evidence with regard to potential differential risks to health of smoking menthol versus non-menthol cigarettes. The evidence reviewed includes studies on differences in the ways that menthol cigarettes are smoked versus non-menthol cigarettes; studies on levels of biomarkers of dose of tobacco smoke components in smokers; studies on the toxicity of menthol and smoke from menthol cigarettes; and studies on the comparative risks of smoking menthol and non-menthol cigarettes in human populations. For some of these topics, the number of studies is limited for some of these major lines of evidence. For example, only six epidemiological studies address lung cancer and lesser numbers were identified for other health outcomes.

The in vitro studies show that menthol has activity in various systems. Chapter 3 addresses the pharmacologic actions of menthol which may lead to some of these effects. The very limited bioassay data does not indicate that smoke from menthol cigarettes has greater toxicity than smoke from non-menthol cigarettes. The epidemiological literature, albeit limited in scope, suggests that there is not greater risk for disease development for smokers of menthol versus non-menthol cigarettes. For lung cancer, the studies are consistent in this regard.

TPSAC concludes, based on the evidence reviewed in this chapter, that:

- The evidence is insufficient to conclude that it is more likely than not that menthol cigarette smokers inhale more smoke than non-menthol cigarette smokers. Because of methodologic issues in studying smoking topography, the generalizability of these findings to the smoking of menthol cigarettes in daily life is questionable.

- The evidence is insufficient to conclude that it is more likely than not that menthol cigarette smokers are exposed to higher levels of nicotine and other tobacco smoke toxins, at least in regular daily smokers of more than 5 or 10 cigarettes per day. There are insufficient data to know if menthol cigarettes result in greater smoke intake and more exposure to tobacco smoke toxins among smokers of relatively few cigarettes per day.

- The evidence is insufficient to conclude that smokers of menthol cigarettes face a different risk of tobacco-caused diseases than smokers of non-menthol cigarettes. Some toxicology studies raise concern, particularly the finding that the addition of menthol is associated with greater fine particles which are suspected to contribute to cardiovascular disease. Available epidemiologic data do not demonstrate increased disease risk in people, but the data are largely limited to lung cancer. The hypothesis that menthol cigarette smoking increases the risk of cardiovascular disease is biologically plausible and needs to be investigated.

# CHAPTER 8: CONCLUSIONS AND RECOMMENDATIONS

## INTRODUCTION

In this chapter, TPSAC synthesizes the evidence included in chapters 3–6 to address the charge given to it in the Act. Using the methodology described in chapter 2, TPSAC has systematically identified and evaluated relevant studies and other evidence, including papers published in the peer-reviewed literature, documents supplied to the committee by tobacco companies, FDA white papers and unpublished tobacco company documents. Here, TPSAC provides its conclusions to the seven key questions in chapter 1 related to individual smokers and the two key questions related to effects at the population level. These conclusions are expressed in the classification set out in Chapter 2 that is based around the anchoring point of "equipoise" in the strength of evidence for and against a relationship. Answers to these questions underlie TPSAC's qualitative judgment as to whether there is an adverse impact on public health from menthol cigarettes; the results of models are used to provide a quantitative picture of the adverse impact. Because the answers to questions 1 and 2 utilize the same evidence, these closely related questions are answered together. For the same reason, questions 3 and 4, which also are closely related, are answered together. Chapter 8 concludes with recommendations to the FDA and a discussion of contraband, as called for under section 907 (b).

## EVIDENCE SYNTHESIS FOR KEY QUESTIONS

### Related to Individual Smokers

***1. Does availability of menthol cigarettes increase the likelihood of experimentation?***

***2. Does availability of menthol cigarettes increase the likelihood of becoming a regular smoker?***

Regular cigarette smoking begins with experimentation, typically during adolescence, as noted in chapter 6. To understand the role of menthol cigarettes in the continuum that ends with regular smoking, TPSAC closely examined data presented in chapters 4 and 6 on the prevalence and patterns of menthol cigarette smoking in youths ages 12 to 17. TPSAC considered studies, summarized in chapters 3 and 6, about the sensory impacts of menthol cigarette smoke and reviewed evidence from internal tobacco company documents and consumer research, presented in chapter 5, on the influences of menthol cigarette advertising and marketing on smoking of menthol cigarettes.

TPSAC's review in these chapters led to key findings related to these two questions. (1) The proportion of youth smokers who smoke menthol cigarettes is higher than the proportion of adult smokers who smoke menthol cigarettes. (2) Younger adolescent smokers have a higher proportion of menthol cigarette smokers than older adolescent smokers. African Americans, who tend to begin smoking later, are an exception. (3) There is some evidence that new smokers—those who have been smoking for less than a year—have a greater prevalence of menthol cigarette use than established smokers. (4) The proportion of menthol cigarette use among youth smokers is trending upward while non-menthol cigarette use is trending downward or is flat. (5) Menthol's cooling and anesthetic properties reduce the harshness of cigarette smoke for new smokers. Menthol cigarettes produce sensory cues, such as a minty taste and odor, a cooling sensation and throat irritation or impact—all of which may provide strong cigarette-associated cues that reinforce smoking behavior. Thus, it is biologically plausible that menthol cigarettes lead to increased experimentation and higher risk for continued regular smoking among youth. (6) Menthol cigarette marketing influences the anticipated sensory experience of smoking menthol cigarettes, thereby enhancing consumers' subjective sensory experience and liking. (7) Initiating with menthol cigarettes is more likely to lead to established smoking than initiating with non-menthol cigarettes, according to one key cohort study of youth initiators. (8) These findings, coming from multiple lines of investigation, are coherent in supporting a role for menthol cigarettes in increasing experimentation and progression to regular smoking.

TPSAC finds, based on its review, that:

> **The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases experimentation and regular smoking. (Above Equipoise)**

***3. Does inclusion of menthol in cigarettes increase the likelihood of the smoker becoming addicted?***

***4. Does inclusion of menthol in cigarettes increase the degree of addiction of the smoker?***

TPSAC considered these two questions separately for adults and adolescents. Due to a lack of relevant evidence, TPSAC was unable to reach a conclusion about the relationship between menthol cigarettes and nicotine addiction in adults. Evidence about the severity of addiction in adult menthol cigarette smokers was mixed.

TPSAC found clear evidence of a relationship between menthol cigarettes and nicotine addiction in youth. This evidence, presented in chapters 3 and 6, produced three key findings. (1) Youth who initiated with menthol cigarettes were more likely to become daily, regular, or established smokers than youth who initiated with non-menthol cigarettes. (2) Adolescent menthol cigarette smokers have a higher prevalence of nicotine dependence and degree of addiction than in those who smoke non-menthol cigarettes. (3) Studies of sensory cues and self-administration of addicting drugs in animals show that sensory factors enhance and sustain self-administration of addictive drugs. These animal studies provide biological plausibility for a role of menthol in cigarettes in increasing the likelihood of addiction in youth and increasing the degree of addiction of the young smoker. TPSAC finds, based on its review, that:

> **The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases the likelihood of addiction and the degree of addiction in youth smokers. (Above Equipoise)**
>
> **There is insufficient evidence to conclude that menthol cigarettes increase the likelihood of addiction and the severity of addiction in adults. (Below Equipoise)**

***5. Are smokers of menthol cigarettes less likely to quit successfully than smokers of non-menthol cigarettes?***

TPSAC examined data from national population surveys and other studies to determine the comparative success of quit attempts among smokers of menthol compared with non-menthol cigarettes. The national surveys provide data on quit ratios (the ratio of former to ever smokers) or rates of quitting among menthol smokers and non-menthol smokers as a measure of the success of quitting. In addition, TPSAC reviewed other types of research, including secondary analyses of data from cohort and treatment studies, both of which have limitations that were discussed in chapter 6. The evidence for whites is mixed. Across the most informative national surveys, the preponderance of evidence for non-white adults showed lower success rates for quitting among menthol smokers compared to non-menthol smokers, particularly among African Americans. Of the other studies found to be informative and of sufficient quality by TPSAC, the evidence was mixed. Considering all of the evidence, TPSAC concluded that non-white, particularly African American menthol smokers, are less likely to quit successfully than non-menthol smokers.

TPSAC reviewed experimental and pharmacological evidence, presented in chapter 3, that provided a plausible biological explanation for lower cessation success among menthol smokers. Several animal studies showed that once drug self-administration is established, taste and other sensory factors can function as stimuli that substantially enhance the strength and persistence of drug self-administration. Stimuli associated with drug intake can come to evoke craving that promotes resumption of drug self-administration after a period of abstinence. As discussed in chapters 5 and 6, empirical and qualitative research—including consumer research conducted by tobacco companies— showed consumers hold beliefs about the implicit health benefits of menthol cigarettes, which could undermine quitting intentions and attempts. As discussed in chapter 5, these beliefs about the implicit benefits of menthol cigarettes are especially apparent among African Americans.

TPSAC finds, based on evidence reviewed in chapter 6, that:

> **The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes results in lower likelihood of smoking cessation success in African Americans, compared to smoking non-menthol cigarettes. (Above Equipoise)**
>
> **The evidence is sufficient to conclude that a relationship is as likely as not that the availability of menthol cigarettes results in lower likelihood of smoking cessation success in other racial/ethnic groups (At Equipoise)**

***6. Do biomarker studies indicate that smokers of menthol cigarettes receive greater doses of harmful agents per cigarette smoked compared with smokers of non-menthol cigarettes?***

To examine the question of whether menthol cigarette smokers are exposed to higher levels of harmful agents, TPSAC reviewed studies directed at the topography of smoking (puffing behavior and exposure to nicotine and carbon monoxide from single cigarettes) and studies comparing levels of biomarkers of tobacco smoke exposure in smokers of menthol and non-menthol cigarettes. This evidence was presented in chapter 7. Because of methodologic issues in studying smoking topography, including small numbers of subjects, imbalance between race and menthol use, smoking through cigarette holders and/or artificial patterns of smoking, the generalizability of the topography findings to the smoking of menthol cigarettes in daily life is questionable. The biomarker studies are more generalizable in that they typically include larger numbers of smokers smoking their own cigarettes in a naturalistic way, and the studies involve larger numbers of smokers than the topography studies. There is some evidence from one large study that while daily exposure is not different, the intake of nicotine per cigarette is higher for menthol compared to non-menthol smokers. There are insufficient data to know if smoking menthol cigarettes is associated with greater smoke intake and more exposure to tobacco smoke toxins among smokers of relatively few cigarettes per day.

TPSAC finds, based on the evidence reviewed, that:

> **The evidence is insufficient to conclude that it is more likely than not that menthol smokers inhale more smoke per cigarette or that they are exposed to higher levels of nicotine and other tobacco toxins. (Below Equipoise)**

**7.** ***Do smokers of menthol cigarettes have increased risk for diseases caused by smoking compared with smokers of non-menthol cigarettes?***

Chapter 7 summarizes the diverse lines of evidence relevant to this question, including the findings of toxicological and epidemiological studies. The findings pertaining to biomarkers and smoking topography, leading to the conclusion for Question 6 related to individual smokers, are also relevant. That conclusion does not give support to increased risk for diseases in smokers of menthol compared to non-menthol cigarettes.

The toxicological studies considered in Chapter 6 use diverse in vivo and in vitro systems. The evidence is mixed. The in vitro studies show that menthol has activity in various systems. Chapter 3 addresses the pharmacologic actions of menthol which may lead to some of these effects. The very limited bioassay data does not indicate that smoke from menthol cigarettes has greater toxicity than smoke from non-menthol cigarettes. The epidemiological literature, albeit limited in scope, suggests that there is not greater risk for disease development for smokers of menthol versus non-menthol cigarettes. For most of the diseases caused by smoking, the evidence is extremely limited. For lung cancer, the most studied disease, there are only six epidemiological studies and lesser numbers were identified for other health outcomes.

TPSAC finds, based on the evidence reviewed in this chapter, that:

> **The evidence is insufficient to conclude that it is more likely than not that smokers of menthol cigarettes have increased risk for diseases caused by smoking compared with smokers of non-menthol cigarettes. (Below Equipoise)**

**Smoking at the Population Level**

***1. Does the availability of menthol cigarettes increase the prevalence of smoking in the population, beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?***

The prevalence of adult smoking is substantially driven by the experimentation and subsequent regular smoking by youth and adolescents. As noted in chapter 6, the proportion of menthol cigarette smoking is highest in the 12–15 year age group and decreases progressively within every older age group to age 25. The early use of menthol cigarettes by between one-half to one-third of youth smokers most likely contributes to nicotine dependence in at least the 30 percent of adult smokers who use menthol cigarettes. The evidence for Question 5 above, which indicates that menthol cigarette smokers are less likely to quit smoking than non-menthol cigarette smokers, is also relevant.

In addition, a substantial number of smokers who initiate with menthol cigarettes later switch to non-menthol cigarettes. Thus, menthol initiation also contributes to the prevalence of non-menthol cigarette smoking in the general population. Because of the high prevalence of smoking menthol cigarettes in these early ages and because of the likelihood that smoking menthol cigarettes increases their dependence on smoking and makes quitting less likely, TPSAC concludes that the availability of menthol cigarettes increases the prevalence of smoking in the general population and particularly in African Americans, beyond the anticipated prevalence if such cigarettes were not available.
TPSAC finds, based on the evidence reviewed, that:

**The evidence is sufficient to conclude that it is more likely than not that the availability of menthol cigarettes increases the likelihood of experimentation and regular smoking beyond the anticipated prevalence if such cigarettes were not available, in the general population and particularly in African Americans. The evidence is sufficient to conclude that it is more likely than not there is a causal relationship between the availability of menthol cigarettes and regular smoking among youth. (Above Equipoise)**

***2. Does tobacco company marketing of menthol cigarettes increase the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available? In subgroups within the population?***

Chapter 4 provided an introduction to the history of marketing of menthol cigarettes. Chapter 5 summarized strategies for marketing of menthol cigarettes, menthol marketing messages, target groups for menthol marketing and consumer perceptions of menthol cigarettes. The findings pertaining to patterns of menthol smoking for the population overall, and for population subgroups, as reviewed in chapter 4 and 6 are also relevant. In addition, chapter 3 provided information on the sensory properties of menthol cigarettes which are relevant for considering consumer perception issues.

TPSAC found there to be sufficient evidence that marketing messages for menthol cigarettes have been different from those used in non-menthol cigarette marketing. Menthol cigarettes have been and continue to be marketed with a set of associated branding elements and labels that connote health benefits. Early messages featured explicit references to health benefits through medicinal assistance (such as soothing a sore throat or clearing a blocked nose) and later messages emphasized implicit health benefits, through the promotion of the particular features of menthol cigarettes that refer to their 'freshness' and sensory cooling properties. Studies show consumer perceptions of the taste/sensory experience of cigarettes are correlated with perceptions of harm, including for menthol cigarettes. Against a background of consumer research studies demonstrating that taste perception is subjective and highly amenable to suggestion from product advertising, branding and labeling, menthol cigarette marketing influences the anticipated sensory experience of menthol cigarettes, thereby enhancing consumers' subjective sensory experience and liking. There is sufficient evidence from tobacco industry document reviews and empirical studies to conclude that consumers hold beliefs about the implicit health benefits of menthol cigarettes and this is particularly the case among African Americans.

In addition to messages that implied health reassurance, menthol marketing messages promoted a more youthful brand image than for non-menthol cigarettes, and emphasized the role of menthol cigarettes in peer group acceptance. There is substantial evidence that menthol marketing has been especially targeted to youth and African Americans, with youthful imagery, messages promoting an appealing sensory experience, and peer group acceptance. There is also evidence from tobacco industry documents that the tobacco industry designed menthol cigarettes with lower menthol levels, with an awareness that, at these lower levels, the sensory effects of menthol reduce the harshness of cigarettes for new smokers. Menthol smoking is higher in more youthful smoker population groups and among African American smokers.

The evidence is sufficient to conclude that Hispanics have been disproportionately more targeted by menthol than non-menthol marketing. Menthol smoking is also higher among Hispanic smokers. Although menthol smokers comprise a higher proportion of Asian American and Hawaiian/Pacific Islander smokers, there is insufficient evidence to conclude that these population groups have been disproportionately more targeted by menthol than non-menthol marketing. Finally, although female smokers have higher menthol smoking rates than male smokers, there is insufficient evidence to conclude that they have been disproportionately more targeted by menthol than non-menthol marketing.

TPSAC finds, based on the evidence reviewed, that:

> **The evidence is sufficient to conclude that it is more likely than not that menthol cigarette marketing increases prevalence of smoking beyond anticipated prevalence if such cigarettes were not available for the whole population, and for youth and African Americans.(Above Equipoise)**
>
> **The evidence is sufficient to conclude that it is as likely as not that menthol cigarette marketing increases prevalence of smoking beyond anticipated prevalence if such cigarettes were not available for Hispanics. (At Equipoise)**
>
> **The evidence is insufficient to conclude that it is more likely than not that menthol cigarette marketing increases prevalence of smoking beyond anticipated prevalence if such cigarettes were not available for Asian Americans, Hawaiians/Pacific Islanders and women. (Below Equipoise)**

**OVERALL CONCLUSIONS**

Based on the conclusions to the nine questions, TPSAC provides the following general conclusions:

- Menthol cigarettes have an adverse impact on public health in the United States.
- There are no public health benefits of menthol compared to non-menthol cigarettes.

## PUBLIC HEALTH IMPACT

The Family Smoking Prevention and Tobacco Control Act charges the Tobacco Products Scientific Advisory Committee (TPSAC) with developing a report and recommendations that address "the issue of the impact of the use of menthol in cigarettes on the public health including such use among children, African Americans, Hispanics, and other racial and ethnic minorities." The availability of menthol cigarettes in the marketplace could adversely affect public health through two consequences: (1) increasing the risk for the diseases caused by smoking cigarettes; and (2) increasing the number of people who smoke. These two consequences are captured in the population attributable risk statistic, used to calculate the disease burden attributable to a causal factor, such as cigarette smoking.

The committee finds that the evidence does not indicate increased disease risks in smokers of menthol cigarettes compared to non-menthol cigarettes. TPSAC does conclude that the availability of menthol cigarettes has led to an increase in the number of smokers and that this increase does have adverse public health impact in the United States. TPSAC found evidence that the availability of menthol cigarettes increases initiation; of particular concern was the high rate of menthol cigarette smoking among youth and the trend over the last decade of increasing menthol cigarette smoking among 12 to 17 year olds, even as smoking of non-menthol cigarettes declines. TPSAC also concluded that cessation is less likely to be successful among smokers of menthol cigarettes. Thus, the availability of menthol cigarettes increases initiation and reduces cessation, thereby increasing the number of people who are smoking. This increase in the number of smokers represents an adverse impact of the availability of menthol cigarettes on public health.

To gain an understanding of the quantitative impact of menthol cigarettes on public health, TPSAC turned to the results of models of smoking in the United States, one developed for the entire population and the other for the African American population (Appendix A). Details of the models developed by Mendez are provided in Appendix A. Mendez expanded a previously developed compartmental model of smoking in the population of the United States to incorporate smoking of menthol and non-menthol cigarettes (see references in Appendix A for background). Based on the review provided in this report, TPSAC provided specifications for model parameters, including a central or "best" estimate and plausible lower and upper bounds. For parameters not covered in the TPSAC review, parameter values were based on documents available to TPSAC. Table 1 below ( Table 3 in Appendix A) documents these choices.

The model compares two scenarios: a scenario based on the current pattern of smoking of menthol and non-menthol cigarette smoking and a counterfactual or comparison scenario representing smoking in the United States, but without the availability of menthol cigarettes. These two scenarios match at the outset in every way except for the availability of menthol cigarettes. Over time, the patterns of experimentation, initiation, and cessation differ as described in Table 1 of Appendix A and switching occurs between the two types of cigarettes in the menthol cigarette scenario. Models were implemented for the boundary conditions defined by the lower and upper bounds for the model parameters. The results provide insight into the sensitivity of findings to values of model parameters.

## Table 1.Results – General Population

| Scenario | Description | Cumulative Excess Deaths | | | | Cumulative Excess Smoking Initiation | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 2020 | 2030 | 2040 | 2050 | 2020 | 2030 | 2040 | 2050 |
| 1 | TPSAC Estimates | 17,182 | 67,817 | 164,590 | 327,565 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 2 | Low Menthol Initiation | 17,181 | 67,812 | 164,555 | 327,396 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 3 | High Menthol Initiation | 17,182 | 67,822 | 164,625 | 327,733 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 4 | Low Menthol Experimentation | 15,411 | 61,041 | 147,794 | 292,601 | 2,019,295 | 3,908,229 | 5,920,677 | 8,051,353 |
| 5 | High Menthol Experimentation | 20,723 | 81,367 | 198,181 | 397,489 | 2,827,013 | 5,471,520 | 8,288,948 | 11,271,894 |
| 6 | Low Yield from Experimenter to Smoker | 2,127 | 10,220 | 21,810 | 30,346 | 0 | 0 | 0 | 0 |
| 7 | High Yield from Experimenter to Smoker | 19,838 | 77,980 | 189,784 | 380,008 | 2,692,393 | 5,210,972 | 7,894,236 | 10,735,137 |
| 8 | Low Menthol Cessation | 18,495 | 74,138 | 178,061 | 346,122 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 9 | High Menthol Cessation | 11,023 | 38,336 | 101,964 | 241,409 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 10 | Low Menthol Mortality Risk | -239,508 | -293,535 | -220,657 | -41,279 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 11 | High Menthol Mortality Risk | 238,551 | 378,451 | 494,892 | 644,022 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 12 | Low Switch Rate Menthol to Non-menthol | 17,227 | 68,265 | 166,070 | 330,538 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 13 | High Switch Rate Menthol to Non-Menthol | 17,138 | 67,397 | 163,252 | 324,972 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 14 | Low Switch Rate Non-menthol to Menthol | 17,139 | 67,399 | 163,249 | 324,993 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |
| 15 | High Switch Rate Non-menthol to Menthol | 17,224 | 68,223 | 165,874 | 329,989 | 2,288,534 | 4,429,326 | 6,710,101 | 9,124,867 |

The model results indicate that the availability of menthol cigarettes increases the numbers of people who initiate smoking, as well as leading to premature death from smoking caused diseases. Table 1 provides the numbers of excess initiators and of premature deaths. The first row of the table provides the results based on TPSAC's best estimates of the model parameters. The findings provide an approximate indication of the magnitude of the public health impact of the availability of menthol cigarettes. For example, assuming the best estimates, by 2020 about 17,000 premature deaths will occur and about 2.3 million people will have started smoking, beyond what would have occurred absent availability of menthol cigarettes. The cumulative figures mount over time. The remaining rows of the table provide similar results for the additional scenarios. All show excess mortality and numbers of smoking initiators as associated with the availability of menthol cigarettes.

Mendez also explored the public health impact of the high proportion of menthol cigarette smoking among African American smokers. He compared two scenarios: one reflecting the current proportion of menthol use among experiments and initiators (80% for both) compared with a counterfactual identical to that for the general population (40% of experiments using menthol cigarettes and 45% experimenters). Table 2 below (table 6 in Appendix A) provides the findings for the current situation and for the counterfactual, respectively. The difference between the estimates in any cell of the two tables reflects the difference in menthol cigarette use. For example, in 2020, there are an additional 2,025 (4,716 - 2691) excess deaths because of the higher menthol prevalence in the scenario labeled TPSAC estimates. Similarly, there are about 150,000 additional smokers in 2020 attributable to the higher menthol prevalence.

**Table 2. Results-African American Population**

| Description | Cumulative Excess Deaths | | | | Cumulative Excess Smoking Initiation | | | |
|---|---|---|---|---|---|---|---|---|
| | 2020 | 2030 | 2040 | 2050 | 2020 | 2030 | 2040 | 2050 |
| African American Population – TPSAC Estimates | 4,716 | 16,381 | 35,250 | 66,524 | 461,273 | 859,101 | 1,262,086 | 1,656,005 |
| Low Menthol Prevalence Hypothetical African American Population | 2,691 | 10,244 | 23,218 | 44,771 | 307,515 | 572,734 | 841,391 | 1,104,003 |

The results of all models are subject to uncertainty, reflecting incomplete knowledge about underlying relationships and the values of the parameters in the model. Mendez used previously developed and well-characterized models as the starting point for developing the menthol models. The values for parameters were based on the literature reviews carried out by TPSAC. The consequences of assuming particular values for key parameters were explored through sensitivity analyses. As the parameters used as input of the model are subject to the statistical uncertainty inherent to their individual estimation process, a Monte Carlo analysis would be required to capture the combined effect of such uncertainty or the results of the analysis. This analysis would not likely change the magnitude of the results, as the model is linear, and the simulation settings and parameters chosen were conservative.

TPSAC also considered the findings of modeling carried out by Levy et al. (2011) on the future effects of a menthol cigarette ban in the total US population and among African Americans. While TPSAC is not proposing specific policy actions that should be taken by FDA, the modeling of the consequences of a ban provides further insight into the impact of menthol cigarettes on public health. The scenarios considered involved the consequences of implementing a ban in 2011, using the distribution of smoking in the U.S. population as of 2003. Table 2 provides the principal findings for changes in the numbers of smokers and the avoided premature deaths. The comparison scenarios to the status quo involve changes of 10 percent, 20 percent, and 30 percent in the rates of initiation (reduced) and cessation (increased). The authors do not propose that any of these scenarios is most probable. Regardless of scenario, a ban is associated with avoidance of premature mortality for a substantial number of deaths. The figure for a 10% change is similar to the estimate based on TPSAC's best estimates.

The results from Mendez and Levy et al., while based on different models and assumptions, provide comparable insights into the quantitative magnitude of the public health impact of the availability of menthol cigarettes. The burden is substantial; for example, the cumulative excess deaths estimated by Mendez for the 40-year period, 2010-2050, is about 80% of the number of deaths annually currently attributed to cigarette smoking in the United States (US DHHS 2004). Over that same time period, an estimated 9 million people will initiate smoking because of the availability of menthol cigarettes. The models for African Americans show that the high prevalence of menthol cigarette smoking adds to the burden of premature death experienced by this population.

While subject to uncertainty, the model results confirm TPSAC's qualitative judgment on the adverse impact of menthol cigarettes on public health. They do not capture the considerable excess burden of morbidity, coming from chronic diseases, infectious diseases, and diminished well-being that is attributable to smoking.

**RECOMMENDATIONS**

Mentholation of cigarettes was discovered by accident in the 1920s. Even then, the sensory and medicinal properties of menthol were known and these properties, along with cigarette design and marketing, have made menthol cigarettes a substantial component of the cigarette market in the United States. In the decades since the first menthol cigarettes were made, there have been substantial advances in the understanding of the pharmacology of menthol, of how to use menthol to manipulate flavor and the sensory perception of cigarette smoke, and of the interplay between menthol and nicotine. Marketing of menthol cigarettes has been successful. Menthol cigarettes are now smoked by most African American smokers and there is a concerning rise of menthol cigarette smoking among youth. Menthol cannot be considered merely a flavoring additive to tobacco. Its pharmacological actions reduce the harshness of smoke and the irritation from nicotine, and may increase the likelihood of nicotine addiction in adolescents and young adults who experiment with smoking. Furthermore, the distinct sensory characteristics of menthol may enhance the addictiveness of menthol cigarettes, which appears to be the case among youth. TPSAC has found that the availability of menthol cigarettes has adverse impact on public health by increasing the numbers of smokers with resulting premature death and avoidable morbidity.

Consequently, TPSAC makes the following overall recommendation to FDA:

**Removal of menthol cigarettes from the marketplace would benefit public health in the United States.**

The Act offers a variety of mechanisms for FDA to consider, if it concludes that it should pursue this recommendation. At this time, TPSAC has no specific suggestions for follow-up by FDA to this recommendation.

**Contraband**

With regard to any proposed standard, the Act states under section 907(b) that: "The Secretary shall consider all other information submitted in connection with a proposed standard, including information concerning the countervailing effects of the tobacco product standard on the health of adolescent tobacco users, adult tobacco users, or non-tobacco users, such as the creation of a significant demand for contraband or other tobacco products that do not meet the requirements of this chapter and the significance of such demand."

Several presentations in public hearings and written submissions to TPSAC speculated on the potential for contraband as a consequence of a ban on menthol cigarettes. The concerns expressed originated with experience gained from black market activity involving non-menthol cigarettes. The general concern about contraband following a potential ban on menthol cigarettes can be summarized as follows: a black market for menthol cigarettes could be created, criminal activity could ensue, and different methods might be used to supply such a black market. The demand for contraband menthol cigarettes might be met through evasion, illegal production and importation of menthol cigarettes, and after-market mentholation (Public Hearing Date, testimony of from Michael G. Hering, JD deputy chief counsel— Tobacco Master Settlement Agreement, National Association of Attorneys General).

**Evasion**

TPSAC recognizes that the current laws governing the sale and taxation of cigarettes can be evaded. Examples of evasion that might not violate a menthol ban were included in the presentation by Michael G. Hering. One example of such evasion involved the use of menthol cigars, roll your own menthol cigarettes, menthol pipe tobacco, menthol tubes, rolling papers and filters, and the emergence and use of after market mentholation kits. A second example pertained to the FDA tobacco flavoring ban. The flavoring band currently pertains only to cigarettes and not to cigars. Shortly after the FDA flavor ban was implemented, Djarum introduced clove cigars into the market. Other cigars with cherry, peach, strawberry, grape and pina colada and apple tini were also introduced, effectively evading the FDA ban on flavored tobacco.

**Illegal production and importation of menthol cigarettes**

Based on public testimony, TPSAC identified a number of likely sources of menthol cigarettes that would be illegal under a ban. The sources of imported contraband would include foreign manufacturers, domestic manufacturing for foreign markets, and unlicensed domestic manufacturers.

**After Market Mentholation**

If roll your own (RYO) menthol tobacco or menthol pipe tobacco became unavailable, then consumers could purchase their own menthol tubes or rolling paper as well as menthol filter tips. Other forms of aftermarket mentholation were suggested based on current experience with non-menthol cigarettes. Since cigarettes that come off of the manufactures line are mentholated after the fact, it is plausible that after market mentholation kits might become available. After market mentholated kits would allow consumers to create a homegrown menthol cigarette and with the advent of the RYO Filling stations, consumers would not be limited to hand rolling their cigarettes(http://ryofillingstation.com/about.php). Whether such after market mentholation kits could produce levels of mentholation identical to the current branded products or whether 14,000,000 menthol cigarette smokers would make the effort to mentholate their own cigarettes remains unknown.

**Potential Menthol Black Market**

TPSAC recognizes that the potential size of a menthol black market cannot be readily estimated, due to the need to make uncertain assumptions as to the nature and functioning of such a black market. For example, how would distribution of large numbers of contraband menthol cigarettes through illegal channels to the public take place on a daily basis? If the precisely engineered menthol levels in currently available menthol brands cannot be reproduced, is it likely that a substantial black market would develop, particularly since non-menthol cigarettes would be available?
TPSAC did receive industry-supported testimony from Compass Lexecon that attempted to estimate the size of a potential menthol cigarette black market. Based on marketing data provided by Lorillard Inc., Compass Lexecon undertook an analysis that modeled the effect of a menthol cigarette ban. They concluded that a ban would not eliminate menthol cigarette consumption by current menthol smokers in the U.S., and that most current smokers would turn either to a black market for menthol cigarettes or would turn instead to non-menthol cigarettes. Compass Lexecon also speculated on the possible unintended consequences of increased criminal activity as well as concerns about the possibility that youth might have greater access to unregulated cigarettes associated with a black market.

The Compass Lexecon report estimated that a sizable black market would quickly emerge to satisfy the demand for menthol cigarettes. They further estimated that the size of the black market based on the anticipated increased price of black market cigarettes. This report estimated that a 10% increase in the effective price of illegal menthol cigarettes would lead to unit sales of black market menthol cigarettes amounting to about 87% of current legal menthol volumes. Further, the report estimated that a 50% increase in the effective price in black market menthol cigarettes would result in black market menthol sales amounting to about 56% of current legal menthol sales. (Estimating consequences of a Ban on the Legal Sale of Menthol Cigarettes, Compass Lexecon, December 29, 2010). This same analysis predicted that based on the black market price increases noted above, that a 10% price increase would reduce overall smoking rates by 1% and a 50% black market price increase would result in a 3.5% reduction in the overall smoking rates. The authors concluded, based on the above predictions, that less than a 30% reduction in smoking prevalence would be achieved by a ban on menthol cigarettes.

TPSAC noted that this economic analysis did not address the question of a menthol ban's effects on youth smoking initiation or the cumulative effect of a ban after several years. The analysis does not address whether African American smokers who prefer menthol cigarettes and are not yet addicted to nicotine would choose to continue smoking. Because the analysis did not incorporate these possibilities, the results may have underestimated the percentage and number of people who would stop smoking as well as the number of youth who would never begin smoking if menthol cigarettes were not available. Consequently, the model may have overestimated the size of any potential black market.

TPSAC, whose charge is to specifically address issues related to youth smoking, also recognizes that an analysis of the impact of a menthol ban on the overall smoking rates over time should include the effect of price increases on youth. The hypothesis that cigarette smoking by younger persons will be relatively more responsive to price than smoking among older persons is confirmed by studies of cigarette demand based on cross-sectional surveys of youths and young adults. Recent estimates indicate that youths are up to three times more sensitive to price than adults, with a 10- percent price increase estimated to reduce youth smoking prevalence by 5 percent or more and also to reduce cigarette consumption among continuing young smokers (Chaloupka and Grossman, 1996; Evans and Huang, 1998; Lewit et al., 1997,Smoking and Tobacco Control, page 196,NCI Monograph No.14). The greater price sensitivity of youth and young adults, compared to adults 25 years and older, indicates that price increases produced by a black market would reduce initiation and encourage cessation among the youth and young adults.

TPSAC acknowledges that the potential for contraband menthol cigarettes exists, should FDA choose to implement a ban or take some other policy action that restricts availability of menthol cigarettes. Consistent with the requirements of the Act, TPSAC recommends that FDA consult with appropriate experts and carry out relevant analyses depending on the actions taken in response to this report from TPSAC. At present, TPSAC is not constituted to carry out such analyses, and lacking knowledge of FDA's intent on receipt of this report, it concluded that FDA would need to assess the potential for contraband menthol cigarettes as required by the Act.

**Other Considerations**

The removal of menthol cigarettes from the market could result in a substantial reduction in cigarette smoking, according to data from the May 2010 TUS-CPS survey. The survey asked menthol smokers (N=2877)*, "If menthol cigarettes were no longer sold, which of the following would you most likely do?"* According to analysis presented to TPSAC by Anne M. Hartman of the National Cancer Institute (January 2010), 39 percent of menthol smokers would quit, followed by those would switch to non-menthol cigarettes (36.2 percent) or switch to another tobacco product (7.7 percent). Her analysis included a breakdown of potential quitters by race/ethnicity, age and gender: among African American menthol smokers, (47 percent); among non-Hispanic white menthol smokers ( 34 percent) ; among menthol smokers age 18–44 years ( 41 percent) ; among smokers age 45 years and over (37 percent); among female menthol smokers( 42 percent); and among male menthol smokers, (36 percent).

In her presentation, Hartman noted that behavioral intention is associated with actual behavior. She concluded that the results suggest a potential substantial reduction in tobacco use if menthol cigarettes were no longer sold. Should FDA take any action that would remove menthol cigarettes from the marketplace, planning should address the potential demand for cessation services.

## RESEARCH RECOMMENDATIONS

In the course of reviewing the evidence related to its charge, TPSAC noted gaps in understanding of menthol cigarettes and public health that should be addressed with further research. Here, TPSAC makes brief recommendations with acknowledgement that the priority given to particular recommendations may depend on any policy action taken by the FDA.

- **Subliminal menthol**: TPSAC was given the charge of addressing "menthol in cigarettes", but, as set out in Chapter 1, focused this report on menthol cigarettes. Several studies suggested that menthol may be present in some cigarettes in which it is not a characterizing additive. TPSAC suggests that further research should be carried out to characterize the menthol content of cigarettes in general and to assess whether menthol has pharmacologic effects at these concentrations that might affect initiation, dependence or cessation.
- **Susceptible and vulnerable populations**: TPSAC found little data on use of menthol cigarettes by the severely mentally ill, a population with a high prevalence of cigarette smoking. This gap should be addressed, as should data gaps for other potentially vulnerable populations. There is now substantial research on genetic determinants of addiction to nicotine; studies on this topic should incorporate consideration of menthol cigarette smoking into their protocols. In addition, more research is required to assess whether menthol interacts with genetically determined bitterness taste sensitivity (sensitivity to phenylthiocarbamate (PTC) and 6-n-propylthiouracil (PROP)) to facilitate smoking.

- **Strengthen the evidence foundation on the public health impact of menthol cigarettes:**
    - Cohort studies of adolescents and young adults should be carried out that follow participants from experimentation to initiation to dependence. These studies would provide an improved understanding of the risk for moving across this sequence that is associated with menthol cigarette availability.
    - The consequences of menthol cigarette smoking for likelihood of successful cessation need further investigation in the general population. Additionally, the implications of menthol cigarettes for sustained quitting should be addressed in clinical trials of cessation therapy and other databases.
    - Develop surveillance protocols to track industry marketing practices including price promotions and their impact on smoking patterns with attention to menthol cigarettes. The protocols should be sufficiently fine-grained with regard to populations and places and focus on critical periods of policy implementation.

**APPENDIX A**

# Results from a Population Dynamics Model of the Consequences of Menthol Cigarettes for Smoking Prevalence and Disease Risks[1]

David Méndez, PhD
University of Michigan
March 2011

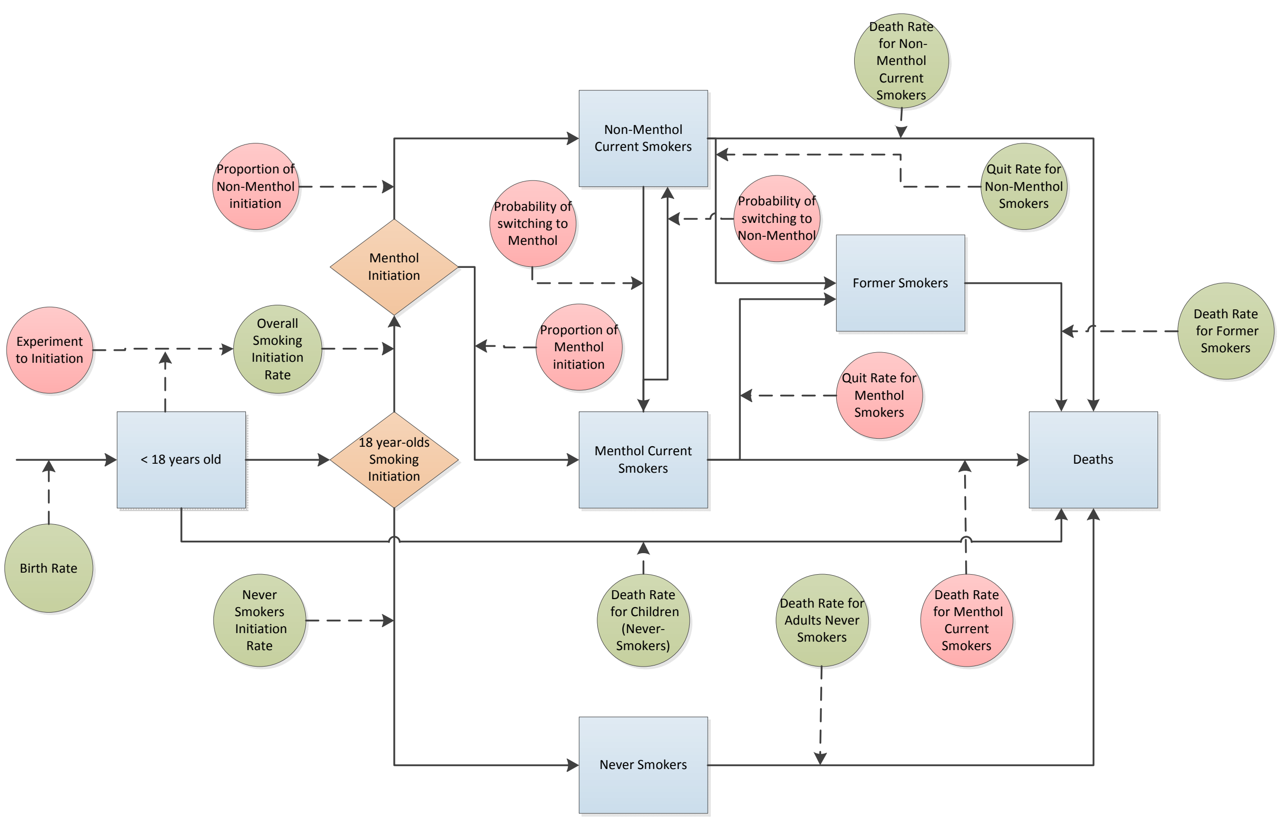
[1] The work reported was done under contract with the Center for Tobacco Products at FDA. The content and conclusions of this report are solely the author's

**Results from a Population Dynamics Model of the Consequences of**

**Menthol Cigarettes for Smoking Prevalence and Disease Risks**

This document describes the constructs of, and results from, the model commissioned by the Tobacco Products Scientific Advisory Committee (TPSAC) to estimate the consequences of menthol cigarette smoking on the U.S population. The model is an extension and modification of a population dynamics model previously developed to track smoking prevalence and smoking related risks, which has been extensively discussed in the literature.[1-7] The following figure shows the general organization of the model, as modified to address menthol cigarettes:

**Menthol Model Block Simulation Diagram**



The boxes (compartments) represent the stock of individuals in different categories at a given time; the arrows represent the flow between compartments; and the circles represent parameters that modify the flow. Red circles refer to parameters related to menthol smoking while green circles refer to the other parameters. Diamonds represent the event of smoking initiation, concentrated at a single age.

Following is a description of the constructs of the model:

**Definition of dynamic (time-dependent) variables:**

$P(a,t) = US\ population\ of\ age\ a\ in\ year\ t$

$N(a,t) = Population\ of\ never - smokers\ of\ age\ a\ in\ year\ t$

$F(a,t,q) = Population\ of\ former - smokers\ of\ age\ a,\ in\ year\ t,\ that\ quit\ q\ years\ ago$

$C(a,t) = Population\ of\ current - smokers\ of\ age\ a\ in\ year\ t$

$C_m(a,t) = Population\ of\ current\ menthol - smokers\ of\ age\ a\ in\ year\ t$

$C_n(a,t) = Population\ of\ current\ non - menthol - smokers\ of\ age\ a\ in\ year\ t$

$\pi_N(a,t) = Prevalance\ of\ never - smokers\ of\ age\ a\ in\ year\ t$

$\pi_N'(t) = Adult\ prevalence\ of\ never - smokers\ in\ year\ t$

$\pi_F(a,t) = Prevalance\ of\ former - smokers\ of\ age\ a\ in\ year\ t$

$\pi_F'(t) = Adult\ prevalence\ of\ former - smokers\ in\ year\ t$

$\pi_C(a,t) = Prevalance\ of\ current - smokers\ of\ age\ a\ in\ year\ t$

$\pi_C'(t) = Adult\ prevalence\ of\ curent - smokers\ in\ year\ t$

$\pi_{C_m}(a,t) = Prevalance\ of\ current\ menthol\ - smokers\ of\ age\ a\ in\ year\ t$

$\pi_{C_m}'(t) = Adult\ prevalence\ of\ current\ menthol - smokers\ in\ year\ t$

$\pi_{C_n}(a,t) = Prevalance\ of\ current\ non - menthol\ - smokers\ of\ age\ a\ in\ year\ t$

$\pi_{C_n}'(t) = Adult\ prevalence\ of\ current\ non\quad menthol\quad smokers\ in\ year\ t$

$D(t) = \mathit{Total\ deaths\ in\ year\ t}$

**Definition of Non-dynamic variables and parameters:**

$\mu(a) = \mathit{Overall\ death\ rate\ for\ individuals\ of\ age\ a}$

$\mu_N(a) = \mathit{Death\ rate\ among\ non - smokers\ of\ age\ a}$

$\mu_F(a, q) = \mathit{Death\ rate\ among\ former\ - smokers\ of\ age\ a\ \ who\ quit\ q\ years\ ago}$

$\mu_C(a) = \mathit{Death\ rate\ among\ current - smokers\ of\ age\ a}$

$\mu_{C_m}(a) = \mathit{Death\ rate\ among\ current\ menthol - smokers\ of\ age\ a}$

$\mu_{C_n}(a) = \mathit{Death\ rate\ among\ current\ non - menthol - smokers\ of\ age\ a}$

$\rho(a) = \mathit{Overall\ smoking\ quit\ rate\ for\ individuals\ of\ age\ a}$

$\rho_{C_m}(a) = \mathit{Smoking\ quit\ rate\ for\ menthol\ smokers\ of\ age\ a}$

$\rho_{C_n}(a) = \mathit{Smoking\ quit\ rate\ for\ non - menthol\ smokers\ of\ age\ a}$

$S_{msn} \quad = \mathit{Switching\ rate\ from\ menthol\ to\ non - menthol\ among\ current\ menthol\ smokers}$

$S_{nsm} = \mathit{Switching\ rate\ from\ non - menthol\ to\ menthol\ among\ current\ menthol\ smokers}$

$I = \mathit{Smoking\ initiation\ age}$

$\gamma = \mathit{Overall\ smoking\ initiation\ rate}$

$\gamma_{C_m} = \mathit{Smoking\ initiation\ rate\ for\ menthol\ smokers}$

$\gamma_{C_n} = \mathit{Smoking\ initiation\ rate\ for\ non - menthol\ smokers}$

$RR(a, q) = \mathit{Relative\ risk\ of\ death\ for\ a\ former\ smoker\ of\ age\ a\ who\ quit\ q\ years\ ago} - q = 0\ \mathit{implie}$

$K_1 = \mathit{Mortality\ risk\ ratio}\ \left(\frac{\mathit{Menthol}}{\mathit{Non - Menthol}}\right)$

$K_2 = \mathit{Quit\ rates\ ratio}\ \left(\frac{\mathit{Menthol}}{\mathit{Non - Menthol}}\right)$

$K_3 = \mathit{Proportion\ of\ Menthol\ among\ Initiators}$

$K_4 = \mathit{Proportion\ of\ Menthol\ among\ Experimenters}$

$$K_E = Ratio\ of\ Yields\ from\ Experimenter\ to\ Established\ Smoker\ \left(\frac{Menthol}{Non-Menthol}\right)$$

**Dynamic (time-dependent) relationships:**

$$N(0,t) = P(0,t)$$

$$N(a,t) = N(a-1,t-1) \times (1 - \mu_N(a))\ \ for\ a \neq I$$

$$N(a,t) = N(a-1,t-1) \times (1 - \mu_N(a)) \times \left(1 - \gamma_{C_m} - \gamma_{C_n}\right)\ \ for\ a = I$$

$$F(a,t,q) = 0\ \ for\ a-q \leq I$$

$$F(a,t,1) = C_m(a-1,t-1) \times \left(1 - \mu_{C_m}(a-1)\right) \times \rho_{C_m}(a-1) + C_n(a-1,t-1) \times \left(1 - \mu_{C_n}(a-1)\right) \times \rho_{C_n}(a-1)$$

$$F(a,t,q) = F(a-1,t-1,q-1) \times \left(1 - \mu_{C_F}(a-1,q-1)\right)\ \ for\ a-q > I\ and\ q > 1$$

$$C_m(a,t) = 0\ for\ a < I$$

$$C_m(a,t) = \gamma_{C_m} \times N(a-1,t-1) \times (1 - \mu_N(a-1))\ \ for\ a = I$$

$$C_m(a,t) = C_m(a-1,t-1) \times \left(1 \quad \mu_{C_m}(a-1)\right) \times \left(1 \quad \rho_{C_m}(a-1)\right) \times (1 \quad S_{mzn}(a-1)) + C_n(a-1,t-1) \times (1$$

$$C_n(a,t) = 0\ for\ a < I$$

$$C_n(a,t) = \gamma_{C_n} \times N(a-1,t-1) \times (1 - \mu_N(a-1))\ \ for\ a = I$$

$$C_n(a,t) = C_n(a-1,t-1) \times \left(1 - \mu_{C_n}(a-1)\right) \times \left(1 - \rho_{C_n}(a-1)\right) \times (1 - S_{nzm}(a-1)) + C_m(a-1,t-1) \times (1 -$$

$$P(a,t) = N(a,t) + \sum_{q=1}^{q=30+} F(a,t,q) + C_m(a,t) + C_n(a,t)$$

$$\pi_N(a,t) = \frac{N(a,t)}{P(a,t)}$$

$$\pi_N'(t) = \frac{\sum_{a=18}^{a=100} N(a,t)}{\sum_{a=18}^{a=100} P(a,t)}$$

$$\pi_F(a,t) = \frac{\sum_{q=1}^{q=30+} F(a,t,q)}{P(a,t)}$$

$$\pi_F'(t) = \frac{\sum_{a=18}^{a=100} \sum_{q=1}^{q=30+} F(a,t,q)}{\sum_{a=18}^{a=100} P(a,t)}$$

$$\pi_{C_m}(a,t) = \frac{C_m(a,t)}{P(a,t)}$$

$$\pi'_{C_m}(t) = \frac{\sum_{a=18}^{a=100} C_m(a,t)}{\sum_{a=18}^{a=100} P(a,t)}$$

$$\pi_{C_n}(a,t) = \frac{C_n(a,t)}{P(a,t)}$$

$$\pi'_{C_n}(t) = \frac{\sum_{a=18}^{a=100} C_n(a,t)}{\sum_{a=18}^{a=100} P(a,t)}$$

$$D(t) = \sum_{a=0}^{a=100} N(a,t) \times \mu_N(a) + \sum_{a=0}^{a=100} \sum_{q=1}^{q=30+} F(a,t,q) \times \mu_F(a,q) + \sum_{a=0}^{a=100} C_m(a,t) \times \mu_{C_m}(a) + \sum_{a=0}^{a=100} C_n(a,t) \times \mu_{C_n}$$

**Non-dynamic relationships:**

- Expressions related to mortality risks and derivation of death rates for current-, former- and never-smokers given overall death rates $\mu(a)$ in 2010.

$$K_1 = \frac{\mu_{C_m}(a)}{\mu_{C_n}(a)}$$

$$\mu_F(a,q) = \mu_N(a) \times RR(a,q)$$

$$\mu_{C_m}(a) = K_1 \times \mu_N(a) \times RR(a,0)$$

$$\mu_{C_n}(a) = \mu_N(a) \times RR(a,0)$$

$$\mu(a) = \mu_N(a) \times \pi_N(a,2010) + \left( \sum_{q=1}^{q=30+} \mu_N(a) \times RR(a,q) \times \pi_F(a,2010,q) \right) + K_1 \times \mu_N(a) \times RR(a,0) \times \pi_{C_m}(a, 201$$

$$\mu_N(a) = \frac{\mu(a)}{\pi_N(a,2010) + \sum_{q=1}^{q=30+} \left( RR(a,q) \times \pi_F(a,2010,q) \right) + K_1 \times RR(a,0) \times \pi_{C_m}(a,2010) + RR(a,0) \times \pi_{C_n}(a,2010)}$$

Expressions related to quit rates and derivation of quit rates for menthol and non-menthol smokers given overall quit rates $\rho(a)$ in 2010.

$$K_2 = \frac{\rho_{C_m}(a)}{\rho_{C_n}(a)}$$

$$\rho_{C_m}(a) = K_2 \times \rho_{C_n}(a)$$

$$\rho(a) = K_2 \times \rho_{C_n}(a) \times \pi_{C_m}(a, 2010) + \rho_{C_n}(a) \times \pi_{C_n}(a, 2010) \rightarrow$$

$$\rho_{C_n} = \frac{\rho(a)}{K_2 \times \pi_{C_m}(a, 2010) + \pi_{C_n}(a, 2010)}$$

- Expressions related to the initiation rate and derivation of initiation rate under the counterfactual scenario (in which menthol cigarettes do not exist) given overall smoking initiation rate $\gamma$ in 2010.

$$\gamma = \gamma_{C_m} + \gamma_{C_n}$$

$$\gamma_{C_m} = K_3 \times \gamma$$

$$\gamma_{C_n} = (1 - K_3 \times \gamma)$$

*Let $W$ be the size of a cohort of potential experimenters, $E$ the proportion of experimenters in that cohort, $Y_m$ the proportion of menthol experimenters that become established smokers, and $Y_n$ the proportion of non – menthol experimenters that become established smokers; then, $W \times E \times K_4$ is the number of menthol experimenters and $W \times E \times (1 - K_4)$ is the number of non – menthol experimenters.*

*It follows that:*

$$W \times E \times K_4 \times Y_m + W \times E \times (1 - K_4) \times Y_n = W \times \gamma$$

*Given that* $\frac{Y_m}{Y_n} = K_5$, *then*

$$W \times E \times K_4 \times K_5 \times Y_n + W \times E \times (1 - K_4) \times Y_n = W \times \gamma \quad or$$

$$Y_n = \frac{\gamma}{E \times (K_A \times K_B + (1 - K_A))}$$

*Let $\gamma'$ be the initiation rate under the counterfactual, then, assuming the same proportion of experimenters as in the status – quo scenario:*

$$W \times E \times Y_n = W \times \gamma' \quad or$$

$$\gamma' = E \times Y_n = \frac{E \times \gamma}{E \times (K_A \times K_B + (1 - K_A))} = \frac{\gamma}{K_A \times K_B + (1 - K_A)}$$

## Description of the Model

The model projects the US population, distinguished by age (0 to 100) and smoking status, over the period 2010-2050. Smoking status is categorized by current smokers of menthol cigarettes, current smokers of non-menthol cigarettes, never smokers and former smokers. The latter group is further divided by years quit. The model tracks former smokers from 1 to 30 years quit.

Each year, for the next 40 years (2010 to 2050) and for every year of age (from 0 to 100), the model follows the number of individuals in each category. Each simulated year the model introduces a birth cohort obtained from the U.S. Census Bureau projections for the period 2010-2050 and ages the population using age- and smoking status- specific death rates. Individuals younger than 18 are consider non-smokers. At age 18 (age 20 for African Americans) a proportion of individuals become menthol smokers, another fraction become non-menthol smokers and the rest remain non-smokers for their remaining life span. After age 18 smokers are given the chance to quit smoking or switch between menthol and non-menthol cigarettes. Those who quit become former smokers and are tracked not just by age but also by years since quit.

The age-specific background cessation rates used in the simulations are the ones estimated by Mendez and Warner (1998)[1]. Those quit rates have been validated since.[5] The quit rates were adjusted to reflect differences between menthol and non-menthol smoking according to the expressions derived on page 6. Age-specific death rates were computed for current (menthol and non-menthol), never, and former smokers by years quit employing smoking relative risks derived from the Cancer Prevention Study II (CPS II) data[8] and the procedure described on pages 5 and 6. Relative risks for current and former smokers specific to the US African American population were derived from CPS II data and supplied by the American Cancer Society (Michael Thun, American Cancer Society, personal communication, March 2011). Background death rates for the general population were obtained from the US Census Bureau. Initial (2010) estimates for overall smoking prevalence for the general and African American populations were obtained from the National Health Interview Survey (NHIS) and the Behavioral Risk Factor Surveillance System (BRFSS) respectively. The initiation rate for the general population was taken to be 21.8%, the smoking prevalence among 18 year-olds reported by the NHIS in 2009. For African Americans, the initiation rate was taken to be 19.8%, consistent with the smoking prevalence at age 20 reported by the BRFSS 2005 for African Americans. Initial (2010) estimates of menthol prevalence were obtained from the National Survey on Drug Use and Health (NSDUH). All data used to produce this report are publicly available.

**Simulation Experiments Settings and Results**

The model was used to evaluate the impact of menthol cigarettes on the entire US population and the US African American population. To do this, a simulation covering the period from 2010 to 2050 was performed assuming that current (2010) initiation and cessation rates will remain constant through that period (status-quo scenario). Then the simulation was repeated, now assuming as the counterfactual that menthol cigarettes have never existed in the U.S. The actual 2010 US smoking prevalence was assumed as the 2010 smoking prevalence under the counterfactual, now produced only by non-menthol smoking. For quit rates under the counterfactual, the same non-menthol age-specific quit rates employed in the comparing status-quo scenario were used; the initiation rate on the counterfactual $(\gamma^{*})$ was computed according to the expression derived on page 6 and 7. The difference in cumulative deaths and cumulative initiation between the status-quo and counterfactual scenarios is reported.

Status quo parameters related to menthol were provided by TPSAC based on literature review findings. An extensive sensitivity analysis of those parameters on the results for the general population was conducted employing parameter ranges also supplied by TPSAC. The results of the analysis for the general population are shown on Tables 1 - 3.

A sensitivity analysis on the African American model was not conducted because of lack of specific data on some parameters and because the rest of the parameters did not show to be sensitive in the general population model. Instead, the results of the African American model were compared to those of a hypothetical population identical to the US African American population in all aspects except menthol prevalence. This hypothetical population was given the same menthol prevalence as the general US population. This comparison highlights the extra burden that menthol imposes on the African American population. The results of the analysis for the African American population are shown on Tables 4 – 6.

**Table 1. Input Parameters – General Population:**

| Parameter | Min | TPSAC Estimate | Max |
|---|---|---|---|
| Proportion of Menthol among Initiators[2] ($K_3$) | 0.35 | 0.40 | 0.45 |
| Proportion of Menthol among Experimenters[2] ($K_14$) | 0.38 | 0.45 | 0.60 |
| Ratio of "Proportion of Menthol Experimenters that become Established Smokers" / "….Non-menthol….."[2] ($K_15$) | 1.00 | 1.68 | 1.85 |
| Cessation Rates Ratio (Menthol/Non-menthol)[2] ($K_12$) | 0.92 | 0.95 | 1.10 |
| Mortality Risk Ratio (Menthol/Non-menthol)[2] ($K_1$) | 0.80 | 1.00 | 1.20 |
| Switching Rate from Menthol to Non-menthol (among Menthol smokers)[3] ($S_1m2n$) | 0.9% | 1.8% | 2.7% |
| Switching Rate from Non-menthol to Menthol (among Non-menthol smokers)[3] ($S_1n2m$) | 0.4% | 0.8% | 1.2% |

[2] Provided by TPSAC
[3] From the switching book adjusted for proper denominator – Range +/- 50%

## Table 2. Scenario Analysis – General Population

| Scenario | Description | Prop of Menthol Initiation | Proportion of Menthol Experimentation | Experimentation to Initiation Yield Ratio Menthol/Non-Menthol | Initiation Rate under Counterfactual | Cessation Ratio Menthol/Non-Menthol | Mortality Ratio Menthol/Non-Menthol | Switching Rate Menthol to Non-Menthol | Switching Rate Non-Menthol to Menthol |
|---|---|---|---|---|---|---|---|---|---|
| 1 | TPSAC Estimates | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 1.8% | 0.8% |
| 2 | Low Menthol Initiation | 0.35 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 1.8% | 0.8% |
| 3 | High Menthol Initiation | 0.45 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 1.8% | 0.8% |
| 4 | Low Menthol Experimentation | 0.40 | 0.38 | 1.68 | 17.3% | 0.95 | 1.00 | 1.8% | 0.8% |
| 5 | High Menthol Experimentation | 0.40 | 0.60 | 1.68 | 15.5% | 0.95 | 1.00 | 1.8% | 0.8% |
| 6 | Low Yield from Experimenter to Smoker | 0.40 | 0.45 | 1.00 | 21.8% | 0.95 | 1.00 | 1.8% | 0.8% |
| 7 | High Yield from Experimenter to Smoker | 0.40 | 0.45 | 1.85 | 15.8% | 0.95 | 1.00 | 1.8% | 0.8% |
| 8 | Low Menthol Cessation | 0.40 | 0.45 | 1.68 | 16.7% | 0.92 | 1.00 | 1.8% | 0.8% |
| 9 | High Menthol Cessation | 0.40 | 0.45 | 1.68 | 16.7% | 1.10 | 1.00 | 1.8% | 0.8% |
| 10 | Low Menthol Mortality Risk | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 0.80 | 1.8% | 0.8% |
| 11 | High Menthol Mortality Risk | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.20 | 1.8% | 0.8% |
| 12 | Low Switch Rate Menthol to Non-menthol | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 0.9% | 0.8% |
| 13 | High Switch Rate Menthol to Non-Menthol | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 2.7% | 0.8% |
| 14 | Low Switch Rate Non-menthol to Menthol | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 1.8% | 0.4% |
| 15 | High Switch Rate Non-menthol to Menthol | 0.40 | 0.45 | 1.68 | 16.7% | 0.95 | 1.00 | 1.8% | 1.2% |

| Scenario | Description | Cumulative Excess Deaths | Cumulative Excess Smoking Initiation |
|---|---|---|---|

**Table 3. Results – General Population**

| | | 2020 | 2030 | 2040 | 2050 | 2020 | 2030 | 2040 | 2050 |
|---|---|---|---|---|---|---|---|---|---|
| **1** | TPSAC Estimates | **17,182** | **67,817** | **164,590** | **327,565** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **2** | **Low Menthol Initiation** | **17,181** | **67,812** | **164,555** | **327,396** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **3** | **High Menthol Initiation** | **17,182** | **67,822** | **164,625** | **327,733** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **4** | **Low Menthol Experimentation** | **15,411** | **61,041** | **147,794** | **292,601** | **2,019,295** | **3,908,229** | **5,920,677** | **8,051,353** |
| **5** | **High Menthol Experimentation** | **20,723** | **81,367** | **198,181** | **397,489** | **2,827,013** | **5,471,520** | **8,288,948** | **11,271,894** |
| **6** | **Low Yield from Experimenter to Smoker** | **2,127** | **10,220** | **21,810** | **30,346** | **0** | **0** | **0** | **0** |
| **7** | **High Yield from Experimenter to Smoker** | **19,838** | **77,980** | **189,784** | **380,008** | **2,692,393** | **5,210,972** | **7,894,236** | **10,735,137** |
| **8** | **Low Menthol Cessation** | **18,495** | **74,138** | **178,061** | **346,122** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **9** | **High Menthol Cessation** | **11,023** | **38,336** | **101,964** | **241,409** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **10** | **Low Menthol Mortality Risk** | **-239,508** | **-293,535** | **-220,657** | **-41,279** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **11** | **High Menthol Mortality Risk** | **238,551** | **378,451** | **494,892** | **644,022** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **12** | **Low Switch Rate Menthol to Non-menthol** | **17,227** | **68,265** | **166,070** | **330,538** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **13** | **High Switch Rate Menthol to Non-Menthol** | **17,138** | **67,397** | **163,252** | **324,972** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **14** | **Low Switch Rate Non-menthol to Menthol** | **17,139** | **67,399** | **163,249** | **324,993** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |
| **15** | **High Switch Rate Non-menthol to Menthol** | **17,224** | **68,223** | **165,874** | **329,989** | **2,288,534** | **4,429,326** | **6,710,101** | **9,124,867** |

**Table 4. Input Parameters – African American Population:**

| Parameter | TPSAC Estimate |
|---|---|
| Proportion of Menthol among Initiators ($K_3$)[4] | .80 |
| Proportion of Menthol among Experimenters[5] ($K_1 1$) | .80 |
| Ratio of "Proportion of Menthol Experimenters that become Established Smokers" / "….Non-menthol….."[6] ($K_1 5$) | 1.68 |
| Cessation Rates Ratio (Menthol/Non-menthol)[6] ($K_1 2$) | 0.95 |
| Mortality Risk Ratio (Menthol/Non-menthol)[5] ($K_1$) | 1 |
| Switching Rate from Menthol to Non-menthol (among Menthol smokers)[7] ($S_1 m2n$) | 0.9% |
| Switching Rate from Non-menthol to Menthol (among Non-menthol smokers)[7] ($S_1 n2m$) | 4% |
| Initiation Rate under Counterfactual[8] ($\gamma'$) | 12.7% |

[4] Same values as experimenters
[5] Provided by TPSAC
[6] Same values as those of the general population
[7] From the switching book adjusted for proper denominator
[8] Computed according to expression on page 7

**Table 5. Input Parameters – Hypothetical Low Menthol African American Population:**

| Parameter | Estimate |
|---|---|
| Proportion of Menthol among Initiators ($K_3$)[9] | .40 |
| Proportion of Menthol among Experimenters[9] ($K_14$) | .45 |
| Ratio of "Proportion of Menthol Experimenters that become Established Smokers" / "….Non-menthol….."[10] ($K_15$) | 1.68 |
| Cessation Rates Ratio (Menthol/Non-menthol)[10] ($K_12$) | 0.95 |
| Mortality Risk Ratio (Menthol/Non-menthol)[10] ($K_1$) | 1 |
| Switching Rate from Menthol to Non-menthol (among Menthol smokers)[10] ($S_1m2n$) | 0.9% |
| Switching Rate from Non-menthol to Menthol (among Non-menthol smokers)[10] ($S_1n2m$) | 4% |
| Initiation Rate under Counterfactual[11] ( $\gamma'$ ) | 15.0% |

[9] Same values as in the general population
[10] Same values as in the African American Population
[11] Computed according to expression on page 7

| Description | Cumulative Excess Deaths | | | | Cumulative Excess Smoking Initiation | | | |
|---|---|---|---|---|---|---|---|---|
| | 2020 | 2030 | 2040 | 2050 | 2020 | 2030 | 2040 | 2050 |
| African American Population – TPSAC Estimates | 4,716 | 16,381 | 35,250 | 66,524 | 461,273 | 859,101 | 1,262,086 | 1,656,005 |
| Low Menthol Prevalence Hypothetical African American Population | 2,691 | 10,244 | 23,218 | 44,771 | 307,515 | 572,734 | 841,391 | 1,104,003 |

**Table 6. Results – African American Population**

**References:**


1. Mendez D, Warner KE and Courant PN. “Has Smoking Cessation Ceased? Expected Trends in the Prevalence of Smoking in the United States.” *American Journal of Epidemiology*, 1998;148(3):249-58.

2. Mendez D and Warner KE. “Smoking Prevalence in the Year 2010: Why the Healthy People Goal is Unattainable.” *American Journal of Public Health*, 2000;90(3):401-403.

3. Mendez D, Warner KE and Courant PN. “Expected Trends in the Prevalence of Cigarette Smoking.” Chapter in Lu R, Mackay J, Niu S and Peto R, eds. *The Growing Epidemic*, Singapore: Springer-Verlag, 2000:49-52.

4. Warner KE, Mendez D and Smith DG. “Cost Effectiveness of Smoking Cessation Programs in Managed Care Organizations.” *Inquiry*, 2004;41(1):57-69.

5. Mendez D and Warner KE. “Smoking Trends in the US: Declining as Expected if not as Desired.” *American Journal of Public Health*, 2004;94:251:252.

6. Mendez D and Warner KE. “Commissioned Simulation Modeling of Smoking Prevalence as an Outcome of Selected Tobacco Control Measures.” Chapter in The Institute of Medicine's Committee on Reducing Tobacco Use, eds. *Ending the Tobacco Problem: A Blueprint for the Nation The Institute of Medicine*, 2007.

7. Mendez D and Warner KE. “Setting a challenging, yet realistic smoking prevalence target for Healthy People 2020: Learning from the California experience.” *American Journal of Public Health*, 2008;98(3):556-9.

8. Mendez D, Warner KE. “The relative risk of death for former smokers: the influence of age and years-quit.” *Unpublished research monograph*, 2001. Available at http://www.umich.edu/~dmendez/tobacco/RRiskmonograph.doc. Accessed March 14, 2011.

**APPENDIX B**

**TPSAC Meeting Dates and Topics**

- March 30-31, 2010 – Summary presentation of published literature on menthol
  - Invited Presenters - Lawrence Deyton, M.S.P.H., M.D., Catherine Lorraine, J.D., Corinne Husten, M.D., M.P.H., Ralph Caraballo, Ph.D., M.P.H., Deirdre Lawrence, Ph.D., M.P.H., Joshua Rising, M.D., M.P.H., Allison C. Hoffman, Ph.D.

- July 15-16, 2010 – Industry presentations on menthol in cigarettes as it relates to characterization of menthol, clinical effects of menthol, biomarkers of disease risk, marketing data, and population effects
  - Invited Presenters - Corinne Husten, M.D., M.P.H., James E. Dillard III, Jane Y. Lewis, Ph.D., Michael W. Ogden, Ph.D., William R. True, Ph.D., Mohamadi A. Sarkar, Ph.D., Pascal A. Fernandez, Monica J. Graves, Leonard H. Jones, Geoffrey M. Curtin, Ph.D., Jennifer L. Hunter, William R. True, Ph.D., David L. Ashley, Ph.D.

- September 27, 2010 – Menthol Report Subcommittee met to discuss timelines and the structure of the Menthol Report.
  - Invited Presenters - Corinne Husten, M.D., M.P.H., Karen Templeton-Somers, Ph.D., Jonathan Samet, M.D.

- October 7, 2010 – Presentations on publicly available industry documents from the Legacy Tobacco Documents Library
  - Invited Presenters - Corinne Husten, M.D., M.P.H., Allison C. Hoffman, Ph.D., Jonathan Samet, M.D., Stacey J. Anderson, Ph.D., Valerie B. Yerger, N.D.

- November 18, 2010 – Updates from the Menthol Report Subcommittee and presentation on secondary analysis of the data requested by the committee at the March 30 and 31, 2010 TPSAC meeting
  - Invited Presenters - Corinne Husten, M.D., M.P.H., Jonathan Samet, M.D., James C. Hersey, Ph.D., Brett R. Loomis

- January 10-11, 2011 – Updates from the Menthol Report Subcommittee , presentation regarding contraband and menthol, presentation on modeling schema, and presentations regarding the data requested by the committee at the March 30 and 31, 2010 TPSAC meeting.
  - Invited Presenters - Jonathan M. Samet, M.D., M.S., Neal L. Benowitz, M.D., Patricia Nez Henderson, M.P.H., M.D.., Dorothy K. Hatsukami, Ph.D., Mark Stuart Clanton, M.D., M.P.H.

- February 10, 2011 – Updates from the Menthol Report Subcommittee, presentation on updated modeling schema, and presentations regarding the data requested by the committee at the March 30 and 31, 2010 TPSAC meeting
  - Invited Speakers - Corinne Husten, M.D., M.P.H., David Mendez, Ph.D., Brian F. Thomas, Ph.D., Hernán Navarro, Ph.D., Kenneth H. Davis, Jr., James Hersey, Ph.D., Jonathan Samet, M.D.

- February 11, 2011– Menthol Report Subcommittee met to discuss timelines and the structure of the Menthol Report.
    - Invited Speakers - Corinne Husten, M.D., M.P.H., Jonathan M. Samet, M.D., M.S., Neal L. Benowitz, M.D., Patricia Nez Henderson, M.P.H., M.D.., Dorothy K. Hatsukami, Ph.D., Mark Stuart Clanton, M.D., M.P.H.

- March 2, 2011 – Updates from the Menthol Report Subcommittee, presentation on updated modeling schema, and presentations regarding the data requested by the committee at the March 30 and 31, 2010 TPSAC meeting
    - Invited Speakers - David L. Ashley, Ph.D., David Mendez, Ph.D., Neal Benowitz, M.D., Jonathan Samet, M.D., M.S., Eric O. Johnson, Ph.D., Daniel J. Heck, Ph.D., DABT

- March 17-18, 2011 – Updates from the Menthol Report Subcommittee (including proposed recommendations) and presentation on updated modeling schema

~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

**Alphabetical list of all invited speakers (consolidated from agendas)**

Stacey J. Anderson, Ph.D.
David L. Ashley, Ph.D.
Neal L. Benowitz, M.D.
Ralph Caraballo, Ph.D., M.P.H.
Mark Stuart Clanton, M.D., M.P.H.
Geoffrey M. Curtin, Ph.D.
Kenneth H. Davis, Jr.
Lawrence Deyton, M.S.P.H., M.D.
James E. Dillard III
Pascal A. Fernandez
Monica J. Graves
Dorothy K. Hatsukami, Ph.D.
Daniel J. Heck, Ph.D., DABT
Patricia Nez Henderson, M.P.H., M.D.
James C. Hersey, Ph.D.
Allison C. Hoffman, Ph.D.
Jennifer L. Hunter
Corinne Husten, M.D., M.P.H.
Eric O. Johnson, Ph.D.
Leonard H. Jones
Deirdre Lawrence, Ph.D., M.P.H.
Jane Y. Lewis, Ph.D.
Brett R. Loomis
Catherine Lorraine, J.D.
David Mendez, Ph.D.
Hernán Navarro, Ph.D.
Michael W. Ogden, Ph.D.
Joshua Rising, M.D., M.P.H.
Jonathan Samet, M.D.
Mohamadi A. Sarkar, Ph.D.
Karen M. Templeton-Somers, Ph.D.
Brian F. Thomas, Ph.D.
William R. True, Ph.D.
Valerie B. Yerger, N.D.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

# Communication from Public

**Name:** Annie Tegen
**Date Submitted:** 07/11/2019 11:04 AM
**Council File No:** 18-1104
**Comments for Public Posting:**

ORIGINAL PAPER

# Racialized Geography, Corporate Activity, and Health Disparities: Tobacco Industry Targeting of Inner Cities

Valerie B. Yerger, ND
Jennifer Przewoznik, MSW
Ruth E. Malone, PhD, RN, FAAN

*Abstract:* Industry has played a complex role in the rise of tobacco-related diseases in the United States. The tobacco industry's activities, including targeted marketing, are arguably among the most powerful corporate influences on health and health policy. We analyzed over 400 internal tobacco industry documents to explore how, during the past several decades, the industry targeted inner cities populated predominantly by low-income African American residents with highly concentrated menthol cigarette marketing. We study how major tobacco companies competed against one another in *menthol wars* fought within these urban cores. Little previous work has analyzed the way in which the inner city's complex geography of race, class, and place shaped the avenues used by tobacco corporations to increase tobacco use in low-income, predominantly African American urban cores in the 1970s–1990s. Our analysis shows how the industry's activities contributed to the racialized geography of today's tobacco-related health disparities.

*Key words:* Smoking, tobacco industry, African Americans, racial disparities, inner city geography.

Despite significant reductions in overall smoking rates in the United States, smoking among poor, less educated, and underserved populations remains higher than among the general population.[1–5] For example, prevalence rates for low-income African Americans have been reported to range from 33% to 59%,[6–11] compared with 21% for the general population.[12] Tobacco company advertising and promotion are associated with increased cigarette consumption; their presence and pervasiveness serve as external cues to smoking.[13] Tobacco companies have strategically targeted marginalized communities,[14–25] who may have limited information about specific and relative health risks of smoking and few social supports and resources such as tailored cessation programs.[26–29] Tobacco-related diseases have hurt lower-income urban communities,

***VALERIE YERGER** and **RUTH MALONE** are affiliated with the Department of Social and Behavioral Sciences, School of Nursing, University of California, San Francisco, California, USA. **JENNIFER PRZEWOZNIK** is affiliated with the Rowan Breast Center at the Abramson Cancer Center of the University of Pennsylvania. Address correspondence to Valerie B. Yerger, ND, Department of Social & Behavioral Sciences, Box 0612, University of California at San Francisco, San Francisco, California, USA 94143-0612; tel: +1(415) 476-2784; fax: +1(415) 476-6552; email: valerie.yerger@ucsf.edu.*

where lack of educational opportunity is compounded by lack of access to health care, few employment opportunities, and environmental injustice.[7,30]

Tobacco use is a major contributor to health disparities in the United States.[5,31] Age-adjusted mortality rates for tobacco-related cancers,[32–37] cardiovascular disease and stroke are higher among African Americans than among White Americans.[38] Tobacco-related health disparities are defined as "differences in the patterns, prevention, and treatment of tobacco use; the risk, incidence, morbidity, mortality, and burden of tobacco-related illness that exist among specific population groups in the United States; and related differences in capacity and infrastructure, access to resources, and environmental tobacco smoke exposure."[30, p. 211] Individual level risk factors account for only part of persistent health disparities. In this paper, we suggest that it is not only tobacco use behavior that shapes disparities, but the disparate distribution of conditions that promote tobacco use. For example, African Americans who report experiencing racial discrimination as subjectively stressful are more likely to smoke.[39] Macro-level factors identified as fundamental causes of disease also influence multiple disease outcomes and affect both individual and social contexts.[40]

The expanding literature on social and environmental injustices recognizes the interplay between individual, social, and geographic factors, including racism and segregation, and their contribution to persistent racial disparities in health.[41–44] This interplay creates what have been called *riskscapes*,[45–46] within which poverty, racial discrimination, segregation, the environment, and other factors work together to shape health disparities. Work from critical geography, public health, and history has drawn attention to localized power relationships, emphasizing that space is neither neutral nor passive.[47–51] Rather, geographic location and social position intertwine and form a loop; places shape one's social station and the social station of a place's residents shapes societal views of that place.[52] *Racialized geography*, as described by Sundstrom, is a complex interplay between race, class, and place, occurring at the nexus of political, economic, and social systems.[52]

One factor shaping the riskscapes of inner cities is corporate activity, which has been identified as a fundamental structural cause of disease through producing and promoting products harmful to health.[53] The tobacco industry's disease-promoting activities[54] are among the most powerful corporate influences on inner city health. Such activities have included targeted marketing, thwarting and undermining tobacco control efforts, deceptive scientific practices, and influencing policymakers and community leadership groups.[55–59]

For this paper, we analyzed previously secret internal documents to explore how, during the past several decades, inner cities populated predominantly by poor African American residents were targeted with highly concentrated menthol cigarette marketing from the entire industry. Today, at least 70% of African American smokers consume menthol cigarettes, compared with 30% of White smokers.[5] Menthol cigarettes, which contain higher amounts of tar and nicotine than non-mentholated brands,[60–64] are associated with nicotine dependence and lower cessation rates,[65–69] and may play a role in increasing systemic exposure to tobacco toxins and carcinogens;[70–76] thus, it is reasonable to consider how activities that promoted tobacco use and mentholated cigarette use specifically have contributed to today's tobacco-related health disparities disfavoring African Americans.

This study shows how the major tobacco companies between the late 1970s–1990s aggressively competed against one another in the *menthol wars* fought within inner city urban cores. The most popular menthol brands were Kool (manufactured by Brown & Williamson, which merged with RJ Reynolds in 2003 to become Reynolds American Tobacco Company), Salem (Reynolds American), Newport (Lorillard), and Philip Morris's Benson & Hedges Menthol. During the time of this marketing blitz, smoking among African Americans increased,[77] the use of menthol cigarettes among African Americans increased,[78] and the overall menthol share of the tobacco market exploded. During the same time period, smoking prevalence among African Americans exceeded that among Whites, and African Americans (especially the poor and less educated) were among those least likely to quit smoking.[79–80] While previous research has described disproportionate levels of menthol cigarette advertising in poor inner city neighborhoods compared with predominantly White neighborhoods,[16,31,81] little work has demonstrated the specific ways in which the inner city's complex geography of race, class, and place shaped the avenues used by tobacco corporations to increase tobacco use in low-income, predominantly African American urban cores during the 1970s–1990s.

## Methods

We used archival approaches[82] to conduct this study, using data from previously undisclosed tobacco industry documents made public under *State of Minnesota versus Philip Morris, Inc.*[83] and electronically available following the 1998 Master Settlement Agreement between 46 state attorneys general and 7 tobacco industry defendants.[84] Between May 2005–August 2006, we collected and analyzed more than 400 documents related to tobacco industry targeting of low-income, inner-city communities. Documents were retrieved in paper form from the Minnesota Depository and electronically from the University of California, San Francisco Legacy Tobacco Documents Library (http://legacy.library.ucsf.edu) and from industry document websites.[85]

We searched using an iterative snowball approach,[86] beginning with combinations of search terms such as *African American*, *Black*, *ethnic*, *ghetto*, *inner city*, *menthol*, *Negro*, and *urban*. Retrieved documents were used to identify additional search terms. We focused primarily on Brown & Williamson, Lorillard, Philip Morris, and RJ Reynolds, as their menthol brands were the most heavily marketed in African American communities.

To begin interpreting the data, the first and second authors reviewed all documents and selected key documents for review by the third author. Drawing on findings from the retrieved tobacco documents and other relevant textual data sources, we developed an account of tobacco industry marketing activities focused on inner cities. Table 1 shows a geographic account, and Figure 1 shows temporal concentration of selected major tobacco marketing initiatives. We organized material by company and by strategy. The results are presented as follows: we first review background information about menthol cigarettes and industry interest in inner city areas, derived predominantly from

**Table 1.**

**TOBACCO ACTIVITIES AND CENSUS DATA, 1980, IN SELECT CITIES**[a]

| City (census year) | Total population | Race | | | | Tobacco company inner city activities | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | White | | Black | | Brown & Williamson | Lorillard | Philip Morris, USA | RJ Reynolds |
| | | Number | Percent | Number | Percent | | | | |
| Atlanta, GA | 425,022 | 137,879 | 32.4 | 282,911 | 66.6 | | X | X | X |
| Baltimore, MD | 786,775 | 345,113 | 43.9 | 431,151 | 54.8 | X | X | X | X |
| Boston, MA | 562,994 | 393,937 | 70.0 | 126,229 | 22.4 | | X | X | |
| Chicago, IL | 3,005,072 | 1,490,216 | 49.6 | 1,197,000 | 39.8 | X | X | X | X |
| Cincinnati, OH | 385,457 | 251,144 | 65.2 | 130,467 | 33.8 | X | X | | |
| Cleveland, OH | 573,822 | 307,264 | 53.5 | 251,347 | 43.8 | | X | X | X |
| Columbus, OH | 564,871 | 430,678 | 76.2 | 124,880 | 22.1 | | X | X | |
| Dallas, TX | 904,078 | 555,270 | 61.4 | 265,594 | 29.4 | | X | X | |
| Detroit, MI | 1,203,339 | 413,730 | 34.4 | 758,939 | 63.1 | X | X | X | X |
| Durham, NC | 100,831 | 52,317 | 51.9 | 47,474 | 47.1 | | | X | |
| Ft. Lauderdale, FL | 153,279 | 118,983 | 77.6 | 32,225 | 21.0 | | X | | |
| Hartford, CT | 136,392 | 68,603 | 50.3 | 46,186 | 33.9 | | X | | |
| Houston, TX | 1,595,138 | 978,353 | 61.3 | 440,346 | 27.6 | X | X | X | |
| Indianapolis, IN | 700,807 | 540,294 | 77.1 | 152,626 | 21.8 | | | X | |
| Jackson, MS | 202,895 | 106,285 | 52.4 | 95,357 | 47.0 | | | X | |
| Jacksonville, FL | 540,920 | 394,756 | 73.0 | 137,324 | 25.4 | | X | X | |
| Los Angeles, CA | 2,966,850 | 1,816,761 | 61.2 | 505,210 | 17.0 | X | X | X | X |
| Louisville, KY | 298,451 | 212,102 | 71.1 | 84,080 | 28.2 | | X | | |
| Memphis, TN | 646,356 | 333,789 | 51.6 | 307,702 | 47.6 | X | X | X | X |

*(Continued on p. 14)*

**Table 1** ***(continued).***

| City (census year) | Total population | Race | | | | Tobacco company inner city activities | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | White | | Black | | | | | |
| | | Number | Percent | Number | Percent | Brown & Williamson | Lorillard | Philip Morris, USA | RJ Reynolds |
| Miami, FL | 346,865 | 231,008 | 66.6 | 87,110 | 25.1 | | X | X | |
| Milwaukee, WI | 636,212 | 466,620 | 73.3 | 146,940 | 23.1 | | X | | |
| New Haven, CT | 126,109 | 78,326 | 62.1 | 40,235 | 31.9 | | X | | |
| New Orleans, LA | 557,515 | 236,987 | 42.5 | 308,149 | 55.3 | X | X | X | |
| New York, NY | 7,071,639 | 4,294,075 | 60.7 | 1,784,337 | 25.2 | X | X | X | X |
| Norfolk, VA | 266,979 | 162,300 | 60.8 | 93,987 | 35.2 | | | | X |
| Oakland, CA | 339,337 | 129,692 | 38.2 | 159,281 | 46.9 | | X | | |
| Paterson, NJ | 137,970 | 70,203 | 50.9 | 47,091 | 34.1 | | X | | |
| Philadelphia, PA | 1,688,210 | 983,084 | 58.2 | 638,878 | 37.8 | | X | X | |
| Pittsburgh, PA | 423,938 | 316,694 | 74.7 | 101,813 | 24.0 | | X | | X |
| Richmond, VA | 219,214 | 104,743 | 47.8 | 112,357 | 51.3 | | X | X | |
| St. Louis, MO | 453,085 | 242,576 | 53.5 | 206,386 | 45.6 | | X | X | |
| San Francisco, CA | 678,974 | 395,081 | 58.2 | 86,414 | 12.7 | | X | X | |
| Washington, D.C. | 638,333 | 171,768 | 26.9 | 448,906 | 70.3 | X | X | X | X |

[a]U.S. Census Bureau selected historical census data, 1980.

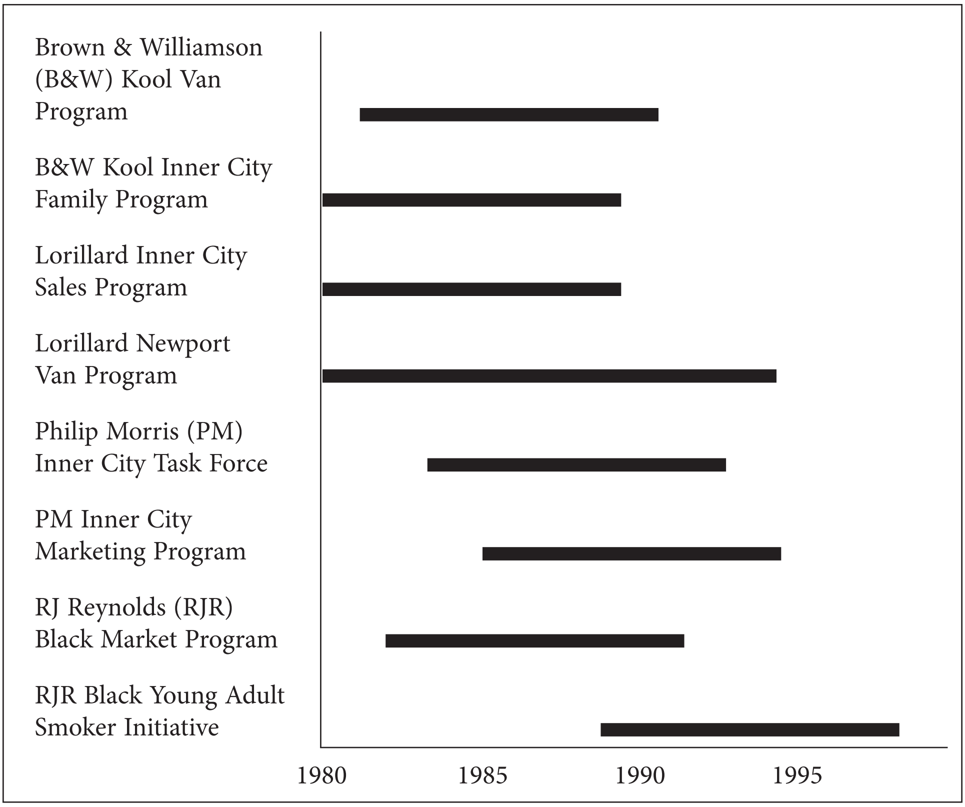



Figure 1. Temporal concentration of selected major tobacco marketing initiatives in U.S. inner cities.

industry documents and secondary sources. We then discuss specific tobacco industry strategies, including studying African American consumers using psychographic and other data; giving out free samples of cigarettes and the use of mobile vans to drive into neighborhoods; specialized inner city retailer programs; and community engagement. We conclude by discussing how today's tobacco-related health disparities were shaped by geographically-specific, intentional and aggressive corporate activity.

## Results

**Background: The tobacco industry and the African American inner city consumer**. Menthol cigarettes have been marketed since the 1920s.[87] Between 1957 and 1963, the menthol share of the total cigarette market grew from 5% to 16%.[88–89] (See Table 2.) By 1964, there were 9 menthol brands, and 23 by 1971.[90] During the 15-year period 1956–1971, the menthol market grew by 48%.[90] By 1982, menthol sales had grown 6 times as fast as sales in the general cigarette market.[91] Salem had dominated the menthol market from its inception in 1956 to 1972, but Kool now led menthol sales. Kool's rise was due in part to its embrace by the African American community.[92]

## Table 2.

### MENTHOL U.S. MARKET SHARE, 1920–2001

| Year | Market share (%) |
|---|---|
| 1920–1955 | 2 |
| 1955–1957 | 5 |
| 1963 | 16 |
| 1978 | 28 |
| 1990–2001 | 27–29 |

Source: Gardiner PS. The African Americanization of menthol cigarette use in the United States. *Nicotine Tob Res* 2004;6 Suppl 1:S55–65. (Used with written permission from Nicotine and Tobacco Research.)

As competitive tobacco companies began noticing Kool's increased popularity, especially among African Americans, they began aggressively marketing their menthol products in inner city African American communities.[78,93–97] (Tobacco companies used the term *inner city* to refer to "the usually older and more densely populated central section of a city with large ethnic populations."[98, p. 5851]) Data collected by or on behalf of tobacco companies revealed that "smoking characteristics of blacks differ significantly from those of whites," requiring "a different marketing strategy . . . for black consumers."[99, p. 9184] For decades, tobacco industry research suggested that African Americans were heavy menthol smokers who presented an opportunity for tobacco companies to increase their menthol market share.[100–101] The tobacco companies used multiple avenues designed specifically for the "difficult to reach"[102, p. 5434] group of inner city Black smokers, including analysis of residents' psychographic profiles, mobile van programs through which free cigarettes were distributed, specialized marketing programs, and tailored retail programs. (See Table 3.) According to a 1982 Philip Morris marketing plan, two segments in the African American market were "becoming increasing polarized—half more affluent than ever, and the other significantly lagging the general market in Education and Income."[103, p. 5627] Tobacco companies were interested in the latter African American consumers, the "younger, less educated, lower in income, urban, [and smoking full-flavor and menthol cigarettes]."[103, p. 5628] Tobacco companies often relied on ethnic marketing firms to provide them with psychographic profiles of African American consumers.[104–110] At least one ethnic marketing firm had multiple tobacco companies as clients.[111–115]

Ethnic marketing firms did more than provide insights into the personalities, behaviors, attitudes, and lifestyles of urban African American consumers. For example, in 1982, SMSi (Special Market Services, Inc.), a Chicago firm that specialized in sampling (giving out for free) cigarettes in minority communities, produced for Philip Morris a report focused on strategies for promoting Benson & Hedges among African American and Hispanic consumers, suggesting specific cities where cigarettes could be sampled.[108] The firm recommended that Philip Morris maintain a "first-class approach" to target

**Table 3.**

**SAMPLING OF TOBACCO INDUSTRY ACTIVITIES IN U.S. INNER CITY NEIGHBORHOODS DURING THE 1970s TO 1990s**

| Marketing activity | Dates | Locations |
|---|---|---|
| ***Brown & Williamson*** | | |
| Marketing Plans Sales Force | 01/73–12/73 | |
| Kool Inner City Music Program | 1982 | Baltimore, MD; Chicago, IL; Cincinnati, OH; Detroit, MI; Houston, TX; Los Angeles, CA; Memphis, TN; New Orleans, LA; New York City, NY; Washington, DC |
| Kool Music on Tour Program | 03/83 | |
| Kool Van Sampling Program | 01/84–12/91 | All regions across the U.S. |
| ***Lorillard*** | | |
| Media Mix | 09/71–12/71 | |
| Criterion (3 Sheet) Program | 08/74–07/75 | Chicago; New York City |
| Newport's 3 and 8 Sheet Showings | 09/74–06/75 | New Jersey; New York City |
| Lorillard Marketing Research Study | | |
| Pre-test | 09/13/78–09/14/78 | Chicago; Detroit |
| Pilot Study | 09/28/78–09/29/78 | Atlanta, GA; Boston, MA; Chicago; Detroit |
| Main Study | 01/02/79–01/06/79 | Atlanta; Boston; Chicago; Detroit; Jacksonville, FL; Los Angeles; Memphis; New York City |
| Vantastic Newport Sampler Van | 09/01/83–09/30/83 | Bronx and Queens, New York City; Dallas, Houston, and San Antonio, TX; Hartford, CT; Los Angeles, Oakland, Sacramento, and San Francisco, CA; Paterson, NJ; Philadelphia, PA; Providence, RI |
| Play Ball with Newport | 01/85–12/85 | New York |
| Krush Groove Concert Van Sampling | 12/27/85 | Madison Square Garden, New York |

*(Continued on p. 18)*

**Table 3 *(continued)*.**

| Marketing activity | Dates | Locations |
|---|---|---|
| Newport Van Program (10 Vans) | 1988–1991 | All regions across the U.S. (including Alabama; Baltimore/Washington, DC; Cincinnati, Cleveland and Columbus, OH; Chicago; Connecticut; Detroit and Flint, MI; Florida; Knoxville and Louisville, KY; Massachusetts; Memphis; Milwaukee, WI; Mississippi; New Orleans; Philadelphia and Pittsburgh, PA; Rhode Island; St. Louis, MO; Texas) |
| Newport Inner City Lighter Promotion | 01/89–03/89 | Baltimore; Boston; Chicago; Detroit; Milwaukee; New York City; Providence; Richmond, VA; Springfield, MA |
| Pleasure on Wheels (P.O.W.) | 11/93–3/31/94 | Detroit; Ft. Lauderdale and Miami, FL; Philadelphia |
| Newport Promotion Plan | 01/94–12/94 | Baltimore/Washington, DC; Albany, Bronx, Brooklyn, Buffalo, Rochester and Syracuse New York; Bridgeport, Hartford, New Haven and Stamford, CT; Chicago; Cleveland; Detroit; Ft. Lauderdale; Philadelphia; Pittsburgh; Miami; New Jersey |
| Newport Special Events Program | 01/94–12/94 | Daytona Beach and Panama City, FL; Jersey Shore, NJ; Virginia Beach, VA |
| ***Philip Morris, USA*** | | |
| Benson & Hedges (B&H) Inner City Sampling Program | 06/03/85–08/23/85 | |
| B & H Inner City Program | 06/87–08/87 | Baltimore; Cleveland/Akron and Columbus/Augusta; Chicago; Dallas/Ft. Worth; Houston; Jackson, MS; Jacksonville; Los Angeles; Memphis; Miami; New Orleans and Shreveport, LA; Philadelphia; Raleigh/Durham, NC; Richmond, VA; St. Louis; San Francisco |
| Marlboro Inner City Bar Nights | 07/88 | |
| Soul Food Picnic | 06/18/88–06/19/88 | Indianapolis, IN |
| Indiana Black Expo Celebration | 07/07/88–07/10/88 | Indianapolis |

*(Continued on p. 19)*

**Table 3 *(continued)*.**

| Marketing activity | Dates | Locations |
|---|---|---|
| Jazz under the Stars | 07/10/88 | Indiana |
| Golden Memories under the Stars | 07/88–12/88 | |
| Region 4 Urban Task Force Cleveland, Chicago, Detroit | 06/94–07/94 | Chicago; Cleveland; Detroit |
| Menthol Urban Program | 06/95–08/95 | Atlanta; Baltimore/Washington, DC; Chicago; Detroit; Houston; Los Angeles; Miami; New York City; Philadelphia |
| Marlboro/B & H Urban Visibility Program | 12/96–01/97 | |
| Wave 1 | | Baltimore/Washington, DC; Boston; Chicago; Detroit; Miami; New York City; Philadelphia |
| Wave 2 | | Atlanta; Houston; Los Angeles; New Orleans |
| Club B & H Club/Bar Program | 07/96–11/96 | Atlanta; Chicago; Dallas/Fort Worth; Houston; Los Angeles; New Orleans |
| ***RJ Reynolds*** | | |
| Bright/Salem Free Pack Coupon In Ebony/Essence Magazines | 04/81–08/82 | |
| Bright Black Smoker Trail Sampling | 03/83–07/83 | |
| Sterling Sampling Plan | 12/83 | Chicago |
| Salem Black Market Promotion Plan | 01/84–11/84 | Atlanta; Baltimore/Washington, DC; Chicago; Detroit; Harlem, New York City; Los Angeles; Memphis; Norfolk, VA; Pittsburgh; Other regions in the North and South Atlantic, North and Mid-Central |
| Black Initiative Program | 04/89–12/89 | Chicago; Cleveland; Memphis |
| Innovative Sales/Marketing Program | 04/89–06/89 | |
| Black YAS Initiative Van Program | 04/89–04/90 | Chicago; Cleveland; Memphis |
| Black Initiative Program Expansion | 07/90 | |

upscale women in beauty salons and boutiques, suggesting that the company present customers in these establishments with the product sample and a single live long stem flower.[108] Philip Morris chose not to implement SMSi's recommendation, perhaps because it had begun to recognize that Benson & Hedges was gaining "acceptance among the important younger Black smoker group,"[91, p. 8889] ages 18–24, a segment of the population that positioned "the brand very well for the future."[91, p. 8889]

**Sampling and mobile vans**. However it could be accomplished, tobacco companies sought to distribute cigarettes for free. They engaged in street sampling, where sales staff on foot handed out free cigarettes. Sampling included both street corner distribution and *quality sampling*.[116] (Quality sampling indicated an interaction wherein the sampler would spend more time with an individual consumer, as opposed to passing out mass quantities within a small window of time.) At times, samplers were expected to pass out as many as 90 packs per hour, approximately 1.5 packs every minute.[116]

A 1985 sampling manual emphasized, "It is important that sampling be confined to the inner city area to maximize the benefits of Benson & Hedges sampling on the target market,"[116, p. 8013] suggesting that the National Urban League would be a "good recruiting source." Sampling programs sometimes lasted only a few weeks, as tobacco companies implemented intensified, short term targeted menthol marketing programs confined to inner cities to generate interest, trial, and brand-switching among residents.[116] For example, during an 8-week promotional period in 1986, Philip Morris carried out sampling in the top 20 African American markets, passing out free 6-cigarette packs and an attached "Buy 1 Get 1 Free" (B1G1F) coupon.[117] The African American population in each of the markets was used to determine the number of samplers allocated to the market. During a 2-month period in 1991, Philip Morris launched a nationwide Benson & Hedges Menthol B1G1F offer in urban markets that hit some 17,000 outlets, expecting to reach almost 350,000 smokers.[118]

However, street sampling in inner city communities presented challenges. Lorillard, for example, was not only concerned about the lack of high traffic locations in these neighborhoods, but also considered these "minority areas" as "high risk" with the threat of product theft and equipment loss or damage.[102] Therefore, after a dalliance with street sampling, Lorillard introduced an innovation, the Newport Pleasure Van, in 1979.[102] Lorillard's van program started with a single van in the New York metropolitan area and then expanded to 10 vans circulating across the U.S.[119–125]

Vans allowed sample distributors to be protected from "unruly crowds"[122,126] while handing out free cigarettes. Vans not only offered a sense of safety to tobacco company workers as they penetrated what they perceived to be dangerous territory, but provided a way to distribute cigarettes "with a unique attention getting sampling device specifically targeted to difficult to reach minority groups."[102, p. 5434] Vans were reported to have stopped at street corners, perhaps for only 10 minutes, while playing loud music and distributing free cigarettes.[127–128]

Newport van drivers were provided with a daily schedule, detailing a list of cross-street starting points and street corners of interest in the neighborhoods, where free packs of 10 cigarettes were distributed. Vans were parked near selected stores based on their geographic locations and "to reinforce Newport's image as the 'peer brand' among young adult smokers."[129, p. 2731] In a 1981 memo to all division managers in the

Cincinnati, Dayton, and Columbus, Ohio regions, an assistant Newport brand manager wrote that "The Newport Van is proving to be a uniquely effective vehicle for reaching this target market in their own enviroment [*sic*]," as "Newport's target group of young adults/blacks is difficult to reach via coupons and standard street corner crew sampling."[120, p. 6117] The van program catch phrase, shown as a signature on Lorillard van-related documents, was: "When your target group is hard to reach / With a standard marketing plan, / Get out and sample them on their streets / With the 'Vantastic' Newport Sampler Van."[120, p. 6117]

In March 1983, Brown & Williamson instituted its Kool van program for inner cities, determining that vans had "proven to be an intrusive non-traditional media venue as well as an effective, cost-efficient sampling device."[130, p. 0535] The Kool van program, also known as Kool Music on Tour,[131] was created to access "Kool's hard-to-reach, low readership starter market and target audience,"[130,132] specifically targeting "inner city, young adult competitive smokers."[133, p. 1291] (The phrase *starter market* is usually interpreted as referring to youth, since the great majority of smokers take up tobacco before the age of 18.[134]) Kool vans were staffed with a professional DJ and a tobacco company employee who handed out free cigarettes.

By 1985, vans were the primary sampling medium for distributing Kool cigarettes, entering neighborhoods in more than 50 cities where Newport, Salem, and Benson & Hedges Menthol sales were strong.[133] Brown & Williamson evaluated demographic information from the Chambers of Commerce, regional festival directors and groups, state fairs, trade shows and exhibitions to identify sampling opportunities.[130] The Kool Music on Tour program continued until at least 1991 with 3 vans, concentrated in the Northeast and Midwest.[135]

RJ Reynolds had determined that Lorillard's van program was instrumental to Newport's growth among African American young adult smokers.[127] Inspired by Lorillard, Reynolds also established a van sampling program, aimed to increase Salem's visibility in Chicago. Brightly-painted video vans were fitted with state-of-the-art electronic equipment and displayed music videos.[136] Sent to Chicago nightclubs, the vans caught potential Salem customers entering and leaving the clubs. The vans also displayed live video coverage of the inside club action, thereby entertaining the younger crowd hanging around outside the club.[136]

During the day, the three video vans called on retailers and Salem sales teams in the Chicago area.[136] The vans also traveled to parks, construction sites, bingo halls, street corners, parking lots, and local sports events.[128,137] They made appearances at urban street malls, public aid offices, currency exchanges, housing projects, public transit stops, and other venues.[138] Vans were also used to increase Salem's visibility at street festivals and other neighborhood events. A Reynolds marketing representative proposed that the video vans display community service messages focusing on drug awareness, staying in school, and African American History.[139] Each van took part in as many as 60 events per week. A field marketing manager reported that the vans "work the streets and stores all day and the clubs at night. It can be 20 hours a day, seven days a week."[136, p. 8941]

Although other companies used vans to distribute cigarettes in inner cities, Lorillard's van program was the most far-reaching. In 1993, Lorillard decided to change "the strategic thrust of the Newport Van Program from a sampling vehicle to a more aggressive approach,"[140, p. 4259] whereby retail store sales were tracked and smokers were offered inducements to generate impulsive purchases of Newports.[140–141] Participant "name capture" cards were used to collect contact information from Newport and competitive brand smokers in exchange for a promotional item.[142–143] Lorillard ran this POW (Pleasure On Wheels) van program from February through November 1994. The program drew business away from competitors (especially Kool)[144] in the inner city neighborhoods of New York, Miami/Fort Lauderdale, Philadelphia, St. Louis, and Detroit.[145–147] After Newport came to dominate the urban menthol market, Lorillard reduced the number of vans it operated and then shifted its van program to the general market, though the company continued to focus on lower socioeconomic groups.[148] According to a March 1992 memo to regional sales managers, Lorillard's plan was to "move out of the inner City Core to the general market . . . van sampling will be targeted to blue collar smokers."[149, p. 7856]

In some cities, such as Atlanta, public restrictions prevented van sampling. There, sampling specialists were used to gain access to privately owned areas including bars, small events, and other allowable venues.[125] Philip Morris relied on local samplers to use their area-specific knowledge to identify the best locations. Samplers were to work at inner city high traffic locations or events, such as sporting events, concerts, factory shift changes, bowling alleys, and outside movie theaters, and "where a relaxed, personalized message can be delivered."[116, p. 8014] Other locations included nightclubs, beauty salons, barbershops, fashion boutiques, and restaurants. Samplers were instructed not to get involved in conversations about smoking and health. Rather, they were urged to respond to such inquiries with, "I respect your opinion, and I'm sorry that you feel that way. Thank you" or "I'm afraid I am not sufficiently qualified to comment on that question. Thank you."[116, p. 8025]

**Specialized marketing programs**. All the companies developed special inner city sales programs for menthol brands. For example, during the early to mid-1970s, Kool did well in the inner city market; in 1976, 38% of African American smokers used Kools,[92] a jump of 24 percentage points in 8 years. Among African American male smokers under age 35, nearly 60% smoked Kool. Increased competition for these African American menthol smokers led to a marketing blitz.[150] A summary provided by Brown & Williamson's advertising and brand management team noted, "Competitors have been increasing their efforts to counter Kool's success, and means to combat this activity will be a continuing effort."[151, p. 9109] For the next 10 years, Brown & Williamson focused on maintaining Kool's visibility in inner cities.

To compete with Kool, Lorillard increased Newport's marketing efforts in geographical areas with large concentrations of African Americans.[96] Lorillard aggressively targeted Kool smokers, developing inner city sales programs to support markets where Newport sales were already strong and seeking to narrow the sales ratio in those markets where Newport was trailing Kool.[152] Lorillard initially decided to target both African American and Hispanic young adults with a high school education or less who resided "in tough inner city neighborhoods;"[153–154] however, the company soon found that "Newport, along with other menthol brands, have [sic] been unable to crack this [Hispanic] market."[96, p. 7635] Field sales reps reported that Newport was succeeding "predominantly among males, in the Black inner city."[155, p. 4936] Therefore, the company reallocated funds to the African American inner city market's "more promising opportunities."[96] By 1988, Lorillard had implemented inner city sales programs in the urban markets of Detroit and Flint, Michigan.[152] Within 2 years, these efforts reached over 30 "ethnic niches" in the Northeast and Midwest, including Chicago, Baltimore, Detroit, Boston, and Cleveland; and nightclubs in New Orleans, Atlanta, St. Louis, Los Angeles, San Francisco, and Indianapolis.[156–157]

Lorillard's strategies included maintaining a highly visible Newport brand presence, focusing on trial and conversion from smokers of competitive brands, distribution drives, increased numbers of point-of-sales materials, sampling, special event coverage, increased levels of advertising support, and rewarding retailers for promoting Newport.[158] Promotional items such as key chains, sports bags, sunglasses, lighters, and B1G1F offers were used as tools to encourage smokers of other menthol brands, but particularly Kool smokers, to switch to Newport.[96,153,159]

Recognizing minority markets as "virgin territories,"[103] Philip Morris implemented African American ethnic and urban programs beginning in 1982 and continuing through the early 1990s. In its 1982 minority marketing plan, Philip Morris proposed to improve the performance of Benson & Hedges among African American smokers.[103] The plan contains pages of demographic profiling of African Americans and Hispanics and charts showing advertising expenditures of competitive brands in African American print media. Philip Morris's action plan recommended company sponsorship of community and national events and included a list of African American organizations.

In 1984, Philip Morris's Black Marketing Task Force met in Washington D.C. to discuss "the very important Black smoker segment."[160, p. 0074] The task force concluded that Benson & Hedges Menthol and Virginia Slims were the only Philip Morris brands "that can be really 'worked' [in the] inner city."[161, p. 1444] Strategies presented by the task force included promotional plans, incentives, advertising, sampling programs, materials, communication, and the assignment of African Americans samplers to the inner city. As with Lorillard, a heavy emphasis was placed on B1G1F deals, incentives for inner city retailers, and promotional items that would appeal to African American consumers, such as playing cards, blank cassette tapes, cigarette cases, and lighters.[162]

With its share of the menthol market declining from 22.4% in 1981 to 15.8% in 1987, Reynolds began to focus heavily on Black young adult smokers (BYAS), who were considered critical to the success of all menthol styles.[127] Inner city African American young adults were also important because they were seen as trendsetters. As a marketing research report presented to RJ Reynolds suggested, "The daring, flamboyant aspect of YA [young adult] Black smokers' personalities are evident in **the many trends they start.** And the fact that these trends often spread to the general population speaks to the **unrecognized power and influence** this subgroup yields on society. . . . Trends are often started by lower income Black males who are looking for a way to be important or interesting, to create their own identity . . . [emphases in original]."[163, p. 7657]

Reynolds concluded that Newport was doing so well in the menthol market because Lorillard concentrated its efforts with one brand targeted to one population. Deciding to do the same, Reynolds focused all "BYAS [black young adult smoker] marketing resources" on Salem "since it is an acceptable choice among BYAS and accounts for two-thirds of RJR's BYAS share."[127, p. 0163] From April 1989 to April 1990, Reynolds implemented its BYAS Initiative, targeting high density lower-income African American neighborhoods of Chicago, Cleveland, and Memphis.[127–128] To determine specific boundaries of target neighborhoods within these markets, Reynolds conducted interviews in ZIP code areas pre-defined as inner city, at least 50% African American, and with yearly household incomes under $20,000.[164]

The BYAS Initiative sought to reverse Salem's declining trend among younger adult African American smokers and increase sales by getting African Americans to try Salem. Special advertising, promotions, and "a variety of other carefully coordinated sales and marketing programs"[136, p. 8939] began appearing in these markets. When radio stations featured known performers, Salem would be there, too.[136] Reynolds marketers emphasized that "Salem should be seen as a friend."[163] "The best way to reach minority consumers," they argued, was "through their local communities, . . . [which] tend to support brands that they see are doing something for them. [But these efforts] must be seen as authentic and as being backed by other Blacks—not as a big White company's tactic to sell to Blacks."[163, p. 7655]

**Inner city retailer programs**. Retail outlets located in inner cities presented challenges, including limitations on product availability and visibility, space constraints, retail clutter, high crime rates, and cash flow restrictions.[126,155,160] Additionally, inner city retail outlets were often secured with bullet-proof shields, which not only limited the space available for advertisements and merchandise but also eliminated self-service product selection. Tobacco companies' field representatives and/or ethnic marketing firms developed special efforts aimed at smaller, crowded neighborhood retail outlets in inner cities.[115,136]

Philip Morris acquired "Black accounts," primarily smaller liquor, grocery, and convenience stores in inner cities. These accounts were intended to replace others lost due to the larger supermarkets moving out of inner cities.[162] Philip Morris sought to remove impediments that prevented these small retailers from maintaining and selling cigarettes at acceptable levels. To save space, suction cups were used to hang signs from bullet-proof shielding; pricing signs incorporated personalized messages concerning such matters as the availability of check cashing services.[162] Product displays, existing versions of which were too large and required a major retailer investment, were specially re-designed for inner city retail outlets.[161] To ensure that cigarette displays were visible and well-stocked, inner city retailers were also offered incentives to display promotional items.[156] For example, Philip Morris paid retailers $20 to $40 to expand inventories and maintain visually prominent displays.[165] Additionally, Philip Morris increased the number of promotions offered monthly. This program, described as "the living laboratory," was initially tested in Detroit.[165] The program then expanded nationwide, including only menthol brand extensions of Benson & Hedges, Marlboro, Virginia Slims, and Alpine.[166]

Using ZIP codes to identify inner city neighborhood boundaries, Brown & Williamson implemented its Kool Inner City Point of Purchase (POP) Program in 1978 "to reach the core of Kool's franchise (young, black, relatively low income and education)"[98, p. 5852] and tackle the issues of poor product display and out-of-stock conditions. Later named the Kool Inner City Family Program, it targeted the top 20 African

American markets in the U.S., concentrating in the Northeast, Central, Southeast, and Southwest. Promotions included free gifts for retailers with monthly payments, a free carton of cigarettes for every 10 cartons purchased by distributors, and a multitude of consumer offers.[167]

Ethnic POP materials were employed, including marketing items with African American models that were poised to be "down to earth and not resemble the Harvard Black . . . ."[167, p. 0342] Special community events were also an important part of inner city targeting. In 1974, for example, Reynolds sponsored the Winston/Salem Cadillac sweepstakes in Chicago, in which Cadillacs were the prizes for both smokers and the local retailers of cigarettes. This promotion was intended to "generate excitement" and "strengthen Winston and Salem position [*sic*] in the young urban adult Black community."[168, p. 0004]

In the 1980s, because event sponsorship was a key element of its "Special Market" activities, Reynolds developed Salem Summer Street Scenes.[169,170] These 2-day festivals were held in the early 1980s "inside neighborhoods that [were] predominantly Black" to position Salem as a member of the community while distributing cigarettes. Reynolds reported that Salem Street Scenes reached at least 50% of the African American population in Memphis, Detroit, Chicago, New York, and Washington D.C.[170] The company also sponsored neighborhood events to "create an association between the brand and culturally relevant activities for the inner city Black smoker."[171, p. 7889]

Brown & Williamson also determined that involvement in community events was "critical to the success of its inner city program."[172, p. 3353] It operated the Kool Jazz festivals[173] and Summer Fest inner city music program[174] for years; it also considered funding inner city music festivals that were free to the public as a direct extension of Kool advertising.[175]

Philip Morris, similarly, was urged to "become more intimately involved in community affairs" to increase visibility in inner cities.[160] Philip Morris began sponsoring Black Expos around the country, beginning with the 1988 Indiana Black Expo.[176] Sponsoring national expos gave Philip Morris the opportunity both to advertise its product and to distribute free Benson & Hedges cigarettes to crowds of over 325,000. At the Indiana Black Expo, for example, Philip Morris's promotion included stage signage, a $25,000 check presentation, and remarks made on stage during the concert, and distribution of 10,000 samples, primarily Benson & Hedges cigarettes.[177]

Between 1995 and 1998, Philip Morris activities included "Club Benson & Hedges" promotional bar nights, which targeted 21–45 year-old "urban/ethnic markets."[178] "The brightest up and coming stars in urban music" were showcased in front of an estimated 100,000 consumers, who were "rewarded" with VIP treatment and preferential purchase opportunities. "Passport to 100 Urban Night Clubs," a promotional item billed as "America's only national entertainment guide which features establishments located within the inner city, frequented by African-Americans," was distributed to those attending any Club Benson & Hedges event.[179] It provided information about nightclubs, restaurants, attractions, annual events, and other social happenings in African American communities. After 13 years of using music to promote its Benson & Hedges brand while seeking a "diverse consumer base," Philip Morris suspended the brand's promotional activities in 1999.[180]

**The "menthol wars": Summary**. For 3 decades, the major tobacco companies competed aggressively to attract inner city African American smokers. In 1976, Kool had a 32.1% share of the African American market, and Salem followed with 13.5%. Benson & Hedges and Newport trailed behind with 3.1% and 2% shares, respectively. By 1978, Kool was still in the lead, but with only a 4% increase from 1976, compared with Benson & Hedges's 39% increase.[181] As other brands increased market share, Brown & Williamson grew concerned. Kool's share of the market was leveling off, possibly due to competitive advertising leading to brand switching.[182] Newport, which had consistently received the largest budget of all Lorillard brands, doubled its share of the menthol market from 22.4% in 1981 to 47.8% in 1987, while its competitors all lost half their market share.[127] As a result, Salem, Kool, and Benson & Hedges Menthol sales faltered during the 1980s.

## Discussion

Our study has limitations. The Legacy Tobacco Documents Library contains more than 7 million internal tobacco industry documents (over 40 million pages). Because our search terms retrieved only those documents where our particular search terms were associated with indexed fields (e.g., title, author, date), we were not able to search the full text within the document pages; thus, we may not have retrieved every document relevant to our research topic, and this may have caused us to understate the true extent of tobacco industry activities in inner city neighborhoods during the late 1970s–1990s. Since we completed data collection for this study, a full-text site containing the documents has been developed (http://ltdlftd.library.ucsf.edu/queryform.jsp) which might be used to identify additional documents; however, the sheer quantity of material available forces researchers to make decisions about which search terms retrieve the most relevant material. In any historical or archival study, the possibility always exists that material that later becomes available will shed additional light on the phenomena of interest. However, we believe that the documentary evidence abundantly supports our primary findings, highlighting the consistency of geographical patterns of activities across companies.

Though the targeting of African Americans and poor people has been previously documented,[16,17,78,81] this study shows specifically how temporal intersections between race, class, geography, and corporate marketing shaped and perpetuated "inner cities" as marginalized places and, in turn, how the racialized geography of those places spurred development of innovative technologies for the industrial promotion of menthol cigarettes. Race and class fundamentally shaped the inner city menthol wars described here. While African Americans were not the largest group of menthol smokers, African American smokers overwhelmingly chose menthol, and African Americans were quitting at lower rates than Whites. Thus, geographic areas such as inner cities, with their large concentrations of African American residents, represented efficient sites for promotion and growth opportunities for every menthol brand.

As "White flight" left inner city cores of poverty and racial segregation during the late 20th century,[41–42,183–186] it left behind neighborhoods that were challenging for marketers. Lack of employment opportunities contributed to rising poverty and crime.

These sociogeographic circumstances led tobacco companies to develop the innovation of the mobile van for distributing free samples of cigarettes throughout neighborhoods in which employees felt unsafe on foot. The insulated mobility of vans, accompanied by music and other attractions, enabled tobacco companies to safely counter the threat of crime while covering larger territories.

Other technological innovations were also developed specifically to deal with the geographic particularities of the inner city. As major retailers moved out of urban cores, the multiple small retail outlets that spread throughout these neighborhoods became the only places through which companies could sell goods. As this study shows, the smaller scale of these stores prompted tobacco companies to develop scaled down, specialized display units that served other purposes for retailers, kept products always attractive, visible, and easily accessible, and ensured that retailers did not run out of stock.

The menthol wars were also aided by the refinement during this period of demographic and psychographic profiling that allowed marketers to appeal more effectively to different groups. Even with these tools, however, companies made many missteps in trying to connect with inner city African Americans.[187–189] Companies addressed these missteps by engaging African American marketers who specialized in reaching poor, less educated, and predominantly African American populations.

It would be wrong to suggest that inner city residents were simply passive victims of tobacco marketers. Many within these communities built their capacity and infrastructure to actively resist the targeting of their communities via marketing for deadly products, and in some cases did so with remarkable effectiveness.[16,190–192] One cannot ignore, however, the enormous power differentials that exist between corporations and inner city neighborhood groups, and the ways in which the innovations of tobacco companies allowed them to overcome the disadvantages that inner cities posed for their marketing activities. Those activities, which contributed to increased cigarette smoking, had negative health and economic consequences for inner city residents, reinforcing their marginalized social position and increasing the likelihood that they would be unable to extricate themselves from poverty.[193]

Lung cancer is perhaps the disease most associated with cigarette smoking. Prior to the early 1960s, the mortality rate for lung cancer for White men was higher than for African American men.[194] During the 1960s, African American men and White men were dying of lung cancer at similar rates. However, beginning in the 1970s, the overall age-adjusted death rate for lung cancer for African American men surpassed that of White men. Similarly, beginning in the 1970s, the overall age-adjusted death rate for oral cancer among African American men surpassed that of White men and by the 1980s the death rate was twice as high for African American men than for White men.[194] The overall age-adjusted death rate for cancer of the larynx remained stable for Whites; however, between the 1950s and 1990s the rates had increased by 260% for African American men and approximately 233% for African American women.[194]

This study suggests that the tobacco-related health disparities that disfavor residents of many lower-income urban cores today were not solely determined by factors such as unhealthy habits and unequal access to health services. Tobacco-related health disparities were shaped as well by geographically specific and (when compared with White neighborhoods) intentionally disproportionate levels and *types* of aggressive cigarette marketing and promotion,[16,31,81] carried out over multiple decades. They were in a fundamental way *industrially created*. Ending health disparities, therefore, cannot focus merely on identifying individual health behaviors or risk factors: it also means naming, resisting, and politically organizing resourceful defenses against corporate vectors of disease and attending to the social injustices that shape inner cities as targets. Recent efforts to emphasize community participatory research[195–198] could represent opportunities to organize efforts to counter industry influence and re-shape the racialized geography of health in inner cities.

## Notes


1. Dell JL, Whitman S, Shah AM, et al. Smoking in 6 diverse Chicago communities—a population study. Am J Public Health. 2005 Jun;95(6):1036–42.
2. Haviland L. A silence that kills. Am J Public Health. 2004 Feb;94(2):176–8.
3. Northridge ME, Morabia A, Ganz ML, et al. Contribution of smoking to excess mortality in Harlem. Am J Epidemiol. 1998 Feb 1;147(3):250–8.
4. Parnes B, Main DS, Holcomb S, et al. Tobacco cessation counseling among underserved patients: a report from CaReNet. J Fam Pract. 2002 Jan;51(1):65–9.
5. U.S. Department of Health and Human Services (HHS). Tobacco use among U.S. racial/ethnic minority groups—African Americans, American Indians and Alaska Natives, Asian Americans and Pacific Islanders, and Hispanics: a report of the Surgeon General. Atlanta, GA: HHS, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1998.
6. Ahluwalia JS, McNagny SE. Smoking prevalence and desire to quit in inner city African American walk-in clinic patients. Clin Res. 1993;41:752A.
7. Delva J, Tellez M, Finlayson TL, et al. Cigarette smoking among low-income African Americans: a serious public health problem. Am J Prev Med. 2005 Oct; 29(3):218–20.
8. Hahn LP, Folsom AR, Sprafka JM, et al. Cigarette smoking and cessation behaviors among urban blacks and whites. Public Health Rep. 1990 May–Jun;105(3):290–5.
9. Hyman DJ, Simons-Morton DG, Dunn JK, et al. Smoking, smoking cessation, and understanding of the role of multiple cardiac risk factors among the urban poor. Prev Med. 1996 Nov–Dec;25(6):653–9.
10. Lee D, Cutler BD, Burns J. The marketing and demarketing of tobacco products to low-income African-Americans. Health Mark Q. 2004;22(2):51–68.
11. Resnicow K, Futterman R, Weston RE, et al. Smoking prevalence in Harlem, New York. Am J Health Promot. 1996 May–Jun;10(5):343–6.
12. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2004. MMWR Morb Mortal Wkly Rep. 2005 Nov 1;54(44):1121–4.
13. Centers for Disease Control and Prevention. Cigarette advertising—United States, 1988. MMWR Morb Mortal Wkly Rep. 1990 Apr 27;39(16):261–5.
14. Apollonio DE, Malone RE. Marketing to the marginalised: tobacco industry targeting of the homeless and mentally ill. Tob Control. 2005 Dec;14(6):409–15.
15. Arnett JJ, Terhanian G. Adolescents' responses to cigarette advertisements: links between exposure, liking, and the appeal of smoking. Tob Control. 1998 Summer; 7(2):129–33.

16. Balbach ED, Gasior RJ, Barbeau EM. R.J. Reynolds' targeting of African Americans: 1988–2000. Am J Public Health. 2003 May;93(5):822–7.
17. Barbeau EM, Leavy-Sperounis A, Balbach ED. Smoking, social class, and gender: what can public health learn from the tobacco industry about disparities in smoking? Tob Control. 2004 Jun;13(2):115–20.
18. Barbeau EM, Wolin KY, Naumova EN, et al. Tobacco advertising in communities: associations with race and class. Prev Med. 2005 Jan;40(1):16–22.
19. Ling PM, Glantz SA. Why and how the tobacco industry sells cigarettes to young adults: evidence from industry documents. Am J Public Health. 2002 Jun;92(6):908–16.
20. Luke D, Esmundo E, Bloom Y. Smoke signs: patterns of tobacco billboard advertising in a metropolitan region. Tob Control. 2000 Mar;9(1):16–23.
21. Primack BA, Bost JE, Land SR, et al. Volume of tobacco advertising in African American markets: systematic review and meta-analysis. Public Health Rep. 2007 Oct;122(5):607–15.
22. Pucci LG, Joseph HM J., Siegel M. Outdoor tobacco advertising in six Boston neighborhoods. Evaluating youth exposure. Am J Prev Med. 1998 Aug;15(2):155–9.
23. Robinson RG, Barry M, Bloch M, et al. Report of the Tobacco Policy Research Group on marketing and promotions targeted at African Americans, Latinos, and women. Tob Control. 1992;1(Suppl 1):S24–30.
24. Smith EA, Malone RE. The outing of Philip Morris: advertising tobacco to gay men. Am J Public Health. 2003 Jun;93(6):988–93.
25. Yerger VB, Daniel MR, Malone RE. Taking it to the streets: responses of African American young adults to internal tobacco industry documents. Nicotine Tob Res. 2005 Feb;7(1):163–72.
26. Kiefe CI, Williams OD, Greenlund KJ, et al. Health care access and seven-year change in cigarette smoking. The CARDIA Study. Am J Prev Med. 1998 Aug;15(2):146–54.
27. King G, Polednak A, Bendel RB, et al. Disparities in smoking cessation between African Americans and Whites: 1990–2000. Am J Public Health. 2004 Nov;94(11):1965–71.
28. Lawrence D, Graber JE, Mills SL, et al. Smoking cessation interventions in U.S. racial/ethnic minority populations: an assessment of the literature. Prev Med. 2003 Feb;36(2):204–16.
29. Lew R, Tanjasiri SP. Slowing the epidemic of tobacco use among Asian Americans and Pacific Islanders. Am J Public Health. 2003 May;93(5):764–8.
30. Fagan P, King G, Lawrence D, et al. Eliminating tobacco-related health disparities: directions for future research. Am J Public Health. 2004 Feb;94(2):211–7.
31. Hackbarth DP, Schnopp-Wyatt D, Katz D, et al. Collaborative research and action to control the geographic placement of outdoor advertising of alcohol and tobacco products in Chicago. Public Health Rep. 2001 Nov–Dec;116(6):558–67.
32. Day GL, Blot WJ, Austin DF, et al. Racial differences in risk of oral and pharyngeal cancer: alcohol, tobacco, and other determinants. J Natl Cancer Inst. 1993 Mar 17; 85(6):465–73.
33. Edwards BK, Brown ML, Wingo PA, et al. Annual report to the nation on the status of cancer, 1975–2002, featuring population-based trends in cancer treatment. J Natl Cancer Inst. 2005 Oct 5;97(19):1407–27.
34. Harris RE, Zang EA, Anderson JI, et al. Race and sex differences in lung cancer risk associated with cigarette smoking. Int J Epidemiol. 1993 Aug;22(4):592–9.
35. Hartge P, Silverman DT, Schairer C, et al. Smoking and bladder cancer risk in blacks and whites in the United States. Cancer Causes Control. 1993 Jul;4(4):391–4.

36. Hussain F, Aziz H, Macchia R, et al. High grade adenocarcinoma of prostate in smokers of ethnic minority groups and Caribbean Island immigrants. Int J Radiat Oncol Biol Phys. 1992;24(3):451–61.
37. Ries L HD, Harkins D, Krapcho M, et al., eds. SEER cancer statistics review, 1975–2003. Bethesda, MD: National Cancer Institute, 2006. Available at http://seer.cancer.gov/csr/1975_2003. Based on November 2005 SEER data submission, posted to the SEER web site, 2006.
38. American Heart Association (AHA). Heart disease and stroke statistics—2006 update. Dallas, TX: AHA, 2006.
39. Landrine H, Klonoff EA. Racial discrimination and cigarette smoking among Blacks: findings from two studies. Ethn Dis. 2000 Spring–Summer;10(2):195–202.
40. Link BG, Phelan JC. Fundamental sources of health inequalities. In: Mechanic D, Rogut LB, Colby JC, et al., eds. Policy challenges in modern health care. New Brunswick, NJ: Rutgers University Press, 2005; 71–84.
41. LaVeist TA. Race, ethnicity, and health: a public health reader. 1st ed. San Francisco: Jossey-Bass, 2002; xxxviii, 701.
42. Massey DS, Denton NA. The creation of the underclass communities. In: Massey DS, Denton NA, eds. American apartheid: segregation and the making of the underclass. Cambridge, MA: Harvard University Press, 1993; 115–47.
43. Polednak AP. Segregation, poverty, and mortality in urban African Americans. New York: Oxford University Press, 1997; viii, 184.
44. Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. Public Health Rep. 2001 Sep–Oct;116(5):404–16.
45. Morello-Frosch R, Pastor M, Sadd J. Environmental justice and Southern California's 'riskscape': the distribution of air toxics exposures and health risks among diverse communities. Urban Aff Rev Thousand Oaks Calif. 2001;36(4):551–78.
46. Morello-Frosch R, Shenassa ED. The environmental "riskscape" and social inequality: implications for explaining maternal and child health disparities. Environ Health Perspect. 2006 Aug;114(8):1150–3.
47. Foucault M. The birth of the clinic: an archaeology of medical perception. New York: Vintage Books, 1994; xix, 215.
48. Foucault M. Discipline and punish: the birth of the prison. 2nd Vintage Books ed. New York: Vintage Books, 1995; 333.
49. Lefebvre H. The production of space. Oxford, UK: Blackwell Publishers, 1991; 454.
50. Massey D. A global sense of place. In: Massey D, editor. Space, place, and gender. Minneapolis, MN: University of Minnesota Press, 1994; 146–56.
51. Massey D. The conceptualization of place. In: Massey DB, Jess P, eds. A place in the world? Places, cultures, and globalization. Oxford, UK: Oxford University Press, 1995; 46–85.
52. Sundstrom RR. Race and place: social space in the production of human kinds. Philosophy and Geography. 2003 Feb;6(1):83–95.
53. Wiist WH. Public health and the anticorporate movement: rationale and recommendations. Am J Public Health. 2006 Aug;96(8):1370–5.
54. Freudenberg N. Public health advocacy to change corporate practices: implications for health education practice and research. Health Educ Behav. 2005 Jun;32(3):298–319; discussion 355–62.
55. Glantz SA, Slade J, Bero LA, et al. The cigarette papers. Berkeley, CA: University of California Press, 1996.

56. Hong MK, Bero LA. How the tobacco industry responded to an influential study of the health effects of secondhand smoke. BMJ. 2002 Dec 14;325(7377):1413–6.
57. McDaniel PA, Smith EA, Malone RE. Philip Morris's Project Sunrise: weakening tobacco control by working with it. Tob Control. 2006 Jun;15(3):215–23.
58. Smith EA, Malone RE. "Creative Solutions": selling cigarettes in a smoke-free world. Tob Control. 2004 Mar;13(1):57–63.
59. Yerger VB, Malone RE. African American leadership groups: smoking with the enemy. Tob Control. 2002 Dec;11(4):336–45.
60. Centers for Disease Control and Prevention (CDC). Smoking cessation during previous year among adults—United States, 1990 and 1991. MMWR Morb Mortal Wkly Rep. 1993 Jul 9;42(26):504–7.
61. King G. Attitudes and practices of African-American physicians toward smoking interventions: an earlier study. J Assoc Acad Minor Phys. 1997;8(2):22–8.
62. King G. The "race" concept in smoking: a review of the research on African Americans. Soc Sci Med. 1997 Oct;45(7):1075–87.
63. Massachusetts Tobacco Control Program, Keithly L, Cullen D, et al. Changes in nicotine yields 1998–2004. Boston, MA: Massachusetts Department of Public Health, 2006.
64. Nelson DE, Giovino GA, Shopland DR, et al. Trends in cigarette smoking among US adolescents, 1974 through 1991. Am J Public Health. 1995 Jan;85(1):34–40.
65. Ahijevych KL, Tyndale RF, Dhatt RK, et al. Factors influencing cotinine half-life during smoking abstinence in African American and Caucasian women. Nicotine Tob Res. 2002 Nov;4(4):423–31.
66. Clark PI, Gautam S, Gerson LW. Effect of menthol cigarettes on biochemical markers of smoke exposure among Black and White smokers. Chest. 1996 Nov;110(5):1194–8.
67. Garten S, Falkner RV. Role of mentholated cigarettes in increased nicotine dependence and greater risk of tobacco-attributable disease. Prev Med. 2004 Jun;38(6):793–8.
68. Pletcher MJ, Hulley BJ, Houston T, et al. Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Arch Intern Med. 2006 Sep 25;166(17):1915–22.
69. Sidney S, Tekawa IS, Friedman GD, et al. Mentholated cigarette use and lung cancer. Arch Intern Med. 1995 Apr 10;155(7):727–32.
70. Ahijevych K, Gillespie J, Demirci M, et al. Menthol and nonmenthol cigarettes and smoke exposure in black and white women. Pharmacol Biochem Behav. 1996 Feb; 53(2):355–60.
71. Benowitz NL, Herrera B, Jacob P 3rd. Mentholated cigarette smoking inhibits nicotine metabolism. J Pharmacol Exp Ther. 2004 Sep;310(3):1208–15.
72. Brooks DR, Palmer JR, Strom BL, et al. Menthol cigarettes and risk of lung cancer. Am J Epidemiol. 2003 Oct 1;158(7):609–16; discussion 617–20.
73. Caraballo RS, Giovino GA, Pechacek TF, et al. Racial and ethnic differences in serum cotinine levels of cigarette smokers: Third National Health and Nutrition Examination Survey, 1988–1991. JAMA. 1998 Jul 8;280(2):135–9.
74. Jarvik ME, Tashkin DP, Caskey NH, et al. Mentholated cigarettes decrease puff volume of smoke and increase carbon monoxide absorption. Physiol Behav. 1994 Sep; 56(3):563–70.
75. McCarthy WJ, Caskey NH, Jarvik ME, et al. Menthol vs. nonmenthol cigarettes: effects on smoking behavior. Am J Public Health. 1995 Jan;85(1):67–72.
76. Pérez-Stable EJ, Herrera B, Jacob P 3rd, et al. Nicotine metabolism and intake in black and white smokers. JAMA. 1998 Jul 8;280(2):152–6.

77. Richardson TL. African-American smokers and cancers of the lung and of the upper respiratory and digestive tracts. Is menthol part of the puzzle? West J Med. 1997 Mar; 166(3):189–94.
78. Gardiner PS. The African Americanization of menthol cigarette use in the United States. Nicotine Tob Res. 2004 Feb;6 Suppl 1:S55–65.
79. Office on Smoking and Health. Smoking, tobacco & health, a fact book. Rockville, MD: HHS, Public Health Service (PHS), CDC, Centers for Health Promotion and Education, Office on Smoking and Health, 1986.
80. Novotny TE, Warner KE, Kendrick JS, et al. Smoking by blacks and whites: socioeconomic and demographic differences. Am J Public Health. 1988 Sep;78(9):1187–9.
81. Hackbarth DP, Silvestri B, Cosper W. Tobacco and alcohol billboards in 50 Chicago neighborhoods: market segmentation to sell dangerous products to the poor. J Public Health Policy. 1995;16(2):213–30.
82. Malone R, Balbach E. Tobacco industry documents: treasure trove or quagmire? Tob Control. 2000 Sep;9(3):334–8.
83. The State of Minnesota v. Philip Morris Incorporated. Civil Case No. C1-94-8565. MN District Court, 1998. Available at http://www.library.ucsf.edu/tobacco/litigation/mn/mnsettlement.html.
84. National Association of Attorneys General (NAAG). Master settlement agreement. Washington, DC: NAAG, 1998. Available at http://www.naag.org/upload/1032468605_cigmsa.pdf.
85. Balbach E, Gasior R, Barbeau E. Tobacco industry documents: comparing the Minnesota Depository and internet access. Tob Control. 2002 Mar;11(3):68–72.
86. MacKenzie R, Collin J, Lee K. The tobacco industry documents: an introductory handbook and resource guide for researchers. Center on Global Change and Health, London School of Hyeine & Tropical Medicine, 2003. Available at http://www.Ishtm.ac.uk/cgch/tobacco/Handbook%2030.06.pdf.
87. Reid JR. A history of mentholated cigarettes: this spud's for you. Recent Advances in Tobacco Sciences. 1993;19:71–84.
88. Murdock TK. Lennen & Newell. Newport call report #338. (Memo.) New York: Lennen & Newell, Inc., 1962 Nov 9. Available at http://legacy.library.ucsf.edu/tid/vzp40e00.
89. Yellen M. Lorillard. Lorillard sales position. (Memo.) Greensboro, NC: Lorillard, 1964 Sep 15. Available at http://legacy.library.ucsf.edu/tid/vqa63a00.
90. Lorillard. The menthol cigarette market—a summary—Job number 9016. Greensboro, NC: Lorillard, 1972 Feb. Available at http://legacy.library.ucsf.edu/tid/ipc31e00.
91. Philip Morris. Benson & Hedges Deluxe Ultra Lights slide presentation. Richmond, VA: Philip Morris USA, 1982 Mar15. Available at http://legacy.library.ucsf.edu/tid/wve58d00.
92. Brown & Williamson. The growth of menthols 330000-770000. Macon, GA: Brown & Williamson Tobacco Corporation, 1978. http://legacy.library.ucsf.edu/tid/ank50f00.
93. Cooper R, Simmons BE. Cigarette smoking and ill health among black Americans. N Y State J Med. 1985 Jul;85(7):344–9.
94. Cummings KM, Giovino G, Mendicino AJ. Cigarette advertising and black-white differences in brand preference. Public Health Rep. 1987 Nov–Dec;102(6):698–701.
95. Henningfield JE, Benowitz NL, Ahijevych K, et al. Does menthol enhance the addictiveness of cigarettes? An agenda for research. Nicotine Tob Res. 2003 Feb;5(1):9–11.
96. Liebow MS. Lorillard. Newport field visit: Los Angeles. Greensboro, NC: Lorillard, 1987 Sep 18. Available at http://legacy.library.ucsf.edu/tid/zic98c00.

97. Lorillard. Brand positioning: Shannon & Bounty. Greensboro, NC: Lorillard, 1972 Oct. Available at http://legacy.library.ucsf.edu/tid/man40e00.
98. Hudson RC. Brown & Williamson. Inner city POP Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1979 Oct 15. http://legacy.library.ucsf.edu/tid/icb91d00.
99. Market Facts Inc. Black smoker characteristics study (sex/age) (1971–34). Macon, GA: Brown & Williamson Tobacco Corporation, 1971 May. Available at http://legacy.library.ucsf.edu/tid/fdx79e00.
100. Lorillard. The world of Newport. Greensboro, NC: Lorillard, 1972. Available at http://legacy.library.ucsf.edu/tid/szc41e00.
101. Udow A. Philip Morris. Marketing Research Department report: the Black market, U.S.A. and Metro New York. Richmond, VA: Philip Morris USA, 1976 Mar29. Available at http://legacy.library.ucsf.edu/tid/dbz55e00.
102. Lorillard. Staffing for Newport Pleasure Van sampling program. Greensboro, NC: Lorillard,1979. Available at http://legacy.library.ucsf.edu/tid/nnr31e00.
103. Cohen A, Cutler W. Philip Morris USA. Benson & Hedges 1982 minority marketing plan. Richmond, VA: Philip Morris USA, 1981 Oct 29. Available at http://legacy.library.ucsf.edu/tid/yrq81f00.
104. Action Marketing Ltd. Kool Black market alternatives. Macon, GA: Brown & Williamson Tobacco Corporation, 1978 Nov 22. Available at http://legacy.library.ucsf.edu/tid/kje83f00.
105. Burrell Advertising. Burrell Advertising. Insights into the African-American consumer market. Direct marketing to multicultural market. Richmond, VA: Philip Morris USA, 1998 Apr 8. Available at http://legacy.library.ucsf.edu/tid/rlp28d00.
106. Fraser T. Fraser Smith. Fraser Smith presentation of 870226 Philip Morris Black consumer market development. Richmond, VA: Philip Morris USA, 1987 Feb 27. Available at http://legacy.library.ucsf.edu/tid/mfr75e00.
107. Fraser Smith. Philip Morris USA Benson & Hedges situation analysis Black consumer market promotion department. Richmond, VA: Philip Morris USA, 1987 Jul 8. Available at http://legacy.library.ucsf.edu/tid/czv83e00.
108. Special Market Services. Philip Morris. Recommended product sampling & image building program for Benson & Hedges cigarettes among Black and Hispanic consumers. Richmond, VA: Philip Morris USA, 1982 Apr 22. Available at http://legacy.library.ucsf.edu/tid/hbp54e00.
109. Wall K. FCB/Leber Katz Partners. Expanded consulting. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 Aug 16. Available at http://legacy.library.ucsf.edu/tid/icv61d00.
110. Wall K. Black young adult smoker profile. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1988 Nov 28. Available at http://legacy.library.ucsf.edu/tid/tsn54d00.
111. Hendricks JX. Brown & Williamson. Kool Jazz Festival/Hampton. Macon, GA: Brown & Williamson Tobacco Corporation, 1984 May 14. Available at http://legacy.library.ucsf.edu/tid/isv81d00.
112. Stokes N, SMSI. Brown & Williamson. 850600 Status report. Macon, GA: Brown & Williamson Tobacco Corporation, 1985 Jul 3. Available at http://legacy.library.ucsf.edu/tid/gks73f00.
113. Whitehair T. Brown & Williamson. 1986 Kool Van Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1986 Jun 6. Available at http://legacy.library.ucsf.edu/tid/jmj63f00.

114. Whitehair T. Brown & Williamson. 1986 Kool Van Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1986 Jul 31. Available at http://legacy.library.ucsf.edu/tid/xlj63f00.
115. Smith W. Philip Morris. Benson & Hedges Kings—Urban sampling program. Richmond, VA: Philip Morris USA, 1993 Mar 29. Available at http://legacy.library.ucsf.edu/tid/kyk97d00.
116. Philip Morris. Benson & Hedges part-time Inner City Sampling Program. Richmond, VA: Philip Morris USA, 1985 Jun 3. Available at http://legacy.library.ucsf.edu/tid/jkq24e00.
117. Reich S. Philip Morris. Benson & Hedges Inner City Program. Richmond, VA: Philip Morris USA, 1987 Feb 4. Available at http://legacy.library.ucsf.edu/tid/rws93e00.
118. Smith W. Philip Morris USA. Benson & Hedges Buy 1, Get 1 Free—Urban accounts elements memo. Richmond, VA: Philip Morris USA, 1990 Oct 3. Available at http://legacy.library.ucsf.edu/tid/hrw57c00.
119. Lorillard. Newport Van takes to the streets. Greensboro, NC: Lorillard, 1981 Jun 20. Available at http://legacy.library.ucsf.edu/tid/xtm09c00.
120. Rinns JA. Lorillard, Smoke Signals. Newport van sampling. Greensboro, NC: Lorillard, 1981 Jan 6. Available at http://legacy.library.ucsf.edu/tid/wzc31e00.
121. Schmitz EM. Lorillard. Newport sampling analysis—van, Florida and summer. Greensboro, NC: Lorillard, 1982 Dec 6. Available at http://legacy.library.ucsf.edu/tid/xvh74c00.
122. Liebow MS. Lorillard. Newport Van Program analysis. Greensboro, NC: Lorillard, 1986 Mar 26. Available at http://legacy.library.ucsf.edu/tid/gky88c00.
123. Liebow MS. Lorillard. Newport van program analysis. Greensboro, NC: Lorillard, 1987 Aug 25. Available at http://legacy.library.ucsf.edu/tid/gls54c00.
124. Leong WS. Lorillard. Additional sampling opportunities for the Newport van. Greensboro, NC: Lorillard 28 Aug 1987. Available at http://legacy.library.ucsf.edu/tid/dek44c00.
125. Liebow MS. Lorillard. Newport Van Program. Greensboro, NC: Lorillard, 1988 Jan 11. Available at http://legacy.library.ucsf.edu/tid/wgb98c00.
126. Magid B. Lorillard. Newport Van Program. Greensboro, NC: Lorillard, 1987 Aug 28. Available at http://legacy.library.ucsf.edu/tid/pti44a00.
127. RJ Reynolds. Black YAS Initiative. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1988 Dec 9. Available at http://legacy.library.ucsf.edu/tid/gzh44d00.
128. RJ Reynolds. Black Initiative executional requirements. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1991 Jan26. Available at http://legacy.library.ucsf.edu/tid/xgs28c00.
129. Benson S. Lorillard. Final report: Newport POW promotion evaluation in tiers I and II. Greensboro, NC: Lorillard,1994 Jul 26. Available at http://legacy.library.ucsf.edu/tid/mdz20e00.
130. Lomicka C. Brown & Williamson. Kool Van Sampling Program ("Kool Music on Tour"). Macon, GA: Brown & Williamson Tobacco Corporation, 1984. Available at http://legacy.library.ucsf.edu/tid/mwt13f00.
131. Brown & Williamson. Kool Music On Tour. Macon, GA: Brown & Williamson Tobacco Corporation, 1983 Jun 1. Available at http://legacy.library.ucsf.edu/tid/isr63f00.
132. Brown & Williamson. Kool Targeted Sampling Van Program. Macon, GA: Brown & Williamson Tobacco Corporation, No Date. Available at http://legacy.library.ucsf.edu/tid/anc60f00.

133. Brown & Williamson. Kool Van—Anaheim. Macon, GA: Brown & Williamson Tobacco Corporation, 1985 May 16. Available at http://legacy.library.ucsf.edu/tid/lks73f00.
134. U.S. Department of Health and Human Services. Preventing tobacco use among young people: a report of the Surgeon General. Atlanta, GA: HHS, PHS, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1994.
135. Brown & Williamson. 1991 Kool Van Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1991. Available at http://legacy.library.ucsf.edu/tid/puf02d00.
136. RJ Reynolds. Sales merchandiser. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 Jun. Available at http://legacy.library.ucsf.edu/tid/hbn14d00.
137. Chapa JJ. RJ Reynolds. Camel video van summary—October. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1990 Nov 8. Available at http://legacy.library.ucsf.edu/tid/rul24d00.
138. RJ Reynolds. An overview of the Black Imitative Program in the Chicago market. Winston-Salem, NC: R.J. Reynolds Tobacco Company,1990. Available at http://legacy.library.ucsf.edu/tid/mrj54d00.
139. Stockdale BK. RJ Reynolds. Special markets video van community use. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1990 Apr 23. Available at http://legacy.library.ucsf.edu/tid/xyo28c00.
140. Benson SR. Lorillard. Newport Van Program. Greensboro, NC: Lorillard, 1993 Oct 5. Available at http://legacy.library.ucsf.edu/tid/azb33c00.
141. Lorillard. Evaluation of Newport's "POW" Program. Greensboro, NC: Lorillard,1992. Available at http://legacy.library.ucsf.edu/tid/axp98c00.
142. Benson S. Lorillard. POW Program. Greensboro, NC: Lorillard, 1994 Jun 9. Available at http://legacy.library.ucsf.edu/tid/osm58c00.
143. Benson S. Lorillard. POW sales research status. Greensboro, NC: Lorillard, 1994 Mar 31. Available at http://legacy.library.ucsf.edu/tid/uqp98c00.
144. Benson S. Lorillard. Addendum to Newport POW promotion evaluation analysis. Greensboro, NC: Lorillard, 1994 Jul 29. Available at http://legacy.library.ucsf.edu/tid/ldz20e00.
145. Didonato R. Lorillard. Special Promotions—POW: 'Pleasure on Wheels'. Greensboro, NC: Lorillard, 1993 Nov. Available at http://legacy.library.ucsf.edu/tid/gdz20e00.
146. Sadovnick A. Lorillard. POW Task Force meeting. Greensboro, NC: Lorillard, 1994 Oct 25. Available at http://legacy.library.ucsf.edu/tid/pkc33c00.
147. Didonato RJ. Lorillard. Special promotions—POW. Greensboro, NC: Lorillard, 1994 Nov 15. Available at http://legacy.library.ucsf.edu/tid/vwq23c00.
148. Giacoio AJ. Lorillard. Special promotions—Newport field programs. Greensboro, NC: Lorillard, 1992 Mar 20. Available at http://legacy.library.ucsf.edu/tid/bad54a00.
149. Benson SR. Lorillard. Measuring Newport's van sampling effort. Greensboro, NC: Lorillard, 1992 Mar 26. Available at http://legacy.library.ucsf.edu/tid/pxm58c00.
150. Smith RE. Lorillard. Menthol marketing direction. Greensboro, NC: Lorillard, 1973 Feb 5. Available at http://legacy.library.ucsf.edu/tid/etl81e00.
151. Brown & Williamson. Brown & Williamson Tobacco Corporation marketing plans. Macon, GA: Brown & Williamson Tobacco Corporation, 1973. Available at http://legacy.library.ucsf.edu/tid/afk40f00.
152. Richardson RW. Lorillard. Special promotions—Inner City Sales Program. Greensboro, NC: Lorillard,1989 Jan 20. Available at http://legacy.library.ucsf.edu/tid/eiv44a00.
153. Liebow MS. Lorillard. Newport Inner City Sales Program. Greensboro, NC: Lorillard, 1988 Jan 12. Available at http://legacy.library.ucsf.edu/tid/nqq13c00.

154. Lorillard. Newport Inner City Sales Program implementation meeting. Greensboro, NC: Lorillard, 1987 Oct 12.Available at http://legacy.library.ucsf.edu/tid/fyk50e00.
155. Davis R. Lorillard. Black marketing research—Findings and recommended actions to date. Greensboro, NC: Lorillard, 1978 Jun 9. Available at http://legacy.library.ucsf.edu/tid/anz30e00.
156. Giacoio A. Lorillard. Special Promotions—Newport inner city lighter promotion. Greensboro, NC: Lorillard, 1988 Nov 1. Available at http://legacy.library.ucsf.edu/tid/xov44a00.
157. Lorillard. Inner City Sales Program. Greensboro, NC: Lorillard,1990 Aug. Available at http://legacy.library.ucsf.edu/tid/mvu44a00.
158. Lorillard. Lorillard retailer merchandising plan II guidelines package counter display offer—Security locations (Plexi-Glass Shielded Only) inner city areas only (ICSP). Greensboro, NC: Lorillard, 1992 Dec. Available at http://legacy.library.ucsf.edu/tid/axv44a00.
159. Liebow MS. Lorillard. Newport field visit: San Francisco. Greensboro, NC: Lorillard,1987 Sep22. Available at http://legacy.library.ucsf.edu/tid/xic98c00.
160. Troupe JM. Philip Morris. Black marketing symposium. Richmond, VA: Philip Morris USA, 1984 Oct 17. Available at http://legacy.library.ucsf.edu/tid/gyu92e00.
161. Foster HH. Philip Morris. Black Marketing Task Force. Richmond, VA: Philip Morris USA, 1984 Oct 1. Available at http://legacy.library.ucsf.edu/tid/wqp06e00.
162. Philip Morris. Ethnic program development. Richmond, VA: Philip Morris USA, 1984 Jun. Available at http://legacy.library.ucsf.edu/tid/xzu03e00.
163. Leferman Associates Inc., Nassar SC, Marketing Research and Strategic Planning. RJ Reynolds. Salem Black Initiative Program: brand team ideation session. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 Aug 3. Available at http://legacy.library.ucsf.edu/tid/wug34d00.
164. Hawkins SC, Hunter CS, Whitlatch WP, et al. RJ Reynolds. Addendum proposal: inner city Black tracker. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 Aug 2. Available at http://legacy.library.ucsf.edu/tid/gql93a00.
165. Daley T. Philip Morris. Urban Project report. Richmond, VA: Philip Morris USA, 1991 Jun 14. Available at http://legacy.library.ucsf.edu/tid/lbb93e00.
166. Daley T. Philip Morris. Philip Morris Urban Program audit. Richmond, VA: Philip Morris USA, 1991 Sep 13. Available at http://legacy.library.ucsf.edu/tid/alf76e00.
167. Lagreca K. Brown & Williamson. Kool family Inner City Program. Macon, GA: Brown & Williamson Tobacco Corporation, 1981 May. Available at http://legacy.library.ucsf.edu/tid/jxc91d00.
168. RJ Reynolds. Winston/Salem Cadillac Sweepstakes promotion Chicago Black consumer market. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1973 Oct 8. Available at http://legacy.library.ucsf.edu/tid/tbk79d00.
169. RJ Reynolds. 1982 Salem Summer Street Scenes strategic direction. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1982. Available at http://legacy.library.ucsf.edu/tid/glr13a00.
170. RJ Reynolds. Black Street Scenes: review and recommendations. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1983. Available at http://legacy.library.ucsf.edu/tid/onb19d00.
171. RJ Reynolds. Inner city Black targeted brand. (Blank file cover). Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 (estimate). Available at http://legacy.library.ucsf.edu/tid/mbv61d00.

172. C, RL. Brown & Williamson. Kool inner city meeting—recap. 1982 Jun 21. Available at http://legacy.library.ucsf.edu/tid/wgt50f00.
173. Santangelo J. Brown & Williamson. [Kool Jazz Festivals contributions]. Macon, GA: Brown & Williamson Tobacco Corporation, 1976 Sep 23. Available at http://legacy.library.ucsf.edu/tid/knd91d00.
174. Steele M. Brown & Williamson. Kool Summer Fest inner city program outline. Macon, GA: Brown & Williamson Tobacco Corporation, 1982 Aug 20. Available at http://legacy.library.ucsf.edu/tid/otm21c00.
175. Steele M. Brown & Williamson. Inner city music program. Macon, GA: Brown & Williamson Tobacco Corporation, 1982 Jul 1. Available at http://legacy.library.ucsf.edu/tid/zdb91d00.
176. Robinson J. Philip Morris. Benson & Hedges command performance involvement at the 1989 Indiana Black Expo—American Legion Mall/ Hoosier Dome. Richmond, VA: Philip Morris USA, 1987 Jun 19. Available at http://legacy.library.ucsf.edu/tid/abd45d00.
177. Biedermann EM. Phillip Morris. Indiana Black Expo—status report. Richmond, VA: Philip Morris USA, 1988 Jul 21. Available at http://legacy.library.ucsf.edu/tid/qdd65e00.
178. Philip Morris. 1996 Club Benson & Hedges Club/Bar Program. Richmond, VA: Philip Morris USA, 1995 Jan 30. Available at http://legacy.library.ucsf.edu/tid/sqf57d00.
179. Excel. Passport to 100 urban nightclubs. Richmond, VA: Philip Morris USA, 1998. Available at http://legacy.library.ucsf.edu/tid/ybj71c00.
180. Philip Morris. Club Benson and Hedges message point—event marketing. Richmond, VA: Philip Morris USA, 1999 Oct 26. Available at http://legacy.library.ucsf.edu/tid/epf16c00.
181. Brown & Williamson. Black market overview. Macon, GA: Brown & Williamson Tobacco Corporation, 1979. Available at http://legacy.library.ucsf.edu/tid/byz43f00.
182. Kates S. Brown & Williamson. Kool Black market research. Macon, GA: Brown & Williamson Tobacco Corporation, 1976 Jun 11. Available at http://legacy.library.ucsf.edu/tid/qbz40f00.
183. Avila E. Popular culture in the age of white flight: fear and fantasy in suburban Los Angeles. Berkeley, CA: University of California Press, 2004; 308.
184. Jargowsky PA. Poverty and place: ghettos, barrios, and the American city. New York: Russell Sage Foundation, 1997; xiv, 288.
185. Schulz AJ, Williams DR, Israel BA, et al. Racial and spatial relations as fundamental determinants of health in Detroit. Milbank Q. 2002;80(4):677–707, iv.
186. Williams DR. Race and health: basic questions, emerging directions. Ann Epidemiol. 1997 Jul;7(5):322–33.
187. RJ Reynolds. Sterling repositioning agenda. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1988 Mar. Available at http://legacy.library.ucsf.edu/tid/oak54d00.
188. RJ Reynolds. Project Uptown test market plan: Briefing summary. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1989 Nov 16. Available at http://legacy.library.ucsf.edu/tid/lih24d00.
189. PR News Wire via Dow Jones. Brown & Williamson Tobacco Corporation announces start of KOOL MIXX market finals. Macon, GA: Brown & Williamson Tobacco Corporation, 2000 Dec (estimate). Available at http://legacy.library.ucsf.edu/tid/guc65c00.
190. Community of Saint Sabina. Billboard Statement (fax). Chicago, IL: Community of Saint Sabina to R.J. Reynolds, 1991 Aug 14. http://legacy.library.ucsf.edu/tid/fbs14d00.

191. Robinson RG, Pertschuk M, Sutton C. Smoking and African Americans: spotlighting the effects of smoking and tobacco promotion in the African American community. In: Samuels SE, Smith MD, eds. Improving the health of the poor: strategies for prevention. Menlo Park, CA: Henry J. Kaiser Family Foundation, 1992; 122–81.
192. Slade J. Commission on Smoking OR Health. [Letter to R.J. Reynolds regarding the cancellation of test marketing in Uptown Philadelphia]. Trenton, NJ: Commission on Smoking OR Health, 1990 January 20. Available at http://legacy.library.ucsf.edu/tid/ffq14d00.
193. Zagorsky JL. The wealth effects of smoking. Tob Control. 2004 Dec;13(4):370–4.
194. Centers for Disease Control and Prevention (CDC). Mortality trends for selected smoking-related cancers and breast cancer—United States, 1950–1990. MMWR Morb Mortal Wkly Rep. 1993 Nov;42(44):857, 863–6.
195. Green LW, Mercer SL. Can public health researchers and agencies reconcile the push from funding bodies and the pull from communities? Am J Public Health. 2001 Dec;91(12):1926–9.
196. Hennessey Lavery S, Smith ML, Esparza AA, et al. The community action model: a community-driven model designed to address disparities in health. Am J Public Health. 2005 Apr;95(4):611–6.
197. Minkler M, Blackwell AG, Thompson M, et al. Community-based participatory research: implications for public health funding. Am J Public Health. 2003 Aug;93(8):1210–3.
198. Viswanathan M, Ammerman A, Eng E, et al. Community-based participatory research: assessing the evidence. Evid Rep Technol Assess (Summ). 2004 Aug;(99):1–8.

# Communication from Public

**Name:** Campaign for Tobacco-Free Kids
**Date Submitted:** 07/11/2019 11:05 AM
**Council File No:** 18-1104
**Comments for Public Posting:**

# PRELIMINARY SCIENTIFIC EVALUATION OF THE POSSIBLE PUBLIC HEALTH EFFECTS OF MENTHOL VERSUS NONMENTHOL CIGARETTES

Food and Drug Administration

TABLE OF CONTENTS

I. Executive Summary ........................................................................................... 3
II. Science Reviews ............................................................................................... 7
  A. Smoke Chemistry and Nonclinical Toxicology ................................................ 8
  B. Physiology ................................. .................................................................. 22
  C. Biomarkers ..................................................................................................... 37
  D. Patterns of Use ............................................................................................... 53
  E. Marketing and Consumer Perception of Risk .................................................. 66
  F. Initiation and Progression to Regular Use ....................................................... 90
  G. Dependence .................................................................................................... 106
  H. Cessation ......................................................................................................... 124
  I. Disease Risk ..................................................................................................... 138

# I. Executive Summary

Menthol is widely used in consumer and medicinal products and has long been used in cigarettes, often as a flavor-characterizing additive. In medical products, menthol is regulated as a drug with restrictions on allowable doses and use. There are no product standards for menthol when used in cigarettes.

Approximately one-fourth of all cigarettes sold in the United States are menthol (Giovino, 2004). The vast majority (88%) of adult smokers in the United States start to smoke before age 18 (U.S. Department of Health and Human Services, 2012). Thus, youth and young adulthood appear to be a critical age-span for initiation of cigarette smoking, and research suggests that menthol cigarettes may have an impact on initiation rates that differ from nonmenthol cigarettes. Further, the impact of menthol cigarettes on dependence, cessation, and health risks has been the topic of scientific inquiry and intense debate.

The Federal Food, Drug, and Cosmetic Act (FD&C Act) (Section 907 (e)) requires FDA's Tobacco Products Scientific Advisory Committee (TPSAC) to submit a report and recommendation to the Secretary of Health and Human Services (HHS) on the impact of the use of menthol in cigarettes on public health – including use among children, women, African Americans, Hispanics, and other racial or ethnic minorities – by March 23, 2011. In March 2010, TPSAC began its process of reviewing the available evidence as well as soliciting and receiving valuable input from researchers, tobacco industry representatives, consultants to the tobacco industry, representatives of the public health sector, and others. On July 21, 2011, TPSAC voted on its final report and recommendations on menthol, which concluded "removal of menthol cigarettes from the marketplace would benefit public health in the United States." TPSAC noted that a variety of options were available for FDA to consider, and they made no specific suggestions for follow-up by FDA should the agency decide it should pursue this recommendation. In addition, the non-voting industry representatives of TPSAC submitted a separate document reflecting the industry perspective. That document acknowledged the inherent risks of all tobacco products, including those that have menthol as a characterizing flavor, and raised the possibility of countervailing effects, including potential risks of contraband menthol products, should a ban be imposed.

Independently, FDA has undertaken a thorough review of the available science concerning menthol cigarettes. To accomplish this task, FDA weighed the collective body of evidence for the impact of the use of menthol in cigarettes on public health. One of the first considerations in weighing the value of a particular study was the relevance of the information to the consumption of menthol cigarettes in the United States. Findings that were replicated in different studies, especially different types of studies, were given greater weight. FDA also considered the source of information, the type of study, and the quality of study methods and data. In drawing conclusions, more consideration was given to peer-reviewed studies, studies in humans, and studies that were appropriately powered and designed. In this process, FDA evaluated the peer- reviewed literature, industry submissions and other materials provided to TPSAC, and performed or commissioned additional analyses in an attempt to fill in and inform some of the gaps in the literature.

In making its assessment, FDA used a "weight of scientific evidence" approach. Studies were evaluated to determine the strength of both negative and positive associations of menthol in cigarettes with the impact under consideration. Scientific determinations fell into one of five categories, where x is the impact under consideration:

- The weight of evidence supports the conclusion that menthol in cigarettes is associated with x
- The weight of evidence supports the conclusion that menthol in cigarettes is likely associated with x
- The weight of evidence supports the conclusion that menthol in cigarettes is likely not associated with x
- The weight of evidence supports the conclusion that menthol in cigarettes is not associated with x
- The evidence is not sufficient to support a conclusion of an association of menthol in cigarettes with x

The purpose of this evaluation was to determine whether there are independent associations between menthol in cigarettes and various outcomes of interest. In doing so, FDA evaluated the weight of evidence, taking into account potential threats to validity, such as bias or confounding, and whether the findings were generalizable to the U.S. population The evaluations were not an attempt to establish causality. In reviewing the science of menthol smoking, FDA divided the scientific evidence into the following broad categories:

**Smoke Chemistry and Nonclinical Toxicology**: This review assessed information on *in vitro* and *in vivo* studies, as well as studies that examined menthol alone or tobacco smoke from menthol cigarettes. Two particular areas of interest were the comparison of menthol to nonmenthol cigarettes and whether the addition of menthol impacted the presence and levels of harmful and potential harmful constituents in the smoke. The studies examined did not show increased toxicity in menthol cigarettes compared to the already-toxic nonmenthol cigarettes. From the available studies, the weight of evidence supports the conclusion that, from a nonclinical toxicity standpoint, menthol in cigarettes is not associated with increased or decreased smoke toxicity.

**Physiology:** FDA considered information on menthol's effect on cooling, desensitization, anesthesia, and potential effect on nicotine and tobacco specific nitrosamines (TSNAs). FDA reviewed both *in vitro* and *in vivo* studies in human and animal models. In addition, analysts reviewed studies looking at the effect of menthol on smoking topography. There are some *in vivo* and *in vitro* studies that show menthol has cooling, desensitizating, and proanalgesic effects. Menthol acts primarily through receptors on sensory nerves. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with altered physiological responses to tobacco smoke.

**Biomarkers:** FDA analyzed studies measuring biomarkers of exposure in smokers of menthol and nonmenthol cigarettes. Biomarkers included levels of smoke constituents or their metabolites in exhaled air, saliva, blood, and urine such as expired carbon monoxide (CO) and plasma carboxyhemoglobin (COHb) for levels of CO exposure; cotinine (main nicotine metabolite) and other nicotine equivalents in plasma and urine for exposure to nicotine. Some studies show that smoking menthol cigarettes modulates the exposure or metabolism of nicotine and tobacco-specific nitrosamines (TSNAs), while other studies fail to show a significant association. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely not associated with increased or decreased levels of biomarkers of exposure.

**Patterns of Use:** FDA reviewed scientific literature focusing on the general trends and patterns in menthol smoking. Articles reporting data on national estimates or very large representative populations were given highest priority in order to draw estimations of patterns of use that would be applicable and generalizable for the U.S. population overall. Data support that a majority of African American smokers smoke menthol cigarettes, but other minority groups are also more likely to smoke menthol cigarettes as compared to Whites. Further, younger populations have the highest rate of smoking menthol cigarettes, and female smokers are more likely to smoke menthol cigarettes than male smokers. Also, the use of menthol cigarettes is associated with lower socioeconomic status (SES). From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is associated with particular patterns of smoking.

**Marketing and Consumer Perception of risk:** FDA reviewed studies of brand preference, advertising receptivity, marketing strategies, and consumer perception of risk in an effort to determine what role, if any, marketing and consumer perception of risk play in the use of menthol cigarettes. Of particular interest was whether there is a stronger relationship between marketing and/or consumer perceptions and the use of menthol among subpopulations (e.g. youth, African Americans, Hispanics, women). The available data show that advertising is a strong driver of brand preference among adolescents and that it is likely that the standard marketing mix approach of price, promotion, product, and place has been used to drive menthol cigarette preference among the urban African American community. From the available studies, the weight of evidence supports the conclusion that, like nonmenthol cigarettes, the marketing of menthol cigarettes is associated with brand preference. The marketing of menthol cigarettes is associated with menthol brand preference among adolescents and the African American community. Given the limited data reviewed and mixed results reported, the weight of evidence is not sufficient to support a conclusion that consumer perceptions are associated with the use of menthol cigarettes.

**Initiation and Progression to Regular Use:** FDA assessed data on the possible impact of menthol cigarettes on initiation and progress to regular use of cigarette smoking with a particular focus on smoking behavior by youth and young adults. Included in the analysis were studies looking at differences in prevalence rates, age of first cigarette, and progression to regular smoking. Data show that newer smokers prefer menthol at levels substantially above that of the general population, with an inverse correlation between age and menthol preference that reaches a plateau in adulthood. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased initiation and progression to regular of cigarette smoking.

**Dependence:** FDA reviewed studies utilizing a variety of measures of nicotine dependence and/or craving. This included studies measuring: time to first cigarette (TTFC), cigarettes per day (cpd), the Fagerström Test for Nicotine Dependence (FTND), and craving.

Night waking to smoke was also included since it is emerging as a reliable indicator of strength of dependence. Data are included on other scales of nicotine dependence and craving if there were direct menthol versus nonmenthol assessments. There were consistent findings that menthol smokers are more likely to smoke their first cigarette within five minutes of waking. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased dependence.

**Cessation:** FDA analyzed studies addressing questions of whether menthol smokers were differentially successful in smoking cessation. These included cross-sectional studies, community-based or population-based prospective cohort studies, and clinical trial cessation studies. None of the studies were specifically designed to prospectively evaluate the effect of menthol on cessation. Several of the studies that failed to find an association between menthol smoking and cessation may have "over-adjusted" their analyses by controlling for the level of dependence. In the reviewed studies, menthol smokers, especially African American menthol smokers, were less likely to successfully stop smoking than their nonmenthol smoking counterparts. This is consistent with the observation that menthol smokers appear to be more nicotine dependent than nonmenthol smokers which can be an important factor in smoking cessation success. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with reduced success in smoking cessation, especially among African American menthol smokers.

**Disease Risk:** FDA analyzed studies that addressed the impact of smoking menthol cigarettes on disease risk as compared to those risks posed by smoking nonmenthol cigarettes. Studies investigating impact on lung cancer, non-lung smoking-related cancers (esophageal cancer, oropharyngeal cancer), cardiovascular disease, and respiratory outcomes in addition to one study that evaluated health wellness and health conditions such as body mass index (BMI) and emergency room visits were reviewed. No studies found an increased risk of cancer or non-cancer diseases in menthol smokers compared to nonmenthol smokers. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is not associated with an increase in disease risk to the user compared to non-menthol cigarette smokers.

**Summary of Evidence**

The impact of cigarette smoking upon public health is indisputable. More than 400,000 deaths per year in the United States are caused by tobacco use. Consistent patterns have emerged as a result of FDA's evaluation of the scientific evidence relevant to the impact of menthol tobacco products on public health. While there is little evidence to suggest that menthol cigarettes are more or less toxic or contribute to more disease risk to the user than nonmenthol cigarettes, adequate data suggest that menthol use is likely associated with increased smoking initiation by youth and young adults. Further, the data indicate that menthol in cigarettes is likely associated with greater addiction. Menthol smokers show greater signs of nicotine dependence and are less likely to successfully quit smoking. These findings, combined with the evidence indicating that menthol's cooling and anesthetic properties can reduce the harshness of cigarette smoke and the evidence indicating that menthol cigarettes are marketed as a smoother alternative to nonmenthol cigarettes, make it likely that menthol cigarettes pose a public health risk above that seen with nonmenthol cigarettes.

This document is a scientific assessment of public health issues related to the use of menthol in cigarettes. **This document does not constitute a decision about what regulatory action, if any, FDA might take with respect to menthol in cigarettes.** If FDA determines, after reviewing all of the available information from this assessment and the anticipated public comments, from the TPSAC report and associated public comments, and from the tobacco industry perspective document, that restrictions on the sale and/or distribution of menthol cigarettes or product standards should be established, the Agency would do so pursuant to rulemaking procedures that include public notice and an opportunity for public comment. There is no required deadline or timeline for FDA to make a determination about what regulatory action, if any, is appropriate.

References


1. Giovino, GA, Sidney, S, Gfroerer, JC, O'Malley, PM Allen, JA. et al. (2004) Epidemiology of menthol cigarette use. Nicotine and Tobacco Research 6 Suppl 1:S67-S81. [No funding source(s) provided. Authors affiliated with the Roswell Park Cancer Institute, Kaiser Permanente Medical Care Program, Substance Abuse and Mental Health Services Administration, University of Michigan, American Legacy Foundation, Centers for Diease Control and Prevention]
2. U.S. Department of Health and Human Services (2012). Preventing tobacco use among youth and young adults – A report of the Surgeon General. Rockville, MD.


# II. Science Reviews

The following is a list of abbreviations commonly used in this report:
1-OHP: 1-hydroxypyrene
3-HPMA: 3-hydroxypropyl mercapturic acid
3OH: 3-hydroxy
4-ABP: 4-ABP
AOR: Adjusted odds ratio
BMI: Body Mass Index
CARDIA: Coronary Artery Risk Development in Young Adults
CDC: Centers for Disease Control and Prevention
CI: Confidence interval
CO: Carbon monoxide
COHb: carboxyhemoglobin
COMMIT: Community Intervention Trial for Smoking Cessation
COPD: Chronic obstructive pulmonary disease
CPD: Cigarettes per day
CPS-TUS: Tobacco Use Supplement to the Current Population Survey
DHBMA: 1, 2-dihydroxybutyl mercapturic acid
FDA: Food and Drug Administration
FEV1: Forced expiratory volume in one second
FTC: Federal Trade Commission

FTND: Fagerstrom Test for Nicotine Dependence
FVC: Forced vital capacity
HDL: high-density lipoprotein
HHS: Health and Human Services
HR:Hazard Ratio
LDL: low-density lipoprotein
MCh: methacholine
MHBMA: monohydroxy-3-butenyl mercapturic acids
MTF: Monitoring the Future Survey
NDI: National Death Index
NE: Nicotine equivalents
NHANES: National Health and Nutrition Examination Survey
NHIS: National Health Information Survey
NHIS-CCS: National Health Interview Survey – Cancer Control Supplement
NHIS-LMF: National Health Interview Survey Linked Mortality File
NNAL: 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol
NSDUH: National Survey on Drug Use and Health
NTP: National Toxicology Program
NYTS: National Youth Tobacco Survey
OR: Odds ratio
RTI: Research Triangle Institute
SES: Socio-economic status
TDC: Tar delivery category
TES: Total Exposure Study
TPSAC: Tobacco Products Scientific Advisory Committee
TSNA: Tobacco specific nitroamine
TTFC: Time to first cigarette upon waking

## A. Smoke Chemistry and Nonclinical Toxicology

Scientific studies have investigated the smoke chemistry and nonclinical toxicology of nonmenthol cigarettes, but very few studies have directly compared the exposure of nonmenthol cigarettes to menthol cigarettes. Nonmenthol cigarettes produce an array of harmful chemicals during combustion and result in significant and substantial toxicological effects. Studies that evaluate whether menthol cigarettes produce greater quantities of harmful chemicals or result in more pronounced toxicological outcomes are limited. FDA reviewed scientific papers in order to examine differences in the smoke chemistry and nonclinical toxicology.

*Smoke chemistry*

The comparison of menthol to nonmenthol cigarettes is of interest to determine if the addition of menthol impacts the presence or measured levels of and occurrence of harmful smoke constituents. Schmeltz and Schlotzhauer (1968) evaluated the pyrolysis of menthol and reported the formation of phenols and polyaromatic hydrocarbons. But their study examined the pyrolysis of menthol alone and not as part of the process of burning tobacco. So while it is informative, it must be interpreted with this consideration.

In two papers from 2004, Baker et al. reported only minimal differences in harmful smoke constituents. They reported their results normalized to the levels of total particulate matter in smoke which provides relative increases or decreases between constituents, but does not necessarily reflect overall changes to the amount of harmful smoke constituents delivered per cigarette. They reported an increase in aldehydes in the smoke from the menthol cigarettes, likely due to the combustion of simple and complex sugars, as well as increased lead. Some constituents were lower compared to the nonmenthol cigarette, such as benzo[a]pyrene. From the limited data and differences in how these data can be interpreted, there is a lack of evidence showing that menthol in cigarettes yields substantial changes in smoke chemistry.

*Menthol as a singular compound – toxicology, pharmacology and therapeutic applications*

A review of the National Toxicology Program (NTP) database (Ashby and Tennant, 1991) shows that menthol has neither a structural alert for DNA reactivity or mutagenic activity. Menthol is listed in the database as Level F on their carcinogenicity scale, which indicates that adequate tests have been conducted and the compound is concluded to be non-carcinogenic.

The racemic mixture of menthol was tested in an Ames, sister chromatid exchange and chromosomal aberration assays. In these studies, menthol alone had no effect under the conditions of these assays (Ishidate et al., 1984; Ivett et al., 1989; and Murthy et al., 1991).

Rabinoff et al. (2007) reviewed industry documents looking for information on the pharmacological activity of tobacco additives. Possible effects listed for menthol include anesthetic action, complex interaction with nicotine, and increase in P1-N2 amplitudes, an objective electrophysiological measure of brain activity.

Harris (2006) presented a review of the therapeutic applications of menthol alone, based on the interaction at the thermoreceptor. Some therapeutic actions discussed include local anesthesia, nasal decongestant and cough relief.

*Antiproliferative effects of menthol as a singular compound*

There were several papers that examined the effects of menthol on *in vitro* cell proliferation and have shown that in several cancer cell lines, menthol had a significant growth inhibition effect (Bernhardt et al., 2008; Li et al., 2009; Lu et al., 2006; Lu et al., 2007; Sidell et al., 1991; Tatman and Mo 2002; Yamamura et al., 2008; and Zhang and Barritt 2004).

Ruch and Sigler (1994) examined a mechanism for terpene-induced growth inhibition of rat liver epithelial cells and found that while some terpenes (such as limonene and pinene) appeared to inhibit 3-hydroxy-3-methylglutaryl CoA reductase and mevalonic acid synthesis, menthol did not act through this mechanism. It is important to note that any anti-proliferative effects of menthol have been shown with menthol alone, and not with menthol in combination with tobacco or in a smoke condensate. In fact, as has already been stated, menthol smoke condensate from burned tobacco is genotoxic. Additionally, one should not assume that a compound that had anti-proliferative effects in a tumor cell line or even in a transfected animal model would definitively have oncolytic effects in humans.

*In vitro* studies have examined the pharmacological activity of menthol to help elucidate the mechanism by which it had antiproliferative effects (Kim et al., 2009; Li et al., 2009; Yamamura et al., 2008; and Zhang and Barritt 2004). These studies all show that menthol acts at the transient receptor potential melastatin 8 (TRPM8) thermoreceptor. Activation of this receptor appears to increase intracellular $Ca^{2+}$ levels by increasing the influx of extracellular $Ca^{2+}$ through this channel. These studies also showed the antiproliferative effects of menthol in tumor cell lines.

Lu et al. (2006) showed increased $Ca^{2+}$ levels in human leukemia cells treated with menthol and showed that the decreased cell growth seen could be blocked by the calcium chelator, BAPTA. This is further evidence of the link between the antiproliferative effects of menthol and the increase in intracellular $Ca^{2+}$ that it has been shown to cause cell death.

Sidell et al. (1991) also showed menthol down-regulated the IL-6 receptors in a human myeloma cell line.

*In vitro toxicity of menthol tobacco exposure*

Several reports reviewed here have examined smoke condensate from menthol cigarettes and found no increase in mutagenicity, clastogenicity or cytotoxicity when compared to a comparable nonmenthol cigarette. This was done with mainstream and sidestream smoke, with the same results. Some studies also included cigarettes that heat, but do not burn the tobacco as test cigarettes. These heated cigarettes included menthol and nonmenthol versions. All the cigarettes in which the tobacco was burned were positive in these assays, and cigarettes with added ingredients such as menthol were not significantly different from the control (Baker et al., 2004; Doolittle et al., 1990a and 1990b; Ivett et al., 1989; and Roemer et al., 2002). The cigarettes that heat tobacco but do not burn it were negative in these assays with and without menthol added (Doolittle et al., 1990a and 1990b; Lee et al., 1990).

Other *in vitro* assays showed menthol to be toxic at concentrations greater than 0.1 mM (Bernson and Pettersson 1983). This application produced lesions in biological membranes in the isolated mitochondria assay and increased the permeability over the inner mitochondrial membrane. While interesting, the relevance of these studies to menthol exposure via menthol cigarettes is not strong, as menthol overdose is not likely via this exposure.

*In vivo toxicity of menthol tobacco exposure*

Several studies reported on *in vivo* inhalation toxicity studies with test cigarettes that had menthol added as a flavoring ingredient (Baker et al., 2004; Gaworski et al., 1997). These studies all show no discernable differences in the toxicity of the test cigarettes when compared to the nonmenthol cigarettes.

*In vivo* carcinogenesis studies also have shown no significant effects of menthol compared to nonmenthol. These studies included the SENCAR mouse skin painting assays with smoke condensate from menthol and nonmenthol cigarettes (Gaworski et al., 1999), DMBA-induced rat mammary carcinogenesis model with menthol in the feed (Russin et al., 1989) and azoxymethane-induced neoplasia of the large intestine and duodenum with menthol in the feed (Wattenberg, 1991).

BALB/c mice injected with WEHI-3 leukemia cells also showed effects of menthol exposure, having slowed leukemia-induced spleen growth,and limited differentiation of the precursors of macrophages and granulocytes (Lu et al., 2007).

*Industry reviews of menthol*

Two tobacco industry reviews (Lorillard (Heck 2010); Altria (Werley et al., 2007)) of the available literature on menthol and the possible effects of menthol cigarettes provided no additional information and no information that provided new insight into the potential toxicology of exposure to menthol from a menthol cigarette.

*Conclusion*

While menthol toxicity does occur, the reviewed studies show that this occurs at high levels of menthol as a singular compound and has not been shown with menthol exposure from cigarettes. The nonclinical toxicology data, *in vitro* or *in vivo* indicate that menthol exposure from a menthol cigarette does not cause the menthol cigarettes to be substantially more toxic than nonmenthol cigarettes already are. Menthol in smoke condensate is no more genotoxic than condensate from the control cigarettes. Menthol has not been shown to be carcinogenic or to increase the number of tumors or alter the time to tumor emergence from known carcinogens. In the few *in vivo* inhalation studies comparing menthol cigarette smoke to a control cigarette's smoke, researchers found no increased toxicity due to the added menthol. From the available studies, the weight of evidence supports the conclusion that, from a nonclinical toxicity standpoint, menthol in cigarettes is not associated with increased or decreased smoke toxicity.

Smoke Chemistry and Nonclinical Toxicology: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Ashby J, Tennant RW. | Definitive relationships among chemical structure, carcinogenicity and mutagenicity for 301 chemicals tested by the U.S. NTP. | 1991 | Funded though the National Institute of Environmental Health Sciences | Bioassay | Rodents | Not Applicable | Concepts of genotoxic and non-genotoxic rodent carcinogenicity are worthy of continued attention; it's meaningless to discuss the sensitivity/specificity without defining the broad chemical classes under discussion-> important to any model for screening environmental chemicals for potential carcinogens. |
| Baker RR, Massey, ED, Smith, G. | An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. | 2004 | No funding source(s) provided. Authors affiliated with British American Tobacco Company | Evaluation of series of studies; pyrolysis studies | Not Applicable | Not Applicable | All of these studies have indicated that commonly used tobacco ingredients do not change the toxicity of smoke as measured in specified assays. Also, the ingredients have no effect on the levels of most smoke constituents that may be relevant to smoking-related diseases. |
| Baker RR, Pereira da Silva JA, Smith G. | The effect of tobacco ingredients on smoke chemistry. Part I: flavourings and additives. | 2004 | No funding source(s) provided. Authors affiliated with British American Tobacco Company | Experimental | The levels of the "Hoffmann analytes" in the smoke from the test cigarettes containing the ingredient mixture were compared to those from control cigarettes without the ingredients. | Not Applicable | It was found that, in most cases, the mixtures of flavouring ingredients (generally added in parts per million levels) had no statistically significant effect on the analyte smoke yields relative to the control cigarette. |
| Bernhardt G, Biersack B, Bollwein S, Schobert R, Zoldakova M. | Terpene conjugates of diaminedichlorido platinum(II) complexes: antiproliferative effects in HL-60 leukemia, 518A2 melanoma, and HT-29 colon cancer cells. | 2008 | No funding source(s) provided. Authors affiliated with two German universities | 28 dichloridoplatinum (II) complexes | Not Applicable | Not Applicable | In the melanoma cells, the propane-1,2-cliyl-spacered conjugates of (-)-menthol (1a2,), (+)-neomenthol (1b2), (-)-carvomenthol (1h2,), and (-)-isolongifolol (1n2) displayed growth inhibition at IC50<4 uM which is ten times smaller than that of cisplatin. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoke Chemistry and Nonclinical Toxicology: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| Bernson VS, Pettersson B. | The toxicity of menthol in short-term bioassays. | 1983 | Swedish Work Environment Fund (79/91:3) and the Swedish Tobacco Company | Animal Studies | Short Term Bioassays (trachea from chicken embryos, Ascites sarcoma BP 8 cells, isolated hamster brown adipocytes and rat liver mitochondria) | Not Applicable | Menthol was found to be toxic on in vitro biological model systems in concentrations >0.1mM. One effect of menthol was a lesion of biological membranes as demonstrated by experiments on isolated mitochondria. |
| Doolittle DJ, Lee CK, Ivett JL, Mirsalis JC, Riccio E, Rudd CJ, Burger GT, Hayes AW. | Comparative studies on the genotoxic activity of mainstream smoke condensate from cigarettes which burn or only heat tobacco. | 1990 | No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company | Short term genotoxicity assays | Mice and hamsters | Not Specified | These results demonstrate that the mainstream CSCs [cigarette smoke concentrate] from the TEST and TEST-menthol cigarettes are neither genotoxic nor cytotoxic under conditions where CSCs from 1R4f, ULT, and ULT-menthol cigarettes are genotoxic and/or cytotoxic in a concentration-dependent manner. |
| Doolittle DJ, Lee CK, Ivett JL, Mirsalis JC, Riccio E, Rudd CJ, Burger GT, Hayes AW. | Genetic toxicology studies comparing the activity of sidestream smoke from cigarettes which burn or only heat tobacco. | 1990 | No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company | Genotoxicity assays | Not Applicable | Not Applicable | Results demonstrate that side stream smoke from cigarettes that heat but do not burn tobacco (TEST and TEST-menthol) was neither genotoxic or cytotoxic under conditions where sidestream smoke from cigarettes which burn tobacco (1R4F, ULT, ULT-menthol) was genotoxic and/or cytotoxic in a concentration-dependent manner. |
| Gaworski CL, Dozier MM, Gerhart JM, Rajendran N, Brennecke LH, Aranyi C, Heck JD. | 13-week inhalation toxicity study of menthol cigarette smoke. | 1997 | No funding source(s) provided. Authors affiliated with Lorillard Tobacco Company | Smoke inhalation study | Groups of male and female rats (21 per sex for reference and 15 per sex for menthol) were exposed at target smoke concentrations of 200, 600 and 1200mg TPM/m 3 for 1 hr/day, 5days/wk, for 13 wk. | N=72 | Addition of menthol to cigarettes does not significantly alter the pattern, incidence, severity or reversibility of any of the effects attributable to smoke exposure in rats. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoke Chemistry and Nonclinical Toxicology: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Gaworski CL, Heck JD, Bennett MB, Wenk ML. | Toxicologic evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice. | 1999 | No funding source(s) provided. Authors affiliated with Lorillard Tobacco Company | Skin painting biassays; experimental design | Female SENCAR mice | N=30-50 | Study did not indicate any substantive effect of flavoring ingredients. |
| Harris, B. | Menthol: A review of its thermo receptor interactions and their therapeutic applications. | 2006 | No funding source(s) provided. Author affiliated with Essential Oil Resource Consultants | Literature Review | Not Applicable | Not Applicable | This review has confirmed the therapeutic benefits of menthol containing oils in: topical applications for cooling, warming, relief of pain and itch; inhaled preparation and chest rub for relief of cough; and oral preparations such as lozenges for relief of cough. |
| Heck JD. | A review and assessment of menthol employed as a cigarette flavoring ingredient. | 2010 | No funding source(s) provided. Author affiliated with Lorillard Tobacco Company | Literature Review | Not Applicable | Not Applicable | …a broad convergence of findings supports a judgment that menthol employed as a cigarette tobacco flavoring ingredient does not meaningfully affect the inherent toxicity of cigarette smoke or the human risks that attend smoking. |
| Ishidate, Jr, M, Sofuni T, Yoshikawa K, Hayashi M, Nohmi T, Sawada M, and Matsuoka A | Primary mutagenicity screening of food additives currently used in Japan. | 1984 | The Food Chemistry Division, Environmental Health Bureau, Ministry of Health and Welfare of Japan | In Vitro | Chinese hamster fibroblast cells | Not Specified | [No narrative. Listed in Table 1] |
| Ivett JL, Brown BM, Rodgers C, Anderson BE, Resnick MA, Zeiger E. | Chromosomal aberrations and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. IV. Results with 15 chemicals. | 1989 | National Institute of Environmental Health Sciences. Grant Number NO1-ES-3–5030 | In Vitro | Chinese hamster ovary cells | Not Specified | There was no increase in the trial with activation, and the chemical was judged negative in the SCE assay. The aberration assays were both negative. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Kim SH, Nam JH, Park EJ, Kim BJ, Kim SJ, So I, Jeon JH. | Menthol regulates TRPM8-independent processes in PC-3 prostate cancer cells. | 2009 | Funded by a grant of the Korea Health 21R and D project, Ministry of Health, Welfare and Family Affairs, Republic of Korea (A060058), and by the Seoul National University Hospital Research Fund (03-2005-026-0), and the BK21 project from Ministry of Education, Science and Technology | Experimental | Prostate cancer cells | Not Specified | There is an apparent lack of causality between TRPM8 activation and menthol-induced cell death and that menthol can regulate TRPM8-independent Ca(2+)-transport and cellular processes. |
| Lee CK, Doolittle DJ, Burger GT, Hayes AW. | Comparative genotoxicity testing of mainstream whole smoke from cigarettes which burn or heat tobacco. | 1990 | No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company | Comparative | Not Applicable | Not Applicable | Mainstream whole smoke from the heat tobacco (TEST) cigarettes, with either regular or menthol flavor, was neither cytotoxic nor mutagenic in any of these assays. |
| Li Q, Wang X, Yang Z, Wang B, Li S. | Menthol induces cell death via the TRPM8 channel in the human bladder cancer cell line T24. | 2009 | National Natural Science Foundation of China (No. 30872572/C160603) | Experimental | Cells of the human bladder cancer cell line T24. | Not Specified | Menthol can induce mitochondrial membrane depolarization via the TRPM8 channel in cells of the human bladder cancer cell line T24, resulting in cell death. It would be helpful to explore the precise mechanism of action of menthol in bladder cancer with a view to its possible use as intravesical chemotherapy. |
| Lu HF, Liu JY, Hsueh SC, Yang YY, Yang JS, Tan TW, Kok LF, Lu CC, Lan SH, Wu SY, Liao SS, Ip SW, Chung JG. | (-)-Menthol inhibits WEHI-3 leukemia cells in vitro and in vivo. | 2007 | grant CMU94-103 from the China Medical University, Taichung, Taiwan, and by grant 95-31 from the Cheng Hsin Rehabilitation Medical Center, Paipei, Taiwan | Experimental | In vivo Mice cells | Not Specified | (-)- menthol was found to induce cell death and inhibited leukemia-related spleen growth. |
| Lu HF, Hsueh | The role of Ca2+ | 2006 | Grant 93-32 from the | Experimental | Human promyelocytic | Not | Ca2+ production is associated with the induction |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| SC, Yu FS, Yang JS, Tang NY, Chen SC, Chung JG. | in (-)-menthol-induced human promyelocytic leukemia HL-60 cell death. | | Cheng Hsin Rehabilitation Medical Center (Taipei, Taiwan, R.O.C.) | | leukemia HL-60 cell line | Specified | of (-)-Menthol-induced cell death. |
| Murthy PBK, Ahmed MM, Regu K. | Lack of genotoxicity of menthol in chromosome aberration and sister chromatid exchange assays using human lynphocytes in vitro. | 1991 | Department Science and Technology, Government of India (SP/YS/L35/85) | Experimental | Heparinized peripheral blood samples obtained from male and female adult non-smokers. | N=24 (12 male, 12 female) | These results suggest that menthol does not have a chromosomal-damaging effect in human lymphocytes. |
| Rabinoff M, Caskey N, Rissling A, Park C. | Pharmacological and chemical effects of cigarette additives. | 2007 | National Institute of Mental Health (NRSA training grant MH 14585) | Review | Tobacco industry documents and other sources | 5 Primary Sources | Findings indicated that more than 100 of 599 documented cigarette additives have pharmacological actions that camouflage the odor of environmental tobacco smoke emitted from cigarettes, enhance or maintain nicotine delivery, could increase the addictiveness of cigarettes, and mask symptoms and illnesses associated with smoking behaviors. |
| Roemer E, Tewes FJ, Meisgen TJ, Veltel DJ, Carmines EL. | Evaluation of the potential effects of ingredients added to cigarettes. Part 3: In vitro genotoxcity and cytotoxicity. | 2002 | No funding source(s) provided. Author affiliated with R.J. Reynolds Tobacco Company | In vitro | Ingredients commonly used in cigarette manufacturing | N=333 | Within the sensitivity and specificity of the test systems, the in vitro mutagenicity and cytotoxicity of the cigarette smoke were not increased by the addition of the ingredients. |
| Ruch RJ, Sigler K. | Growth inhibition of rat liver epithelial tumor cells by monoterpenes does not involve | 1994 | Grant from the American Institute for Cancer Research to RJ Reynolds Tobacco Company | In Vitro | Rat liver epithelial cells | Not Applicable | Monoterpene-induced growth inhibition of rat liver epithelial cells was dissimilar to lovastatin and did not appear to involve altered Ras plasma membrane association. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Smoke Chemistry and Nonclinical Toxicology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | Ras plasma membrane association. | | | | | | |
| Russin WA, Hoesly JD, Elson CE, Tanner MA, Gould MN. | Inhibition of rat mammary carcinogenesis by monoterpenoids. | 1989 | Grant from the National Cancer Institute CA38128 | Experimental | Terpenes | Not Specified | Dietary additions of each of the monocyclic terpenes, d-limonene or (-)-menthol resulted in a significant inhibition of mammary carcinogenesis. Furthermore, menthol was found to be a more potent chemopreventive agent than limonene during the DMBA initiation of rat mammary tumors. |
| Schmeltz I, Schlotzhauer WS. | Benzo(a)pyrene, phenols and other products from pyrolysis of the cigarette additive, (d,1)-menthol. | 1968 | No funding source(s) provided. Authors affiliated with the U.S. Dept of Agriculture | Experimental | Menthol | Not Specified | The contribution of menthol to the chemical and biological effects of cigarette smoke must be weighed in relation to the amount used as an additive, and the amount that undergoes pyrolytic conversion. |
| Sidell N, Taga T, Hirano T, Kishimoto T, Saxon A. | Retinoic acid-induced growth inhibition of a human myeloma cell line via down-regulation of IL-6 receptors. | 1991 | United States Public Health Service Grants A115251. A115332, CA30515. CA43503 and CA12800 from the National Institutes of Health and Grant-in-Aid for Specially Promoted Research from the Ministry of Education. Science and Culture. Japan | Experimental | Human B cell lines | Not Specified | Menthol, a structurally unrelated compountdo RA, also suppressed IL-6R expression and, correspondingly, inhibited cell growth. |
| Tatman D, Mo H. | Volatile isoprenoid constituents of fruits, vegetables and herbs cumulatively suppress the proliferation of murine B16 melanoma and | 2002 | Public Health Service grant CA 73418 | Experimental | Fruits, vegetables, herbs | Not Applicable | The cancer-protective property of fruits, vegetables, and related products is partly conferred by the cumulative impact of volatile isoprenoid constituents. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | human HL-60 leukemia cells. | | | | | | |
| Wattenberg LW. | Inhibition of azoxymethane-induced neoplasia of the large bowel by 3-hydroxy-3,7,11-trimethyl-1,6,10-dodecatriene (nerolidol). | 1991 | Funded by grant SIG 5A from the American Cancer Society | Experimental | Male F344 rats | Not Applicable | The chemical structure of nerolidol suggests the possibility that the compound might have an impact on protein prenylation or some other aspect of the mevalonate pathway, but this remains to be established. |
| Werley MS, Coggins CR, Lee PN. | Possible effects on smokers of cigarette mentholation: a review of the evidence relating to key research questions. | 2007 | No funding source(s) provided. Authors affiliated with Philip Morris USA | Review | Not Applicable | Not Applicable | Smoking mentholated cigarettes did not affect the rate of decline in lung function in Year 1 or between Year 1 and Year 5 (p=0.229 and 0.64, respectively, data not shown). |
| Yamamura H, Ugawa S, Ueda T, Morita A, Shimada S. | TRPM8 activation suppresses cellular viability in human melanoma. | 2008 | Grants-in-Aid for Young Scientists from the Ministry of Education, Culture, Sports, Science and Technology (to H. Yamamura) and for Scientific Research and Exploratory Research from the Japan Society for the Promotion of Sciences (to S. Shimada). | In situ hybridization | Human melanoma | Not Specified | The viability of melanoma cells was dose-dependently depressed in the presence of menthol. These results reveal that a functional TRPM8 protein is expressed in human melanoma cells to involve the mechanism underlying tumor progression via the Ca(2+) handling pathway, providing us with a novel target of drug development for malignant melanoma. |
| Zhang L, Barritt GJ. | Evidence that TRPM8 is an androgen-dependent Ca2+ channel required for the survival of | 2004 | No funding source(s) provided. Authors affiliated with Flinders University | Experimental | Prostate cancer cell lines | Not Specified | TRPM8 is an important determinator of Ca2+ homeostasis in prostate epithelial cells and may be a potential target for the action of drugs in the management of prostate cancer. |

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | prostate cancer cells. | | | | | | |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

References


1. Ashby J, Tennant RW. (1991) Definitive relationships among chemical structure, carcinogenicity and mutagenicity for 301 chemicals tested by the U.S. NTP. Mutatation Research: Reviews in Genetic Toxicology 257(3):229–306. [Funded though the National Institute of Environmental Health Sciences]
2. Baker RR, Massey, ED, Smith, G (2004a) An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. Food and Chemical Toxicology 42S: S53-S83. [No funding source(s) provided. Authors affiliated with British American Tobacco Company]
3. Baker RR, Pereira da Silva JA, Smith G (2004b) The effect of tobacco ingredients on smoke chemistry. Part I: flavourings and additives. Food and Chemical Toxicology 42(suppl):S3–S37. [No funding source(s) provided. Authors affiliated with British American Tobacco Company]
4. Bernhardt G, Biersack B, Bollwein, S, Schobert R, Zoldakova, M (2008) Terpene conjugates of diaminedichloridoplatinum(II) complexes: antiproliferative effects in HL-60 leukemia, 518A2 melanoma, and HT-29 colon cancer cells. Chemistry and Biodiversity 5(8):1645–1659. [No funding source(s) provided. Authors affiliated with two German universities]
5. Bernson VS, Pettersson B (1983) The toxicity of menthol in short-term bioassays. Chemico-Biological Interactions 46(2):233–246. [Funded by grants from the Swedish Work Environment Fund (79/91:3) and the Swedish Tobacco Company]
6. Doolittle DJ, Lee CK, Ivett JL, Mirsalis JC, Riccio E, Rudd CJ, Burger GT, Hayes AW (1990a) Comparative studies on the genotoxic activity of mainstream smoke condensate from cigarettes which burn or only heat tobacco. Environmental and Molecular Mutagenesis 15(2):93–105. [No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company]
7. Doolittle DJ, Lee CK, Ivett JL, Mirsalis JC, Riccio E, Rudd CJ, Burger GT, Hayes AW (1990b) Genetic toxicology studies comparing the activity of sidestream smoke from cigarettes which burn or only heat tobacco. Mutation Research 240(2):59–72. [No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company]
8. Gaworksi CL, Dozier MM, Gerhart JM, Rajendrans N, Brennecke LH, Aranyi C, Heck JD (1997) 13-week inhalation toxicity study of menthol cigarette smoke. Food and Chemical Toxicology 35(7):683–692. [No funding source(s) provided. Authors associated with Lorillard Tobacco Company]
9. Gaworski CL, Heck JD, Bennet MB, Wenk ML (1999) Toxicologic evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice. Toxicology 139(1–2):1–17. [No funding source(s) provided. Authors affiliated with Lorillard Tobacco Company]
10. Harris B (2006) Menthol: a review of its thermoreceptor interactions and their therapeutic applications. International Journal of Aromatherapy 16(3–4):117–131. [No funding source(s) provided. Author affiliated with Essential Oil Resource Consultants]
11. Heck JD (2010) A review and assessment of menthol employed as a cigarette flavoring ingredient. Food and Chemical Toxicology 48(suppl):S1–S38. [No funding source(s) provided. Author affiliated with Lorillard Tobacco Company]

12. Ishidate, Jr, M, Sofuni T, Yoshikawa K, Hayashi M, Nohmi T, Sawada M, and Matsuoka A (1984) Primary mutagenicity screening of food additives currently used in Japan. Food and Chemical Toxicology 22(8):623–636. [Funding provided by the Food Chemistry Division, Environmental Health Bureau, Ministry of Health and Welfare of Japan.
13. Ivett JL, Brown BM, Rodgers C, Anderson BE, Resnick MA, Zeiger E (1989) Chromosomal aberrations and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. IV. Results with 15 chemicals. Environmental and Molecular Mutagenesis 14:165–187. [Funded by contract number N01-ES-3-5030 with the National Institute of Environmental Health Sciences]
14. Kim SH, Nam JH, Park EJ, Kim BJ, Kim SJ, So I, Jeon JH (2009) Menthol regulates TRPM8-independent processes in PC-3 prostate cancer cells. Biochimica et Biophysica Acta 1792(1):33–38. [Funded by a grant of the Korea Health 21R and D project, Ministry of Health, Welfare and Family Affairs, Republic of Korea (A060058), and by the Seoul National University Hospital Research Fund (03-2005-026-0), and the BK21 project from Ministry of Education, Science and Technology]
15. Lee CK, Doolittle DL, Burger GT, Hayes AW (1990) Comparative genotoxicity testing of mainstream whole smoke from cigarettes which burn or heat tobacco. Mutation Research 242(1):37–45. [No funding source(s) provided. Authors affiliated with R.J. Reynolds Tobacco Company]
16. Li Q, Wang X, Yang Z, Wang B, Li S (2009) Menthol induces cell death via the TRPM8 channel in the human bladder cancer cell line T24. Oncology 77:335–341. [Funded by the National Natural Science Foundation of China (No. 30872572/C160603).
17. Lu HF, Liu JY, Hsueh SC, Yang YY, Yang JS, Tan TW, Kok LF, Lu CC, Lan SH, Wu SY, Liao SS, Ip SW, Chung JG (2007) (-)-Menthol inhibits WEHI-3 leukemia cells in vitro and in vivo. In Vivo 21(2):285–289. [Funded by grant CMU94-103 from the China Medical University, Taichung, Taiwan, and by grant 95-31 from the Cheng Hsin Rehabilitation Medical Center, Paipei, Taiwan]
18. Lu HF, Hsueh SC, Yu FS, Yang JS, Tang NY, Chen SC, Chung JG (2006) The role of Ca2+ in (-)-menthol-induced human promyelocytic leukemia HL-60 cell death. In Vivo 20(1):69–75. [Funded by grant 93-32 from the Cheng Hsin Rehabilitation Medical Center, Taipei, Taiwan]
19. Murthy PBK, Ahmend MM, Regu K (1991) Lack of genotoxicity of menthol in chromosome aberration and sister chromatid exchange assays using human lynphocytes in vitro. Toxicology in Vitro 5(4):337–340. [Funded by the Department Science and Technology, Government of India (SP/YS/L35/85)]
20. Rabinoff M, Caskey N, Rissling A, Park C (2007) Pharmacological and chemical effects of cigarette additives. American Journal of Public Health 97(11):1981–1991. [Funded by a pilot grant from the National Institute of Mental Health (NRSA training grant MH 14585)]
21. Roemer E, Tewes FJ, Meisgen TJ, Veltel DJ, Carmines EL (2002) Evaluation of the potential effects of ingredients added to cigarettes. Part 3: In vitro genotoxcity and cytotoxicity. Food and Chemical Toxicology 40:105–111. [No funding source(s) provided. Author affiliated with R.J. Reynolds Tobacco Company]

22. Ruch RJ, Sigler K (1994) Growth inhibition of rat liver epithelial tumor cells by monoterpenes does not involve Ras plasma membrane association. Carcinogenesis 15(4):787–789. [Funded by a grant from the American Institute for Cancer Research to RJ Reynolds Tobacco Company]
23. Russin WA, Hoesly JD, Elson CE, Tanner MA, Gould MN (1989) Inhibition of rat mammary carcinogenesis by monoterpenoids. Carcinogenesis 10(11):2161–2164. [Funded by a grant from the National Cancer Institute CA38128]
24. Schmeltz I, Schlotzhauer WS (1968) Benzo(a)pyrene, phenols and other products from pyrolysis of the cigarette additive, (d,1)-menthol. Nature 219(5152):370–371. [No funding source(s) provided. Authors affiliated with the U.S. Dept of Agriculture]
25. Sidell N, Taga T, Hirano T, Kishimoto T, Saxon A (1991) Retinoic acid-induced growth inhibition of a human myeloma cell line via down-regulation of IL-6 receptors. Journal of Immunology 146(11):3809–3814. [Funded by United States Public Health Service Grants A115251. A115332, CA30515. CA43503 and CA12800 from the National Institutes of Health and Grant-in-Aid for Specially Promoted Research from the Ministry of Education. Science and Culture. Japan]
26. Tatman D, Mo H (2002) Volatile isoprenoid constituents of fruits, vegetables and herbs cumulatively suppress the proliferation of murine B16 melanoma and human HL-60 leukemia cells. Cancer Letters 175(2):129–139. [Funded by Public Health Service grant CA 73418]
27. Wattenberg LW (1991) Inhibition of azoxymethane-induced neoplasia of the large bowel by 3-hydroxy-3,7,11-trimethyl-1,6,10-dodecatriene (nerolidol). Carcinogenesis 12(1):151–152. [Funded by grant SIG 5A from the American Cancer Society]
28. Werley MS, Coggins CRE and Lee PN (2007) Possible effects on smokers of cigarette mentholation: a review of the evidence relating to key research questions. Regulatory Toxicology and Pharmacology 47:189–203. [No funding source(s) provided. Authors affiliated with Philip Morris USA]
29. Yamamura H, Ugawa S, Ueda T, Morita A, Shimada S (2008) TRPM8 activation suppresses cellular viability in human melanoma. American Journal of Physiology: Cell Physiology 295(2):C296–C301. [Funded by Grants-in-Aid for Young Scientists from the Ministry of Education, Culture, Sports, Science and Technology and for Scientific Research (B) and Exploratory Research from the Japan Society for the Promotion of Sciences]
30. Zhang L, Barritt GJ (2004) Evidence that TRPM8 is an androgen-dependent Ca2+ channel required for the survival of prostate cancer cells. Cancer Research 64(22):8365–8373. [No funding source(s) provided. Authors affiliated with Flinders University]

## *B. Physiology*

Menthol is widely used in drug products, foods, cosmetic products, and cigarettes, and generates a minty taste and a cooling sensation. The flavor and sensation may be pleasing, and can impact the way a smoker experiences a menthol cigarette. Menthol's effect on cooling, desensitization, anesthesia, and the potential effect on nicotine and tobacco specific nitrosamines (TSNAs) using both *in vitro* and *in vivo* studies in human and animal models can inform how researchers understand and policy-makers address menthol in cigarettes and its impact on individual behavior and public health outcomes, as well as effect of menthol on smoking topography. This assessment focuses on the actions of menthol alone rather than tobacco smoke from menthol cigarettes.

*Sensory Effects*

Green and Schullery (2003) conducted a study that focused primarily on the bitterness stimulation induced by capsaicin and menthol. On average, capsaicin and menthol produced "moderate" bitterness in the edges and side of the tongue and weaker bitterness on the side and tip of the tongue. Sensory irritation from capsaicin was rated significantly higher at the tongue tip, whereas menthol coolness was rated higher in the edges and side of the tongue.

Kuhn et al. (2009) carried out an *in vitro* study on TRPM8, a cation channel activated by cold and menthol, and found that menthol and menthol derivatives were indistinguishable in their ability to evoke currents through channels in a $Ca^{2+}$-independent manner and by producing $Ca^{2+}$- dependent desensitization in human embryonic kidney (HEK-293) cells.

Sherkheli (2008) found that WS-12, a menthol derivative, is more potent and selective than menthol as a TRPM8 agonist in Xenopus laevis oocytes.

Ito et al. (2008) investigated the impact of menthol and icilin on airway smooth muscle contraction in guinea pigs. The study found that as a cold receptor agonist, menthol inhibited contractions elicited by MCh and high $K^+$ concentrations with a reduction in $Ca^{2+}$. Lowering the temperature to room temperature enhanced the relaxing effects of menthol on MCh-induced contractions. The result indicated that stimulation of an unknown cold receptor may be involved in the relaxation mediated by menthol in guinea pig tracheal smooth muscle.

Menthol gives a sense of cooling. Campero et al. (2009) used microneurography to search for C fibers (a type of sensory cell) in human skin that are activated by cooling and menthol. Menthol activated only Type 2 C fibers, which showed a strong reaction to harmless cooling and were strongly activated and sensitized to cooling by menthol.

Orani et al. (1991) found in guinea pigs that cooling of the larynx and application of l-menthol to the laryngeal lumen reduced ventilation. Application of menthol to the nasal cavity markedly enhanced the ventilatory inhibition. Although l-menthol did not actually reduce laryngeal temperature, the laryngeal lumen responded as though it did. In fact, l-menthol seems to be more effective in reducing ventilation than physical cooling.

Sant'Ambrogio et al. (1991, 1992) investigated the effect of l-menthol on laryngeal and upper airway cold receptors in dogs. The study found that l-menthol acted as a specific stimulant of laryngeal cold receptors. Trials with cold air and warm air plus l-menthol exposure on upper airway cold receptors greatly reduced ventilation in newborn dogs. The menthol-induced respiratory depression occured even earlier than the cold-induced effect. The faster onset of reflex response could be because the menthol stimulation of cold receptors was greater or because nasal cold receptors were involved in the menthol response.

By monitoring the action potentials of the ethmoidal nerve, Sekizawa (1996) characterized the responsiveness of nasal cold receptors to menthol and capsaicin in guinea pigs. Both cold air and l-menthol stimulated the ethmoidal afferent activity. Topical anesthesia of the nasal cavity with 2 percent lidocaine eliminated these responses. This study dovetails with those discussed earlier; it provides electrophysiological support for the breathing inhibition that other studies also found (Orani et al., 1991; Sant'Ambrogio et al., 1991; Sant'Ambrogio et al., 1992).

*Mechanisms of Menthol Action*

In an *in vivo* human study, Dessirier et al. (2001) assessed the responses of participants' tongues to menthol application. Repeated application of menthol produced desensitization as characterized by a progressive reduction in the ratings of the intensity of irritation across trials. This appeared to generalize, as menthol exposure also significantly weakened nicotine-evoked irritation. The desensitization and cross-desensitization was temporary, with a return to normal sensations after a rest period.

Cold temperatures and some chemical stimuli (like menthol) activate the TRPM8 receptor. Kuhn et al. (2009) found that prolonged menthol exposure desensitized TRPM8 receptors. Galeotti et al. (2002) found that menthol could induce analgesia in mice, regardless of the noxious stimulus used: thermal (hot-plate) or chemical (abdominal constriction test). The analgesic properties were mediated through a selective activation of κ-opioid receptors.

An *in vivo* study demonstrated that menthol is an effective cough suppressant in chemically induced coughing in conscious guinea pigs (Laude et al, 1994).

Sekizawa et al. (1996) found that topical anesthesia of the nasal cavity eliminated the responsiveness of nasal cold receptors to cold air and l-menthol in guinea pigs. The desensitization and analgesic effect of menthol may reduce sensitivity of human response to irritation induced by smoking constituents.

Wright et al. (1997) found that menthol exposure promotes bronchodilatation both *in vitro* and *in vivo* in guinea pigs. The authors also proposed that menthol might act as an antagonist of calcium ($Ca^{2+}$) channels.

Sidell et al. (1990) demonstrated that exposure to menthol could block the depolarization-induced $Ca^{2+}$ influx though both dihydropyridine (DHP)-sensitive and DHP-insensitive $Ca^{2+}$ channels in LA-N-5 human neuroblastoma cells. Whether menthol blocks $Ca^{2+}$ channels was concentration-dependent, rapid in onset, and readily reversible. In addition, applying menthol to neuroblastoma cells in culture resulted in morphologic differentiation and inhibition of cell growth that correlated with menthol's ability to block the dihydropyridine-insensitive $Ca^{2+}$ current.

Lin et al. (2005) found menthol to have potential antitumor qualities. Menthol inhibited the growth of cancer cells in a dose- and time-dependent manner. Menthol inhibited topoisomerase I, IIα and IIβ, but promoted the levels of NF-κB gene expression. These data suggest that menthol may induce cytotoxicity through inhibiting gene expression of topoisomerase I, IIα and IIβ and promoting the gene expression of NF-κB in SNU-5 cells.

*Metabolic Effects*

MacDougall et al. (2003) found that menthol and synthetic congeners inhibited the microsomal oxidation of nicotine to cotinine (the primary metabolite of nicotine) in human liver microsomal testing systems. The data suggested that smoking menthol cigarettes may lead to inhibition of nicotine metabolism and allow the smoker to achieve prolonged exposure to nicotine.

Azzi et al. (2006) found menthol donor solution (0.08%) decreased the flux of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and significantly increased the tissue reservoir formation in porcine esophageal mucosa. The magnitude of the reservoir formed was similar for control and menthol, but was significantly higher in the presence of both ethanol and menthol.

Squier et al. (2010) found that the presence of menthol significantly increased the uptake of both N′-nitrosonornicotine (NNN) and nicotine over that of controls with no menthol in porcine buccal and floor of mouth mucosa. According to the authors, the presence of menthol might increase exposure of carcinogens and nicotine, which in turn might increase the risk of cancer and dependence, however there are no disease outcome data that support this hypothesis.

In a crossover study with 14 subjects, Benowitz et al. (2004) found that mentholation of cigarettes did not affect systemic intake of nicotine and carbon monoxide. Researchers reported that menthol smoking inhibits the metabolism of nicotine through slower oxidative metabolism to cotinine and slower glucuronide conjugation.

*Effects of Menthol on Smoking Topography*

Ahijevych & Parsley (1999) assessed smoking topography in a clinical research setting using a two-factor study design involving 95 women, half of whom smoked menthol cigarettes. Menthol smokers (n=49) had significantly larger puff volumes compared to nonmenthol smokers (n=46). Larger puff volumes can result in smokers' exposure to more chemicals.

Pickworth et al. (2002) found that mentholation of cigarettes had no effect on topography, with menthol smokers (n=18) and nonmenthol smokers (n=18) each taking approximately 8 puffs per commercial cigarette, and approximately 11 puffs per high nicotine yield cigarette and per low nicotine yield cigarette.

Using a two-factor factorial design and a sample of 37 women divided by menthol or nonmenthol cigarette use, Ahijevych et al. (1996) found nonmenthol smokers had a trend toward higher puff volumes as compared to menthol smokers (mean = 48.5 vs. 42.7 ml), however this did not reach signficance.

Jarvik et al. (1994) measured smoking topography in 20 smokers (10 were menthol smokers) and found menthol cigarettes decreased the average and total cumulative puff volumes and increased the mean puff flow rates of inhaled smoke. Researchers noted no significant differences in the depth of inhalation of the smoke or in the amount of insoluble smoke particulates delivered to or retained in the respiratory tract between the two types of cigarettes.

McCarthy et al. (1995) studied 29 male smokers who smoked either a regular or a menthol cigarette in two separate sessions one week apart. Researchers used commercial brands with comparable tar, nicotine, and CO content. When smoking the nonmenthol cigarettes, participants took 22 percent more puffs and had 13 percent higher mean volumes per puff than they did when smoking the menthol cigarettes.

The tobacco industry is aware that menthol has cooling, anaesthetic, and analgesic properties that moderate the harshness and irritation of tobacco. Yerger and McCandless (2011) reviewed publicly available tobacco industry documents and concluded that the documents suggest the amount of menthol in a cigarette is associated with how the cigarette is smoked and how satisfying it is to the smoker. According to these documents, menthol's physiological effects contribute to the sensory qualities of the smoke and affect smoking topography.

*Industry Assessment of Menthol Effects*

Heck (2009) found median blood carboxyhemoglobin values, total urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), and urinary nicotine equivalents were not significantly different between the menthol and nonmenthol smokers.

Wang et al. (2010) found smoking menthol cigarettes does not increase daily exposure to smoke constituents as measured by nicotine equivalents (total and per cigarette), serum cotinine, and COHb after adjusting for cpd and the smoking behavior characteristics of the participants.

In its presentation to TPSAC, Altria Client Services presented analysis of the Total Exposure Study (TES) that also showed no differences between users of menthol and nonmenthol brands for a wide variety of biomarkers of exposure, biomarkers of potential harm, nicotine metabolite ratios, measures of smoker topography, and nicotine dependence, after adjustment for cpd and smoking behavior characteristics.

*Conclusion*

Menthol generates a minty taste and a cooling sensation. At lower concentrations menthol has a soothing effect, while it is irritating at high concentrations. Smokers experience the cooling sensation of menthol in cigarettes, and menthol is perceived as reducing the irritation and harshness of smoking. Several *in vitro* and *in vivo* studies investigated the sensory effects of menthol and discussed mechanisms for these effects. In addition, a few studies suggested that menthol might have a role on exposure and metabolism of nicotine and TSNAs. Due primarily to menthol's sensory effects, the weight of evidence supports the conclusion that menthol in cigarettes in likely associated with altered physiological responses to tobacco smoke.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Ahijevych K, Garrett BE. | Menthol pharmacology and its potential impact on cigarette smoking behavior. | 2004 | Funded in part by National Institute on Drug Abuse grant 10809 and General Clinical Research Center grant M01 RR00034 | Literature Review | Not Applicable | Not Applicable | Menthol smokers have been shown to score higher on a measure of nicotine dependence, and Black smokers who prefer mentholated cigarette brands have lower quit rates than White smokers Industry findings also have shown that menthol is capable of increasing nicotine impact in cigarette smokers. These findings provide some support for increased tobacco addiction in mentholated cigarette smokers but are still inconclusive. |
| Ahijevych K, Gillespie J, Demirci M, Jagadeesh J. | Menthol and nonmenthol cigarettes and smoke exposure in black and white women. | 1996 | The Ohio State University Seed Grant and The Ohio State University General Clinical Research Center Grant MO1 RROO034 | Cross sectional 2 factor factorial design | Black and White Women 19-59 years old, smoked ≤20 cpd | N=37 (18 Black, 19 White) | In the current study, lower CO boost with mentholated cigarettes suggests that factors beyond mentholation may affect differences in cotinine levels in black and white women. |
| Ahijevych K, Parsley LA. | Smoke constituent exposure and stage of change in black and white women cigarette smokers. | 1999 | American Lung Association Research Grant; General Clinical Research Center M01 RR00034 | Two-factor design | Black and White Women | N=95 total women (48 black with 27 smoking menthol cigarettes, and 47 white with 22 smoking menthol cigarettes) | Black women had significantly higher beliefs about the negative aspects of smoking than did White women; menthol smokers had a shorter time to first cigarette, indicating greater nicotine dependence. |
| Azzi C, Zhang J, Purdon CH, Chapman JM, Nitcheva D, Hebert JR, Smith EW. | Permeation and reservoir formation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo[a]pyrene (B[a]P) across | 2006 | MUSC/USC/HCC Department of Defense Funds, Phase VI, Cancer Prevention and Control Research Development Grant | Confocal microscopy studies | Porcine esophageal mucosa | Not Applicable | We have observed markedly different extents of permeation and reservoir formation for the tobacco carcinogens applied to porcine esophageal mucosa in the presence of ethanol and menthol. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | porcine esophageal tissue in the presence of ethanol and menthol. | | | | | | |
| Benowitz NL, Herrera B, Jacob P 3rd. | Mentholated cigarette smoking inhibits nicotine metabolism. | 2004 | State of California Tobacco Related Disease Research Program Grant 1RT-0521, by U.S. Public Health Service Grants DA02277 and DA12393 awarded by the National Institute on Drug Abuse and CA32389 awarded by the National Cancer Institute, and by the General Clinical Research Center at San Francisco General Hospital Medical Center with the support of the Division of Research Resources, National Institutes of Health (RR-00083) | Cross Over | 14 healthy cigarette smokers recruited through local papers. (7 African-Americans and 7 whites, 12 men and 2 women. Participants were selected as typically smoking 20 or more cigarettes per day and having a prior experience of smoking both mentholated and nonmentholated cigarettes. | N=14 | Our finding of impaired metabolism of nicotine while mentholated cigarette smoking suggests that mentholated cigarette smoking enhances systemic nicotine exposure. |
| Campero M, Baumann TK, Bostock H, Ochoa JL. | Human cutaneous c fibres activated by cooling, heating, and menthol. | 2009 | NIH Grant no. R01-NS48932 | Not Applicable | 18 adult volunteers over 4 years (11 males and 7 females) ages 17-52 years (mean age 27.3) | N=18 | We propose that the Type 2 C fibres, although resembling Aδ cold fibres in their repsosnes to innocuous cooling and menthol, have a more complex sensory function, colouring with a 'hot-burning' quality the perceptions of low and high temperatures. |
| Dessirier JM, O'Mahony M, Carstens E. | Oral irritant properties of menthol: sensitizing and desensitizing effects of repeated application and cross- | 2001 | Grant from the California Tobacco-Related Disease Research Program No. 6RT-0231 | 3 Experimental Design | Experiment 1: Healthy Males and females ages 18-43 yrs who were students and staff at University of California at Davis Experiment 2: Healthy | Experiment 1: N=22 (6 males and 16 females) Experiment 2: | These studies demonstrate 3 new properties of menthol as oral irritant chemical (a) exposure to menthol cross-desensitized irritation elicited by nicotine (b) When applied at a short (5-s) ISI, a significant proportion of subjects perceived the menthol irritation to increase briefly before desensitization appeared (c) when menthol was |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | desensitization to nicotine. | | | | Males and females ages 18-50 yrs who were students and staff at University of California at Davis, non smokers, and did not participate in Experiment 1. Experiment 3 was same as Exp 1 & 2 | N=27 (5 males and 22 females) | reapplied following a rest period, most subjects appeared to exhibit recovery from desensitization. |
| Galeotti N, Di Cesare Mannelli L, Mazzanti G, Bartolini A, Ghelardini C. | Menthol: a natural analgesic compound. | 2002 | No funding source(s) provided. Authors affiliated with University of Florence, Italy | Experimental | Not Applicable | Not Applicable | Menthol cross-desensitizes a class of capsaicin-sensitive nociceptors, resulting in analgesic activity. In rodents, menthol produced dose-dependent analgesic effects, postulated to work via activation of the K opioid system |
| Green BG, Schullery MT. | Stimulation of bitterness by capsaicin and menthol: differences between lingual areas innervated by the glossopharyngeal and chorda tympani nerves. | 2003 | Funded by a grant from the National Institutes of Health R01 DC 05002 | Not Specified | Adults between ages of 18-45 yrs. old at Yale. | Exp 1: 15 (11 females and 4 males) Exp 2: 16 (9 females and 7 males) | Study suggests that Capsaicin and menthol are capable of stimulating a subset of taste neurons that respond to bitter substance and that the glossopharyngeal nerve may contain more such neurons than the chorda tympani nerve. |
| Heck JD. | Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. | 2009 | No funding source(s) provided. Author affiliated with Lorillard Tobacco Company | Cross-sectional | male and female subjects 24 to 70 yrs of age, having a minimum smoking history of 3 pack-years, and reporting consumption of $\geq$15 menthol or nonmenthol cigarettes daily for the past year, | N=112 (54 menthol, 58 nonmenthol) | The present findings indicate that moderately heavy smokers of menthol and nonmenthol cigarettes of similar machine-generated smoke yield exhibit essentially identical levels of biomarkers of smoke constituent exposure. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| Ito S, Kume H, Shiraki A, Kondo M, Makino Y, Kamiya K, Hasegawa Y. | Inhibition by the cold receptor agonists menthol and icilin of airway smooth muscle contraction. | 2008 | Grant-in-Aid for Young Scientists A, Scientific Research C, and the 21th Century COE Program from the Ministry of Education, Culture, Sports, Science, and Technology of Japan | In Vitro | Male Hartley guinea pigs | Not Specified | Findings support the use of menthol for reducing airflow limitation and chest congestion in patients with symptomatic airway diseases. |
| Jarvik ME, Tashkin DP, Caskey NH, McCarthy WJ, Rosenblatt MR. | Mentholated cigarettes decrease puff volume of smoke and increase carbon monoxide absorption. | 1994 | California Tobacco Related Disease Research Program Grant #1 RT 0087; Medical Research Service, U.S. Departement of Veterans Affairs; Division of Lung Diseases, National Heart, Lung, and Blood Institute Contract NO-HR 46022 | Comparative | Black and white male subjects with a self-reported history of smoking at least 15 cigarettes per day on a regular basis. Half were regular and half were menthol smokers. | N=20 (10 black, 10 white) | Compared to regular cigarettes, mentholated cigarettes produced a significantly greater boost in carbon monoxide measured as both blood carboxyhemoglobin and end-expired carbon monoxide, despite the fact that mentholated cigarettes decreased average and total cumulative puff volumes and increased mean puff flow rates of inhaled smoke. |
| Kühn FJ, Kühn C, Lückhoff A. | Inhibition of TRPM8 by icilin distinct from desensitization induced by menthol and menthol derivatives. | 2009 | the Deutsche Forschungsgemeinschaft Grant DFG KU 2271/1-1 | Experimental | Not Applicable | Not Applicable | In this study we have demonstrated that the menthol derivatives WS-12, CPS-369, and CPS-154 act identically with menthol in terms of Ca2+-independent current activation andCa2+-dependent induction of desensitization on wild-type TRPM8 as well as on the S3 mutant. |
| Laude EA, Morice AH, Grattan TJ. | The antitussive effects of menthol, camphor and cineole in conscious guinea-pigs. | 1994 | No funding source(s) provided. Authors affiliated with University of Sheffield, UK | Experimental | Guinea Pigs | N=13 | Menthol proved the most effective antitussive -- 10 and 30 micrograms/l produced a significant 28 and 56% reduction in cough frequency. |
| Lin JP, Lu HF, Lee JH, Lin JG, Hsia TC, Wu LT, Chung JG. | (-)-Menthol inhibits DNA topoisomerases I, II alpha and beta and promotes NF- | 2005 | Grants CMC90-CM-01 and CMC91-CM-02 from the Research Section of China Medical University, Taichung City, Taiwan, | Experimental | Human gastric SNU-5 cancer cells | Not Specified | (-)-Menthol may induce cytotoxicity through inhibiting gene expression of topoisomerase I, IIalpha and IIbeta and promoting the gene expression of NF-kappaB in SNU-5 cells. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | kappaB expression in human gastric cancer SNU-5 cells. | | R.O.C. | | | | |
| MacDougall JM, Fandrick K, Zhang X, Serafin SV, Cashman JR. | Inhibition of human liver microsomal (S)-nicotine oxidation by (-)-menthol and analogues. | 2003 | University of California Tobacco Related Disease Research Program (Grant 9RT-0196) and a Cornelius Hopper Diversity Award | Comparative, In Vitro | Not Specified | Not Specified | While highly potent inhibition of P450 2A6 was not observed for the menthol analogues examined, it is nevertheless possible that smoking mentholated cigarettes leads to inhibition of nicotine metabolism and allows the smoker to achieve a certain elevated dose of nicotine each day. |
| McCarthy WJ, Caskey NH, Jarvik ME, Gross TM, Rosenblatt MR, Carpenter C. | Menthol vs nonmenthol cigarettes: effects on smoking behavior. | 1995 | Cigarette and Tobacco Surtax Fund of the State of California through the Tobacco-Related Disease Research Program of the University of California, grant 1 RT-87 | Controlled Clinical Trial, Comparative | Healthy male smokers | N=29 | Whatever the mechanism by which menthol facilitates absorption of carbon monoxide (and probably nicotine), the study's repeated-measures data suggest that inferences about the genetic basis for observed racial differences in blood cotinine levels may be premature, and conjectures about the effects of menthol in cigarettes on smoking behavior may need to be modified. |
| Orani GP, Anderson JW, Sant'Ambrogio G, Sant'Ambrogio FB. | Upper airway cooling and l-menthol reduce ventilation in the guinea pig. | 1991 | National Heart, Lung, and Blood Institute Grant HL-20122 | Experimental | Guinea Pigs | N=23 | Both cooling of the larynx and l-menthol in the laryngeal lumen reduce ventilation. Exposure of the nasal cavity to l-menthol markedly enhances this ventilatory inhibition; considering the stimulatory effect of l-menthol on cold receptors, these results suggest a predominant role of nasal cold receptors in this response. |
| Pickworth WB, Moolchan ET, Berlin I, Murty R. | Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery. | 2002 | National Institute on Drug Abuse intramural funds | Randomized Controlled Trial, Comparative | The menthol group was composed of 13 men and 5 women; 17 were African American, 1 was Caucasian. The nonmenthol group was composed of 14 men and 4 women; 3 were African American, 15 | 36 Menthol (n=18) and non-menthol (n=18) cigarette smokers) | Nicotine delivery, but not mentholation, influences cardiovascular and most subjective measures. These results illustrate the importance of threshold levels of nicotine on subjective responses to cigarette smoking. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | were Caucasian. | | |
| Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G. | Effect of l-menthol on laryngeal receptors. | 1991 | National Heart, Lung, and Blood Institute Grant HL-20122 | Experimental | Dogs | N=11 | L-menthol constitutes a specific stimulant of laryngeal cold receptors and could provide a useful tool for the study of their reflex effects. |
| Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G. | Menthol in the upper airway depresses ventilation in newborn dogs. | 1992 | National Institutes of Health Grant HL-20122 | Experimental | Newborn dogs | N=8 | However, a residual depressive effect of/-menthol was still present in 3 of 5 animals and was abolished by nasal anesthesia, suggesting the involvement of nasal cold receptors. |
| Sekizawa S, Tsubone H, Kuwahara M, Sugano S. | Nasal receptors responding to cold and l-menthol airflow in the guinea pig. | 1996 | JSPS Fellowships for Japanese Junior Scientists | In Vitro | Guinea Pigs | Not Specified | L-menthol noticeably stimulated the EN even after repeated capsaicin instillation into the nose, but these values were lower than those following the /-menthol stimulus before the 1st capsaicin treatment. |
| Sherkheli MA, Gisselmann G, Vogt-Eisele AK, Doerner JF, Hatt H. | Menthol derivative WS-12 selectively activates transient receptor potential melastatin-8 (TRPM8) ion channels. | 2008 | IMPRS-CB, Research Excellence School of Bochum and DAAD | Experimental | TRPM8 Ion channels | Not Specified | The selectivity profile of WS-12, its several-fold higher potency and around two-fold increase in efficacy compared to menthol warrants its potential utility for therapy in chronic neuropathic pain states and as a diagnostic probe in prostate cancer. |
| Sidell N, Verity MA, Nord EP. | Menthol blocks dihydropyridine-insensitive Ca2+ channels and induces neurite outgrowth in human neuroblastoma cells. | 1990 | National Institutes of Health grants CA 43503, CA 30515, DK 36351, and DK 41585 | Comparative | Human neuroblastoma cells | Not Specified | The parallel potency for blockade of DHP-insensitive Ca2+ influx with the biologic activity of menthol suggests a role for certain types of Ca2+ channels in triggering growth and morphologic changes in LA-N-5. |
| Squier, CA, MJ Mantz, PW Wertz. | Effect of menthol on the penetration of tobacco carcinogens and | 2010 | The Dows Institute for Dental Research, College of Dentistry, University of Iowa | Experimental | Porcine tissue | Not Specified | Menthol enhances penetration of NNN and nicotine through FM and BM in vitro, even after short exposure. Practical implications are for a potentially increased oral exposure to |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

# Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | nicotine across porcine oral mucosa ex vivo. | | | | | | carcinogens among users of menthol-flavored cigarettes and chewing tobacco. |
| Wang J, Roethig HJ, Appleton S, Werley M, Muhammad-Kah R, Mendes P. | The effect of menthol containing cigarettes on adult smokers' exposure to nicotine and carbon monoxide. | 2010 | No funding source(s) provided. Authors affiliated with Altria Client Services]. | Cross-sectional, observational, ambulatory, multi-centre study | African-American and White adult males and females, 21 years old or older, in generally good health, from 31 states (39 investigative sites across the United States), were enrolled into one of 4 parallel groups based on the smoking machine derived tar categories (i.e., 62.9 mg tar; 3.0–6.9 mg tar; 7.0–12.9 mg tar; and P13.0 mg tar) of the cigarettes they smoked. | N=3341 | Smoking mentholated cigarettes does not increase daily exposure to smoke constituents as measured by NE and COHb. These findings are consistent with the majority of epidemiological studies indicating no difference in smoking related risks between MS and NMS. |
| Wright CE, Laude EA, Grattan TJ, Morice AH. | Capsaicin and neurokinin A-induced bronchoconstriction in the anaesthetised guinea-pig: evidence for a direct action of menthol on isolated bronchial smooth muscle. | 1997 | No funding source(s) provided. Authors affiliated with University of Sheffield | Experimental | Dunkin-Hartley Guinea-pigs | N=24 | Menthol attenuates both capsaicin and NKA-induced bronchoconstriction in vivo and relaxes KCl and ACh preconstricted bronchi in vitro. Menthol inhibition of NKA and capsaicin-induced bronchoconstriction could be, in part, explained by a direct action of menthol on bronchial smooth muscle. |
| Yerger VB, McCandless PM | Menthol sensory qualities and smoking topography: a review of tobacco industry documents | 2011 | Department of Health and Human Services Contract HHSN261201000035I, California Tobacco-Related Disease Research Program, Grant #16RT- | Review of publicly available tobacco industry documents | Not Applicable | 252 publicly available internal tobacco industry documents | Our review of industry studies suggests that the amount of menthol in a cigarette is associated with how the cigarette is smoked and how satisfying it is to the smoker. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Physiology: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | 0149, and National Cancer Institute grant CA113710-05 | | | | |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

References

1. Ahijevych K, Garrett BE. (2004). Menthol pharmacology and its potential impact on cigarette smoking behavior. Nicotine & Tobacco Research 6(suppl 1):S17e28. [Funded by National Institute on Drug Abuse grant 10809 and General Clinical Research Center grant M01 RR00034]
2. Ahijevych K, Gillespie J, Demirci M, Jagadeesh, J. (1996). Menthol and nonmenthol cigarettes and smoke exposure in black and white women. Pharmacology Biochemistry and Behavior 53:355e60. [Funded by The Ohio State University Seed Grant and The Ohio State University General Clinical Research Center Grant MO1 RROO034]
3. Ahijevych K, Parsley LA. (1999). Smoke constituent exposure and stage of change in black and white women cigarette smokers. Addictive Behaviors 24:115e20. [Funded by an American Lung Association Research Grant, and General Clinical Research Center M01 RR00034]
4. Azzi C, Zhang J, Purdon CH, Chapman JM, Nitcheva D, Hebert JR, Smith EW. (2006). Permeation and reservoir formation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo[a]pyrene (B[a]P) across porcine esophageal tissue in the presence of ethanol and menthol. Carcinogenisis 27(1):137-45. [Funded by a MUSC/USC/HCC Department of Defense Funds, Phase VI, Cancer Prevention and Control Research Development Grant]
5. Benowitz NL, Herrera B, Jacob P 3rd. (2004) Menthol cigarette smoking inhibits nicotine metabolism. Journal of Pharmacology and Experimental Therapeutics 310(3):1208-15. [Funded by State of California Tobacco Related Disease Research Program Grant 1RT-0521, by U.S. Public Health Service Grants DA02277 and DA12393 awarded by the National Institute on Drug Abuse and CA32389 awarded by the National Cancer Institute, and by the General Clinical Research Center at San Francisco General Hospital Medical Center with the support of the Division of Research Resources, National Institutes of Health (RR-00083)]
6. Campero M, Baumann TK, Bostock H, Ochoa JL. (2009). Human cutaneous C fibers activated by cooling, heating and menthol. Journal of Physiology 587(Pt 23):5633-52. [Funded by NIH Grant no. R01-NS48932]
7. Dessirier JM, O'Mahony M, Carstens, E. (2001). Oral irritant properties of menthol sensitizing and desensitizing effects of repeated application of cross-desensitization to nicotine. Physiology & Behavior, 73:25-36. [Funded by a grant from the California Tobacco-Related Research Disease Program No. 6RT-0231]
8. Galeotti N, Di Cesare Mannelli L, Mazzanti G, Bartolini A, Ghelardini C. (2002). Menthol: a natural analgesic compound. Neuroscience Letters 322(3):145-8. [No funding source(s) provided. Authors affiliated with University of Florence, Italy]
9. Green BG, Schullery MT (2003). Stimulation of bitterness by capsaicin and menthol: Differences between linguaal areas innervated by the glossopharyngeal and chorda tympani nerves. Chemical Senses 28:45-55. [Funded by a grant from the National Institutes of Health R01 DC 05002]
10. Heck JD (2009) Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. Cancer Epidemiology Biomarkers and Prevention 18(2):622-9. [No funding source(s) provided. Author affiliated with Lorillard Tobacco Company]

11. Ito S, Kume H, Shiraki A, Kondo M, Makino Y, Kamiya K, Hasegawa Y. (2008). Inhibition by the cold receptor agonists menthol and icilin of airway smooth muscle contraction. Pulmonary Pharmacology and Therapeutics21(5):812-7. [Funded by Grant-in-Aid for Young Scientists A, Scientific Research C, and the 21th Century COE Program from the Ministry of Education, Culture, Sports, Science, and Technology of Japan]
12. Jarvik ME, Tashkin DP, Caskey NH, McCarthy WJ, Rosenblatt MR (2004). Menthol cigarettes decrease puff volume of smoke and increase carbon monoxide absorption. Physiology & Behavior 1994;56:563e70. [Funded by California Tobacco Related Disease Research Program Grant #1 RT 0087; Medical Research Service, U.S. Departement of Veterans Affairs; Division of Lung Diseases, National Heart, Lung, and Blood Institute Contract NO-HR 46022]
13. Kühn FJ, Kühn C, Lückhoff A. (2009). Inhibition of TRPM8 by icilin distinct from desensitization induced by menthol and menthol derivatives. Journal of Biological Chemistry 284(7):4102-11. [Funded by the Deutsche Forschungsgemeinschaft Grant DFG KU 2271/1-1]
14. Laude EA, Morice AH, Grattan, TJ. (1994) The antitussive effects of menthol, camphor and cineole in conscious guinea pigs. Pulmonary Pharmacology 7:179-184. [No funding source(s) provided. Authors affiliated with University of Sheffield, UK]
15. Lin JP, Lu HF, Lee JH, Lin JG, Hsia TC, Wu LT, Chung JG. (2005). (-)-Menthol inhibits DNA topoisomerases I, II alpha and beta and promotes NF-kappaB expression in human gastric cancer SNU-5 cells. Anticancer Research 25(3B):2069-74. [Funded by grants CMC90-CM-01 and CMC91-CM-02 from the Research Section of China Medical University, Taichung City, Taiwan, R.O.C.]
16. MacDougall JM, Fandrick K, Zhang X, Serafin SV, Cashman JR. (2003). Inhibition of human liver microsomal (S)-nicotine oxidation by (-)-menthol and analogues. Chemical Research in Toxicology 16(8):988-93. [Funded by the University of California Tobacco Related Disease Research Program (Grant 9RT-0196) and a Cornelius Hopper Diversity Award]
17. McCarthy WJ, Caskey NH, Jarvik ME, Gross, TM, Rosenblatt, MR, Carpenter, C. (1995). Menthol vs.nonmenthol cigarettes: effects on smoking behavior. American Journal of Public Health 1995;85:67e72. [Funded by the Cigarette and Tobacco Surtax Fund of the State of California through the Tobacco- Related Disease Research Program of the University of California, grant 1 RT-87]
18. Orani GP, Anderson JW, Sant'Ambrogio G, Sant'Ambrogio FB. (1991). Upper airway cooling and l-menthol reduce ventilation in the guinea pig. Journal of Applied Physiology 70:2080–2086. [Funded by the National Heart, Lung and Blood Institute Grant HL-20122.]
19. Pickworth WB, Moolchan ET, Berlin I, Murty R. (2002). Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery. Pharmacology Biochemistry and Behavior. 71(1-2):55-61. [Funded by National Institute on Drug Abuse intramural funds]
20. Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G (1991) Effect of l-menthol on laryngeal receptors. Journal of Applied Physiology 70:788–793. [Funded by National Heart, Lung, and Blood Institute grant HL-20122]

21. Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G. (1992). Menthol in the upper airway depresses ventilation in newborn dogs. Respiration Physiology 89(3):299-307. [Funded by National Heart, Lung, and Blood Institute grant HL-20122]
22. Sekizawa SI, Tsubone H, Kuwahara M, Sugana S. (1996). Nasal receptors responding to cold and l-menthol airflow in the guinea pig. Respiration Physiology 103(3):211–219. [Funded by JSPS Fellowships for Japanese Junior Scientists, IMPRS-CB]
23. Sherkheli MA, Gisselmann G, et al. (2008) Menthol derivative WS-12 selectively activates transient receptor potential melastatin-8 (TRPM8) ion channels. Pakistan Journal of Pharmaceutical Sciences, 21(4):370–378. [Funded by IMPRS-CB, Research Excellence School of Bochum and DAAD]
24. Sidell N, Verity MA, Nord EP (1990) Menthol blocks dihydropyridine-insensitive Ca2+ channels and induces neurite outgrowth in human neuroblastoma cells. Journal of Cellular Physiology 142(2):410–419. [Funded by National Institutes of Health grants CA 43503, CA 30515, DK 36351 and DK 41585]
25. Squier CA, Mantz MJ, Wertz PW (2010) Effect of menthol on the penetration of tobacco carcinogens and nicotine across porcine oral mucosa ex vivo. Nicotine and Tobacco Research 12(7):763-7 [Funded by the Dows Institute for Dental Research, College of Dentistry, University of Iowa]
26. Wang J, Roethig HJ, Appleton S, et al. (2010): The effect of menthol containing cigarettes on adult smokers' exposure to nicotine and carbon monoxide. Regulatory Toxicology and Pharmacology 57:24–30. [No funding source(s) provided. Authors affiliated with Altria Client Services].
27. Wright CE, Laude EA, et al (1997) Capsaicin and neurokinin A-induced broncho-constriction in the anaesthetised guinea-pig: evidence for a direct action of menthol on isolated bronchial smooth muscle. British Journal of Pharmacology 121(8):1645–1650. [No funding source(s) provided. Authors affiliated with University of Sheffield]
28. Yerger VB, McCandless PM. (2011) Menthol sensory qualities and smoking topography: a review of tobacco industry documents. Tobacco Control 20(suppl 2):ii37-43. [Funded by the Department of Health and Human Services Contract HHSN261201000035I, California Tobacco-Related Disease Research Program, Grant #16RT-0149, and National Cancer Institute grant CA113710-05]

## *C. Biomarkers*

Biomarkers of exposure are used to objectively measure and evaluate levels of exposure to particular chemicals. Biomarkers that are used to evaluate smoke exposure include particular smoke constituents and/or their metabolites in biological specimens (e.g., exhaled air, saliva, blood, urine). Specifically, biomarkers assessed here include expired carbon monoxide (CO) and blood carboxyhemoglobin (COHb) for levels of CO exposure, cotinine and other nicotine equivalents in serum and urine for exposure to nicotine, and total NNAL in urine for exposure to TSNAs. Very limited data are available for other biomarkers of exposure and biomarkers of potential harm.

*Biomarkers of exposure to CO*

Miller et al. (1994) measured the exhaled CO levels in male smokers (n = 12) who participated in three controlled-dose smoking sessions spaced one week apart. Exhaled CO levels increased along with menthol external dose. The authors proposed that these results suggested that menthol cigarette preference may account for some of the racial differences in smoking behavior and smoking-related outcomes.

In a cross-sectional study, Clark et al. (1996) found that, compared with White smokers (n=96), African American smokers (n=65) had significantly higher breath CO levels per cigarette smoked and per millimeter of the smoked tobacco rod after adjusting for race, cpd, and mean amount of each cigarette smoked.

Williams et al. (2007) examined expired CO for 89 smokers with schizophrenia and 53 control smokers two minutes after smoking an afternoon cigarette. Expired CO was higher in menthol compared with nonmenthol smokers, controlling for group, cpd, and race. The higher exhaled CO in menthol smokers suggests an increased intake of smoke from menthol cigarettes.

One study found menthol cigarettes were associated with decreased breath CO. Ahijevych et al. (1996) conducted a two-factor factorial trial with a sample of 37 women stratified by race and menthol or nonmenthol cigarette use. For CO boost, there was a significant main effect for race (African Americans > Whites) and a main effect for menthol or nonmenthol use (nonmenthol > menthol).

Benowitz et al. (2004) found that mentholation of cigarettes did not affect systemic intake of nicotine and CO in a crossover study with 14 smokers.

*Biomarkers of exposure to nicotine*

In a small, experimental study with 32 women, Ahijevych et al. (2002) examined the effect of selected factors of ethnicity, menthol cigarette preference, body composition and alcohol-use history on cotinine half-life. Being an African American menthol smoker, fewer years of alcohol use, and greater lean body mass explained 52.0 percent of the variance in cotinine half-life and was associated with a longer half-life. Among menthol smokers, baseline cotinine level and cotinine half-life were not significantly different between White and African American women.

Clark et al. (1996) found that, compared with White smokers (n=96), African American smokers (n=65) had significantly higher serum cotinine levels per cigarette smoked and per millimeter of smoked tobacco rod after adjusting for race, cpd, and mean amount of each cigarette smoked.

Using a sample of 359 participants, Mustonen et al. (2005) observed a positive correlation between cotinine and CO in all smokers and a correlation between cotinine and cpd in nonmenthol smokers. Among menthol smokers, cotinine and cpd correlations varied by gender and race. Results showed trends to higher cotinine levels in menthol smokers, although the differences were not statistically significant. The cotinine:cpd ratio was significantly higher among menthol smokers compared to nonmenthol smokers (p=0.004). A significant gender by race by menthol interaction existed on salivary cotinine level as well as cotinine:cpd ratio.

Williams et al. (2007) examined serum nicotine and cotinine for 89 smokers with schizophrenia and 53 control smokers two minutes after smoking an afternoon cigarette. Serum nicotine and cotinine levels were higher in smokers of menthol compared with nonmenthol cigarettes. There were no differences in 3-hydroxycotinine:cotinine ratios between groups when controlling for race. Further linear regression models showed that smoking menthol cigarettes was a significant predictor of nicotine and cotinine levels. The higher exhaled CO in menthol smokers described above suggests that the higher nicotine levels are at least partially related to increased smoke intake from menthol cigarettes. These authors suggested that menthol might be associated with increased health risks of smoking.

In a crossover study of 14 participants, Benowitz et al. (2004) found that mentholation of cigarettes did not affect systemic intake of nicotine. However, menthol cigarette smoking inhibited the metabolism of nicotine by slower oxidative metabolism to cotinine and by slower glucuronide conjugation.

*White and African American Smokers*

Perez-Stable et al. (1998) found higher levels of cotinine per cigarette smoked by African Americans (n=40) compared with Whites (n=39). Both slower clearance of cotinine and higher intake of nicotine per cigarette in African Americans explain this result.

Caraballo et al. (1998) provided evidence from a large national study (n=7182) that African American smokers have higher serum cotinine levels than do White or Mexican American smokers, after adjustment for cpd, age, sex, body weight, number of smokers living in the home, and number of hours exposed at work to environmental tobacco smoke.

Using data from smokers in the the CARDIA longitudinal cohort study (n=1424), Wagenknecht et al. (1990) found signficantly higher serum cotinine levels in African American smokers as compared to White smokers. This difference remained significant after adjusting for cpd, nicotine content of the cigarette, years of smoking, inhalation frequency, and demographic factors. This difference was not explained by reporting bias or nicotine intake differences. The study suggested that the differences in serum cotinine levels may be due to innate differences between the races in the metabolism or excretion of nicotine or cotinine.

In a study of 91 adolescents seeking cessation treatment, Moolchan et al. (2006) found that African Americans (n=30) smoked significantly fewer cpd and had lower nicotine metabolite ratios when compared to White smokers (n=61). Consistent with metabolic variation, mean plasma cotinine:cpd ratio was significantly higher in African American compared to White adolescents. Results remained statistically significant when comparing menthol smokers by ethnicity. The data suggested that observed differences are due to factors other than menthol smoking and suggest that accounting for racial or ethnic differences is crucial for interpreting group differences.

*Menthol and Nonmenthol Smokers*

Using data from 1999–2002 NHANES (n=1520), Gan et al. (2008) found that serum cotinine levels were significantly higher in menthol smokers compared with nonmenthol smokers using a univariate model but not significantly higher using a multivariate model adjusted for gender, cpd, age, race, BMI, poverty status, Federal Trade Commission test nicotine content in each cigarette, and menthol or nonmenthol use.

In a sample of 37 white and African American women, Ahijevych et al. (1996) found no significant differences in nicotine boost by race and/or menthol or nonmenthol use.

In a community-based cross-sectional study (n=525), Muscat et al. (2009) found no significant differences in measures of smoking exposure (metabolites of nicotine or NNAL) by menthol status in either white or African American smokers.

Patterson et al. (2003) investigated the demographic, smoking status, and psychological predictors of nicotine boost in a clinical trial with 190 treatment-seeking smokers. Boost was assessed by comparing plasma nicotine levels before and after participants smoked one of their own brand of cigarettes as desired. Menthol or nonmenthol brand was not associated with the nicotine boost.

Using samples of 255 current smokers from the Southern Community Cohort Study participants, Signorello et al. (2009) found higher serum cotinine levels in African American compared with White smokers, particularly for women, and observed no increase in serum cotinine levels associated with menthol cigarette use after adjusting for age, race, sex, and cpd. The authors concluded that the differences in serum cotinine levels among smokers might be due to racial variation in exposure to and/or metabolism of tobacco smoke constituents.

*Biomarkers of exposure to TSNAs*

In a community-based cross-sectional study, Muscat et al. (2009) found no significant differences in measures of smoking exposure (metabolites of nicotine or NNAL). The NNAL-glucuronide(Gluc):NNAL ratio between smokers of menthol (n=67) and nonmenthol (n=80) cigarettes was 34 percent lower in Whites ($P < 0.01$) and 22 percent lower in African Americans; the difference in African Americans was not statistically significant.

In a study of 109 current smokers, Strasser et al. (2011) found faster nicotine metabolizers had greater total puff volume and total NNAL. Groups with more nonmenthol smokers (quartiles three and four) appeared to have higher mean NNAL than groups with fewer nonmenthol smokers (quartiles one and two) although the difference was not statistically significant.

Richie et al. (1997) found that urinary NNAL-Gluc:NNAL ratios, a likely indicator of NNAL glucuronidation and detoxification, were significantly greater in Whites (n=27) than in African Americans (n=34). The absolute levels of urinary NNAL, NNAL-Gluc, and cotinine were also greater in African Americans than in Whites when adjusted for the cpd. Dissimilarities in exposure or other sociodemographic or dietary factors did not explain observed racial differences. Also, it is unlikely that the dissimilarities are due to racial differences in preference for menthol cigarettes, because chronic administration of menthol to NNK-treated rats did not result in either increases in urinary total NNAL or decreases in NNAL-Gluc:NNAL ratios. Altogether, these results suggest that racial differences in NNAL glucuronidation may explain in part the observed racial differences in lung cancer risk.

*Additional Evidence Based on Altria Total Exposure Study*

FDA analyzed additional data from the Altria TES using unadjusted and adjusted regression models, which were collected from over 5,000 participants. The variables in the adjusted model consisted of gender, race, education, income, Hispanic ethnicity, BMI, number of years and cigarettes smoked, tar delivery category, and total puff volume. Biomarkers of exposure include urine level measures of total nicotine equivalents, total NNAL, total 1-hydroxypyrene (1-OHP), total 3-hydroxypropyl mercapturic acid (3-HPMA), total monohydroxy-3-butenyl mercapturic acids (MHBMA), total 1, 2-dihydroxybutyl mercapturic acid (DHBMA), and serum level measurements of cotinine, carboxyhemoglobin, and red blood cell 4-aminobiphenyl (4-ABP) hemoglobin (Hb) adducts. All biomarkers obtained from urine measurements were analyzed as cigarette-adjusted and creatinine-adjusted measures as well as totals. The analysis found no statistically significant differences between menthol and nonmenthol smokers in any biomarkers of exposure in the adjusted model. The observed statistically significant differences in biomarkers of exposure (unadjusted data) between menthol and nonmenthol smokers may be due to differences in demographic or smoking behavior characteristics between menthol and nonmenthol smokers. In both the total and creatinine-adjusted measures, menthol smokers showed significantly lower levels of exposure to nicotine equivalents ($p<0.0001$ and $p=0.0002$, respectively), NNAL ($p<0.0001$ and $p=0.0002$), 3-HPMA ($p<0.0001$ and $p<0.0001$), MHBMA ($p<0.0001$ and $p<0.0001$), and DHBMA ($p<0.0001$ and $p<0.0001$) in the unadjusted model. However, no per cigarette measure for these outcomes showed any statistically significant differences between menthol and nonmenthol smokers. Menthol smokers showed significantly higher levels of 1-OHP exposure per cigarette than nonmenthol smokers ($p=0.0002$) in the unadjusted model. However, no significant differences in exposure to 1-OHP per cigarette between menthol and nonmenthol smoker were observed in the adjusted model. The unadjusted 3-hydroxycotinine:cotinine ratio was significantly higher (indicating more rapid detoxification) in menthol smokers ($p<0.0001$). However, the significance of this difference did not persist after adjusting for demographic and smoking behavior variables. Neither the nicotine:cotinine ratio in the adjusted or unadjusted model showed any significant differences between menthol and nonmenthol smokers. The likely explanation for this result lies with differences between African American and other racial groups' cotinine levels.

In the TES, biomarkers of potential harm included urine level measures for 8-epi prostaglandin-F2$\alpha$ and 11-dehydrothromboxane-B2 and serum level measures of total bilirubin, white blood cells, C-reactive protein, fibrinogen, von Willebrand factor antigen, total, high density lipoprotein (HDL), low density lipoprotein (LDL), and oxidized LDL cholesterol, triglycerides, forced expiratory volume in one second (FEV1), and forced expiratory vital capacity (FVC). Urine measurements were analyzed as creatinine-adjusted measures as well as totals. In the unadjusted model, menthol smokers showed significantly lower levels of total cholesterol ($p=0.0002$), LDL cholesterol ($p=0.0053$), and triglycerides ($p<0.0001$), and higher levels of HDL cholesterol ($p=0.0016$). However, these differences were no longer significant after adjustment for demographic and smoking behavior variables. Menthol smokers also showed significantly lower unadjusted levels of 8-epi prostaglandin-F2 (p=0.0491), white blood cells (p=0.0002), and total bilirubin (p=0.0012), but higher levels of the van Willebrand antigen factor (p=0.0172). The only difference between menthol and nonmenthol smokers that remained statistically significant in the adjusted model was for 8-epi prostaglandin-F2 (p=0.0318). However, the effect of menthol on 8-epi prostaglandin-F2 reversed direction after adjustment for demographic characteristics and smoking behavior, with menthol smokers showing significantly higher levels of 8-epi prostaglandin of about 99 ng per 24 hour period higher for menthol smokers.

FDA also analyzed demographic, smoking, and biomarker levels for over 5000 smokers participating in the National Health and Nutrition Examination Survey (NHANES) from 1999-2008. Researchers used linear regression, controlling for demographic, health, and smoking characteristics to analyze the associations between menthol cigarette use and biomarker levels. Menthol cigarette use was not associated with higher serum cotinine levels on a per cigarette basis. There was no statistically significant difference for NNAL levels for menthol smokers compared to nonmenthol smokers, although additional data are needed to more precisely estimate any association for this biomarker.

Menthol secondary data analysis (through RTI subcontracts) of the Hersey study examined the relationship in youth (n= 5,511) between smoking menthol cigarettes, salivary cotinine levels, and nicotine dependence. Controlling for age, sex, race or ethnicity, and the length, frequency, and level of smoking, descriptive and regression analysis found that menthol versus nonmenthol cigarette use was not significantly associated with salivary cotinine level models that included cpd smoked. Among youth who smoked for less than one year, a significant interaction exists between menthol use and the number of cigarettes smoked per day -- menthol cigarette use was associated with increased salivary cotinine levels among heavier smokers. Findings were similar for Whites and non-Whites.

*Industry Assessment of Menthol Effects*

Not all studies support the hypothesis that menthol cigarette smoking results in a greater absorption of tobacco smoke chemicals. In an industry-sponsored study, Heck (2009) found median blood carboxyhemoglobin values, total urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), and urinary nicotine equivalents were not significantly different between the menthol and nonmenthol cigarette smokers. In an industry-sponsored study, Wang et al. (2010) found smoking menthol cigarettes does not increase daily exposure to smoke constituents as measured by nicotine equivalents (total and per cigarette), serum cotinine and COHb after adjusting for the number of cigarettes smoked per day and the smoking behavior characteristics of the participants. In its presentation to TPSAC, Altria Client Services presented analysis of the TES that also showed no differences between users of menthol and nonmenthol brands in the TES for a wide variety of biomarkers of exposure, biomarkers of potential harm, nicotine metabolite ratios, and measures of smoker topography and nicotine dependence after adjustment for the number of cigarettes per day and smoking behavior characteristics.

*Conclusion*

Although a few small studies have found that smoking menthol cigarettes may modulate exposure or metabolism of CO, nicotine, and/or TSNAs, several large, well-designed studies failed to find statistically significant differences in biomarkers between smoking menthol or nonmenthol cigarettes. Considering all available studies, but with more emphasis given to the findings of the large, well-controlled studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely not associated with increased or decreased levels of biomarkers of exposure.

Biomarkers: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Ahijevych K, Gillespie J, Demirci M, Jagadeesh J. | Menthol and nonmenthol cigarettes and smoke exposure in black and white women. | 1996 | The Ohio State University Seed Grant; The Ohio State University General Clinical Research Center Grant MO1 RR00034 | Cross sectional 2 factor factorial design | Black and White Women 19-59 years old, smoked ≤20 cpd | N=37 (18 Black, 19 White) | In the current study, lower CO boost with mentholated cigarettes suggests that factors beyond mentholation may affect differences in cotinine levels in black and white women. |
| Ahijevych KL, Tyndale RF, Dhatt RK, Weed HG, Browning KK. | Factors influencing cotinine half-life during smoking abstinence in African American and Caucasian women. | 2002 | National Institute on Drug Abuse DA10809, DA 06889 and The Ohio State University General Clinical Research Center M01 RR00034, and Ohio State University Academic Primary Care Program, USDHHS Bureau of Health Professions 1 D12 HP00027 | Analytic | African American and Caucasian women between 18-50 yrs. old who had smoked a minimum of 5 Cigarettes/day for at least 1 yr; no hx of liver/endocrine disease; not taking Rx or illicit drugs; not pregnant. | N=32 total women (16 African American and 16 White) | African American menthol smoking was a significant predictor of cotinine half-life in comparison to Caucasian non-menthol smoking. |
| Benowitz NL, Herrera B, Jacob P 3rd. | Mentholated cigarette smoking inhibits nicotine metabolism. | 2004 | State of California Tobacco Related Disease Research Program Grant 1RT-0521, by U.S. Public Health Service Grants DA02277 and DA12393 awarded by the National Institute on Drug Abuse and CA32389 awarded by the National Cancer Institute, and by the General Clinical Research Center at San Francisco General Hospital Medical Center with the support of the Division of Research Resources, National Institutes of Health (RR- | Cross Over | 14 healthy cigarette smokers recruited through local papers. (7 African-Americans and 7 whites, 12 men and 2 women. Participants were selected as typically smoking 20 or more cigarettes per day and having a prior experience of smoking both mentholated and nonmentholated cigarettes. | N=14 | Our finding of impaired metabolism of nicotine while mentholated cigarette smoking suggests that mentholated cigarette smoking enhances systemic nicotine exposure. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | 00083) | | | | |
| Caraballo RS, Giovino GA, Pechacek TF, Mowery PD, Richter PA, Strauss WJ, Sharp DJ, Eriksen MP, Pirkle JL, Maurer KR. | Racial and ethnic differences in serum cotinine levels of cigarette smokers: Third National Health and Nutrition Examination Survey, 1988-1991. | 1998 | No funding source(s) were listed. Authors associated with Centers for Disease Control and Prevention, and Batelle Memorial Institute | Third National Health and Nutrition Examination Survey, 1988-1991 | A nationally representative sample of persons aged 17 years or older (non-Hispanic blacks, non-hispanic whites, Mexican Americans) who participated in the survey | Of the 12 391 surveyed, data from 2136 subjects who reported smoking 1 cigarette or more in the past 5 days were included in the analyses. One of the analyses included data from both smokers and nonsmokers (n= 7182) | Blacks had higher cotinine levels than whites, even after ETS exposure and other factors were taken into account. The differences may be influenced by group-specific patterns of smoking behavior and may also be influenced by differences in nicotine pharmacokinetics and brand mentholation. |
| Clark PI, Gautam S, Gerson LW. | Effect of menthol cigarettes on biochemical markers of smoke exposure among black and white smokers. | 1996 | A grant from the American Heart Association, Florida Affiliate | Descriptive cross-sectional | University smoking research lab with 65 black and 96 white adult established smokers. | N=161 | After adjusting for race, cigarettes per day, and mean amount of each cigarette smoked, menthol was associated with higher cotinine levels (p=0.03) and carbon monoxide concentrations (p=0.02). |
| Gan WQ, Cohen SB, Man SF, Sin DD. | Sex-related differences in serum cotinine concentrations in | 2008 | The Canadian Institutes of Health Research (IGH/ICRH), the Canadian Lung Association, and the | Retrospective survey | Data from the National Health and Nutrition Examination Survey (NHANES), 1999–2002; | N=1,520 participants for the present | Menthol can inhibit nicotine metabolism and, as such, may prolong the half-life of nicotine and cotinine. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Biomarkers: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | daily cigarette smokers. | | Heart and Stroke Foundation of Canada. DDS is supported by a Canada Research Chair and a GlaxoSmithKline/Michael Smith/St. Paul's Hospital Foundation Professorship in COPD. | | daily smokers ≥ 20 years old who had smoked at least 100 cigarettes. Excluding those who used nicotine containing products other than cigarettes, and whose cotinine data were available. | analysis: 840 men and 680 women. | |
| Heck JD. | Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. | 2009 | No funding source(s) provided. Author affiliated with Lorillard Tobacco Company | Cross-sectional | male and female subjects 24 to 70 yrs of age, having a minimum smoking history of 3 pack-years, and reporting consumption of ≥15 menthol or nonmenthol cigarettes daily for the past year, | N=112 (54 menthol, 58 nonmenthol) | The present findings indicate that moderately heavy smokers of menthol and nonmenthol cigarettes of similar machine-generated smoke yield exhibit essentially identical levels of biomarkers of smoke constituent exposure. |
| Miller GE, Jarvik ME, Caskey NH, Segerstrom SC, Rosenblatt MR, McCarthy WJ. | Cigarette mentholation increases smokers' exhaled carbon monoxide levels. | 1994 | California Tobacco-Related Disease Research Program Grant 1 RT 87 | Empirical | Male smokers from the inpatient substance abuse ward at the Veterans Administration Medical Center, West Los Angeles. Subjects had to be free of pulmonary and respiratory disease, smoke a minimum of 15 cigarettes per day, and be free of psychotropic medication. | N=12 | Exhaled carbon monoxide levels increased concomitantly with menthol dosage. |
| Moolchan ET, Franken FH, Jaszyna-Gasior | Adolescent nicotine metabolism: | 2006 | National Institute on Drug Abuse, Intramural Research Program | Comparative | Adolescent, tobacco-dependent volunteers 13-17 years of age | N=91 (61 African American, | Menthol was recently shown to inhibit nicotine metabolism, although it did not appear to influence cotinine metabolism; study chose to |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

# Biomarkers: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| M. | ethnoracial differences among dependent smokers. | | | | recruited for a smoking cessation study between September 1999 and September 2003 | 30 White) | repeat the analyses comparing menthol smokers of both ethnicities. Results remained essentially unchanged, which suggests that the observed differences are due to factors other than menthol smoking |
| Mustonen TK, Spencer SM, Hoskinson RA Jr, et al. | The influence of gender, race, and menthol content on tobacco exposure measures | 2005 | National Institute on Drug Abuse grant DA12165 | Comparative | Boston-area participants in a randomized clinical trial of individualizing transdermal patch therapy treatment for cigarette smokers | N=307 | The cotinine/CPD ratio was, however, higher among menthol smokers than nonmenthol smokers, M=23.3 (SD=13.6) versus M=19.4 (SD=9.4), F(1, 303)=8.2, p=.004.<br><br>Post-hoc analyses indicated that White women smoking nonmenthol cigarettes have much lower cotinine values than do Black women smoking nonmenthol or menthol cigarettes (p=.05). |
| Patterson F, Benowitz N, Shields P, Kaufmann V, Jepson C, Wileyto P, Kucharski S, Lerman C. | Individual Differences in Nicotine Intake Per Cigarette. | 2003 | Transdisciplinary Tobacco Use Research Center Grant P50 CA84718 from the National Cancer Institute and National Institute on Drug Abuse and by USPHS Grants DD02277 and DA01696 from the National Institute on Drug Abuse | Not Specified | Male and female treatment-seeking smokers ages 18–75 years who reported smoking at least 10cpd. | N=190 (95 male, 95 female) | Among the smoking-related variables, cotinine level (r = 0.12; P = 0.09) and smoking rate (F= 2.26; P = 0.08) were marginally associated with boost, whereas nicotine/cotinine ratio (r = 0.11; P = 0.13), menthol/nonmenthol brand (t = 0.49; P = 0.63), cigarette type [i.e., light (t =1.6; P =0.11)], and nicotine dependence (r =0.07, P = 0.31) were not. |
| Pérez-Stable EJ, Herrera B, Jacob P 3rd, Benowitz NL. | Nicotine metabolism and intake in black and white smokers. | 1998 | State of California Tobacco-Related Disease Research Program grant 1RT-0521, Public Health Service grants CA39260 and CA32389 awarded by the National Cancer Institute, DA02277 and DA01696 awarded by the National Institute on Drug Abuse, HS07373 awarded by the Agency for Health | Comparative | A total of 40 black and 39 white smokers, average consumption of 14 and 14.7 cigarettes per day, respectively, of similar age (mean, 32.5 and 32.3 years, respectively) and body weight (mean, 73.3 and 68.8 kg, respectively). | N=79 | Higher levels of cotinine per cigarette smoked by blacks compared with whites can be explained by both slower clearance of cotinine and higher intake of nicotine per cigarette in blacks. Greater nicotine and therefore greater tobacco smoke intake per cigarette could, in part, explain some of the ethnic differences in smoking-related disease risks. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Biomarkers: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | Care Policy and Research, 1P30 AG15272 awarded by the National Institute on Aging, the National Institute of Nursing Research, and the Office of Research on Minority Health, and carried out in part in the General Clinical Research Center at San Francisco General Hospital Medical Center with support of the Division of Research Resources, National Institutes of Health (RR-00083). | | | | |
| Richie JP Jr, Carmella SG, et al. | Differences in the urinary metabolites of the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in Black and White smokers. | 1997 | Grants CA-32617 and CA-29580 from the National Cancer Institute | Metabolic epidemiological study | different biomarkers of NNK exposure and metabolism, including the urinary metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and the presumed detoxification product [4-(methylnitrosamino)-1-(3-pyridyl)but-1-yl]-beta-O-D-glucosiduronic acid (NNAL-Gluc), were examined along with questionnaire data on lifestyle habits and diet in a metabolic epidemiological study of | N=61 (34 black and 27 white) | Urinary NNAL-Gluc:NNAL ratios, a likely indicator of NNAL glucuronidation and detoxification, were significantly greater in whites than in blacks (P < 0.02). In addition, two phenotypes were apparent by probit analysis representing poor (ratio < 6) and extensive (ratio > or = 6) glucuronidation groups. The proportion of blacks falling into the former, potentially high- risk group was significantly greater than that of whites (P < 0.05). The absolute levels of urinary NNAL, NNAL-Gluc, and cotinine were also greater in blacks than in whites when adjusted for the number of cigarettes smoked. None of the observed racial differences could be explained by dissimilarities in exposure or other sociodemographic or dietary factors. Also, it is unlikely that the dissimilarities are due to racial |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

# Biomarkers: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | 34 black and 27 white healthy smokers. | | differences in preference for mentholated cigarettes, because chronic administration of menthol to NNK-treated rats did not result in either increases in urinary total NNAL or decreases in NNAL-Gluc:NNAL ratios. Altogether, these results suggest that racial differences in NNAL glucuronidation, a putative detoxification pathway for NNK, may explain in part the observed differences in cancer risk. |
| Signorello LB, Cai Q, Tarone RE, McLaughlin JK, Blot WJ. | Racial differences in serum cotinine levels of smokers. | 2009 | Grant R01 CA092447 from the National Cancer Institute | Comparative | Current smokers sampled from Southern Community Cohort Study participants (65 black men, 65 black women, 63 white men, 62 white women) | N=255 | Differences in cotinine levels among smokers suggest racial variation in exposure to and/or metabolism of tobacco smoke constituents, but our findings do not support a role for menthol preference in this disparity. |
| Strasser AA, Malaiyandi V, Hoffmann E, Tyndale RF, Lerman C. | An association of CYP2A6 genotype and smoking topography. | 2007 | Grants from the National Cancer Institute and the National Institutes on Drug Abuse at the National Institutes of Health: P50 CA/DA84718, CA143187, U01 DA020830, R01 CA120594 and R01 CA130961; and Canadian Institutes of Health Research: MOP86471 | Experimental | Treatment-seeking smokers | N=120 | Smoking topography variables did not differ significantly by level of nicotine dependence or cigarette mentholation (p values >.2). |
| Wagenknecht LE, Cutter GR, Haley NJ, Sidney S, Manolio TA, Hughes GH, Jacobs DR. | Racial differences in serum cotinine levels among smokers in the Coronary Artery Risk Development in (Young) Adults | 1990 | NHLBI Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, and N01-HC-48050 | Multicenter | 18-30 year old, Black and White, men and women participating in the Coronary Artery Risk Development in (Young) Adults Study | N=5,115 | Mentholated cigarettes, smoked by 89 percent of Black smokers but only 30 percent of White smokers, might account for underreporting of inhalation frequency because of the anesthetic effect that menthol provides. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | study. | | | | | | |
| Wang J, Roethig HJ, Appleton S, et al. | The effect of menthol containing cigarettes on adult smokers' exposure to nicotine and carbon monoxide. | 2010 | No funding source(s) provided. Authors affiliated with Altria Client Services Inc, Center for Research and Technology | Cross-sectional, observational, ambulatory, multi-centre study | The 3341 African-American and White adult cigarette smokers included in this analysis were from the TES study, which was a cross-sectional, observational, ambulatory, multi-centered study. Adult males and females, 21 years old or older, in generally good health, from 31 states | N=3,341 | Analyses of variance revealed no statistically significant effects of mentholated cigarettes on NE/24 h, COHb, serum cotinine and NE/cigarette. On average MS smoked 15.0 and NMS 16.8 cigarettes/day. The unadjusted mean differences were as follows: MS had lower NE/24 h (5.4%) and COHb (3.2%), higher serum cotinine (3.0%) and NE/cigarette (5.7%) than NMS. African-Americans MS smoked 40% fewer cigarettes, showed lower NE/24 h (24%) and COHb (10%) and higher NE/cig (29%) and serum cotinine (8%) levels than their White counterparts. Conclusions: Smoking mentholated cigarettes does not increase daily exposure to smoke constituents as measured by NE and COHb. These findings are consistent with the majority of epidemiological studies indicating no difference in smoking related risks between MS and NMS. |
| Williams JM, Gandhi KK, Steinberg ML, Foulds J, Ziedonis DM, Benowitz, NL. | Higher nicotine and carbon monoxide levels in menthol cigarette smokers with and without schizophrenia. | 2007 | Funded by National Institute on Drug Abuse grants DA140090, DA018203, and DA15978, DA015537, DA02277 and DA12393, and a grant from the New Jersey Department of Health and Senior Services, Office of the State Epidemiologist, through funds from New Jersey Comprehensive Tobacco Control Program | Lab study | Expired carbon monoxide (CO) and serum nicotine and cotinine were measured in 89 smokers with schizophrenia and 53 control smokers immediately after smoking an afternoon cigarette | N=142 | Serum nicotine levels (27 vs. 2ng/ml, p=.010), serum cotinine levels (294 vs. 240ng/ml, p=.041), and expired CO (25 vs. 21ppm, p=.029) were higher in smokers of menthol compared with nonmenthol cigarettes, with no differences in 3-hydroxycotinine/cotinine ratios between groups when controlling for race. Backward stepwise linear regression models showed that, in addition to having a diagnosis of schizophrenia, smoking menthol cigarettes was a significant predictor of nicotine and cotinine levels. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

References

1. Ahijevych K, Gillespie J, et al. (1996) Menthol and nonmenthol cigarettes and smoke exposure in black and white women. Pharmacology, Biochemistry, and Behavior, 53(2):355–360. [Funded by The Ohio State University Seed Grant and The Ohio State University General Clinical Research Center Grant MO1 RR00034]
2. Ahijevych KL, Tyndale RF, Dhatt RK, et al. (2002) Factors influencing cotinine half-life during smoking abstinence in African American and Caucasian women. Nicotine and Tobacco Research, 4:423–431. [Funded by National Institute on Drug Abuse DA10809, DA 06889 and The Ohio State University General Clinical Research Center M01 RR00034, and Ohio State University Academic Primary Care Program, USDHHS Bureau of Health Professions 1 D12 HP00027]
3. Benowitz NL, Herrera B, et al. (2004) Menthol cigarette smoking inhibits nicotine metabolism. Journal of Pharmacology and Experimental Therapies, 310(3):1208–1215. [Funded by State of California Tobacco Related Disease Research Program Grant 1RT-0521, by U.S. Public Health Service Grants DA02277 and DA12393 awarded by the National Institute on Drug Abuse and CA32389 awarded by the National Cancer Institute, and by the General Clinical Research Center at San Francisco General Hospital Medical Center with the support of the Division of Research Resources, National Institutes of Health (RR-00083)]
4. Caraballo RS, Giovino GA, et al. (1998) Racial and ethnic differences in serum cotinine levels of cigarette smokers—Third National Health and Nutrition Examination Survey, 1988–1991. JAMA, 280(2):135–139. [No funding source(s) were listed. Authors associated with Centers for Disease Control and Prevention, and Batelle Memorial Institute]
5. Clark PI, Gautam S, et al. (1996) Effect of menthol cigarettes on biochemical markers of smoke exposure among black and white smokers. Chest, 110(5):1194–1198. [Funded in part by a grant from the American Heart Association, Florida Affiliate]
6. Gan WQ, Cohen SB, et al. (2008) Sex-related differences in serum cotinine concentrations in daily cigarette smokers. Nicotine and Tobacco Research, 10(8):1293–1300. [Funded by ICEBERGS (Interdisciplinary Capacity Enhancement: Bridging Excellence in Respiratory Disease and Gender Studies), which is funded by the Canadian Institutes of Health Research (IGH/ICRH), the Canadian Lung Association, and the Heart and Stroke Foundation of Canada. Also by a Canada Research Chair and a GlaxoSmithKline/Michael Smith/St. Paul's Hospital Foundation Professorship in COPD]
7. Heck JD (2009) Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. Cancer Epidemiology, Biomarkers and Prevention, 18(2):622–629. [No funding source(s) provided. Author affiliated with Lorillard Tobacco Company]
8. Miller GE, Jarvik ME, et al. (1994) Cigarette mentholation increases smokers' exhaled carbon monoxide levels. Experimental and Clinical Psychopharmacology, 2(2):154–160. [Funded by California Tobacco-Related Research Program Grant 1 RT 87]
9. Moolchan ET, Franken FH, Jaszyna-Gasior M (2006) Adolescent nicotine metabolism: ethnoracial differences among dependent smokers. Ethnicity and Disease, 16:239–243. [Funded by National Inisttute on Drug Abuse Intramural funds]

10. Mustonen TK, Spencer SM, Hoskinson RA Jr, et al. (2005) The influence of gender, race, and menthol content on tobacco exposure measures. Nicotine and Tobacco Research, 7:581–590. [Funded by National Institute on Drug Abuse grant DA12165]
11. Patterson, F., Benowitz, N, Shields, P, et al. (2003) Individual Differences in Nicotine Intake Per Cigarette. Cancer Epidemiology, Biomarkers, and Prevention, 12:468–471. [Funded by Transdisciplinary Tobacco Use Research Center Grant P50 CA84718 from the National Cancer Institute and National Institute on Drug Abuse and by USPHS Grants DD02277 and DA01696 from the National Institute on Drug Abuse]
12. Perez-Stable EJ, Herrera B, et al. (1998) Nicotine metabolism and intake in Black and White smokers. JAMA, 280(2):152–156. [Funded by State of California Tobacco-Related Disease Research Program grant 1RT-0521, Public Health Service grants CA39260 and CA32389 awarded by the National Cancer Institute, DA02277 and DA01696 awarded by the National Institute on Drug Abuse, HS07373 awarded by the Agency for Health Care Policy and Research, 1P30 AG15272 awarded by the National Institute on Aging, the National Institute of Nursing Research, and the Office of Research on Minority Health, and carried out in part in the General Clinical Research Center at San Francisco General Hospital Medical Center with support of the Division of Research Resources, National Institutes of Health (RR-00083)]
13. Richie JP Jr, Carmella SG, et al. (1997) Differences in the urinary metabolites of the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in Black and White smokers. Cancer Epidemiology, Biomarkers, and Prevention, 6(10):783–790. [Funded by Grants CA-32617 and CA-29580 from the National Cancer Institute]
14. Signorello L, Cai Q, et al. (2009) Racial differences in serum cotinine levels of smokers. Disease Markers, 27(5):187–192. [Funded by grant R01 CA092447 from the National Cancer Institute]
15. Strasser AA, Benowitz NL, Pinto AG (2011). Nicotine metabolite ratio predicts smoking topography and carcinogen biomarkers. Cancer Epidemiol Biomarkers, Prev. 20: 234-238. [Funded by grants from the National Cancer Institute and the National Institutes on Drug Abuse at the National Institutes of Health: P50 CA/DA84718, CA143187, U01 DA020830, R01 CA120594 and R01 CA130961; and Canadian Institutes of Health Research: MOP86471]
16. Wagenknecht LE, Cutter GR, et al. (1990) Racial differences in serum cotinine levels among smokers in the Coronary Artery Risk Development in (Young) Adults study. American Journal of Public Health, 80(9):1053–1056. [Funded by NHLBI Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, and N01-HC-48050]
17. Wang J, Roethig HJ, Appleton S, et al. (2010) The effect of menthol containing cigarettes on adult smokers' exposure to nicotine and carbon monoxide. Regulatory, Toxicology, and Pharmacology, 57:24–30. [No funding source(s) provided. Authors affiliated with Altria Client Services Inc, Center for Research and Technology]
18. Williams JM, Gandhi KK, Steinberg ML, Foulds J, Ziedonis DM, Benowitz, NL (2007) Higher nicotine and carbon monoxide levels in menthol cigarette smokers with and without schizophrenia. Nicotine and Tobacco Research, 9(8):873–881. [Funded by National Institute on Drug Abuse grants DA140090, DA018203, and DA15978, DA015537, DA02277 and DA12393, and a grant from the New Jersey Department of

Health and Senior Services, Office of the State Epidemiologist, through funds from New Jersey Comprehensive Tobacco Control Program]

## D. Patterns of Use

Approximately one-fourth of all cigarettes sold in the United States are menthol (Giovino, 2004). An understanding of menthol cigarette usage patterns can guide health providers, public health professionals, and policy makers to develop effective strategies to reduce smoking prevalence and smoking-attributable morbidity and mortality. Nationwide, there are significant disparities among cigarette use, with higher prevalence among certain racial/ethnic groups and among those of lower socioeconomic status (U.S. Department of Health and Human Services, 2012). Similarly, there are different demographic distribution and characteristics of menthol and nonmenthol smokers. Understanding these patterns of use and relationships are critical to addressing the public health needs of these groups. This section evaluated studies of national survey data examining the patterns of use of menthol cigarettes as compared to nonmenthol cigarettes.

*Tobacco Use Supplement to the Current Population Survey (CPS-TUS)*

The CPS-TUS had a nationally representative sample of respondents and a high response rate with comprehensive demographic data collection. The survey also assumed no switching between cigarette types during subjects' lifetimes, which could also lead to misclassification.The use of mixed interview procedures (most by telephone and some by personal interview) may have affected responses, which may or may not be substantial. Proxy respondents were included which may have affected the reliability of data, particularly on menthol cigarette use. In addition, a relatively small number of minority population subjects (i.e., Asian American/Pacific Islanders and American Indian/Alaska Natives) could limit the ability to provide meaningful estimates of these minority groups.

Alexander et al. (2010) analyzed data from the 2006/2007 CPS-TUS on 30,176 current smokers who were at least 18 years old to examine the relationships among occupational status, menthol smoking preference and employer-sponsored smoking cessation programs and policies on quitting behaviors. The authors of the study found that menthol smokers were more likely to be females compared with nonmenthol smokers (55.1% vs. 43.4%), The authors also found that menthol smokers were more likely to be African American (30.2% vs. 4.4%), less educated (i.e., less than high school) (20.2% vs. 17.9%), never married (35.5% vs. 28.4%), residing in the northeast region (21.1% vs. 15.4%), and service employees (23.2% vs. 18.4%) compared with nonmenthol smokers.

Fagan et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS on 46,273 daily current smokers who were at least 18 years old survey to examine the associations between usual cigarette type (i.e., menthol or nonmenthol) and markers for nicotine dependence and also between cigarette type and quitting behaviors. The study found differences in demographics between menthol and nonmenthol daily current smokers. Menthol smokers were more likely to be females (58.0% vs. 47.3%), younger adults (age 18 to 30 years) (27.4% vs. 24.2%), African American (26.9% vs. 3.5%), never married (32.9% vs. 25.3%), less educated (less than high school diploma or GED) (17.1% vs. 14.5%), and have an annual income of less than $10,000 (13.0% vs. 9.6%) compared to nonmenthol smokers. Among menthol smokers, there were also more respondents who were administrative and office workers, worked in service sectors, unemployed, living in northeastern and midwestern regions, and residing in metropolitan areas compared with nonmenthol smokers. The study also found that menthol smokers reported smoking a mean of 13 cpd compared with 15 cpd among nonmenthol smokers ($p < 0.001$).

Fernander et al. (2010) analyzed data on 66,145 current smokers from the 2003 and 2006/2007 CPS-TUS who were at least 18 years old to examine the relationship between age of cigarette smoking initiation and cigarette purchasing patterns of menthol cigarettes among current smokers. The study found that 24.6 percent of current smokers reported using menthol cigarettes, whereas 70.9 percent reported using nonmenthol cigarettes. The study also found that menthol smokers were more likely to be female (54.8% vs 43.7%), African American (28.7% vs. 3.9%), younger (i.e., 18-24 years old: 17.3% vs. 14.1%), and less educated compared with nonmenthol smokers.

Trinidad et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS involving 283,443 respondents 20-65 years old at the time of the survey. The study showed that a much larger proportion of African American current smokers reported usually smoking menthol cigarettes (69.8% ± 1.6%) compared to other racial groups (20.1% for White; 25.4% for Hispanic/Latino smokers).

Lawrence et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS and presented results of data on 69,193 smokers 18 years old or over. They found that, overall, 27.6 percent of current smokers smoked menthol cigarettes. Of African American current smokers, 73.6 percent smoked menthol cigarettes followed by 27.9 percent of Hispanic, 26.2 percent of Asian American/Pacific Islander, 22.5 percent of American Indian/Alaska Native, and 21.1 percent of White current smokers. The prevalence of smoking menthol cigarettes was highest in the following sociodemographic categories (in order of proportion): African American, born in a US territory, unemployed, annual family income of less than $10,000, residence in the Northeast, never married, consumption of less than 10 cpd, education level of 9-11 years, 18-24 years old, female, smoking on some days, start of regular smoking after age 18, residence in a metropolitan area, and no use of other forms of tobacco. African American smokers were 10-11 times more likely to smoke menthol cigarettes than White smokers were. Most non-White smokers, with the exception of American Indian/Alaska Natives, and women were also more likely to smoke menthol cigarettes than White smokers and male smokers. African American smokers 18-24 years old were four times more likely to smoke menthol cigarettes compared with African American smokers 65 years old or over.

*National Youth Tobacco Survey (NYTS)*

The NYTS had a nationally representative sample from public and private schools with a response rate of 80 percent and oversampled African American, Hispanic, and Asian American students. The survey included two types of data on menthol cigarette use – exclusive brand (Newport or Kool) and self-reported menthol cigarette use. However, the sample size was smaller due to restrictions on the study population, with assumptions made regarding no switching between cigarette brands. Smoking status was based on self-report. Generalizability may be limited since study subjects were students enrolled in regular public and private schools; students in non-traditional schools, such as schools for special education, were excluded from the study. Furthermore, there were insufficient numbers of Asian Americans and Hawaiian/Pacific Islanders (H/PI). The data reflect smoking status in the past 30 days (which is typical for smoking surveys) and did not have information on temporal effects or switching patterns. The response rates were reasonable (84% in 2000 and 75% in 2002), with assessment of the possible misclassification by comparing respondents' reports of menthol use.

Appleyard et al. (2001) analyzed data from the 2000 NYTS of 35,828 middle and high school students in public and private schools across the country to estimate the prevalence of cigarette smoking and describe smoking behaviors among H/PI youth. This study found among those who reported smoking in the past 30 days, 42 percent reported that they smoked menthol cigarettes. While 74 percent of African American youth said their usual brand of cigarette was a menthol brand, 58 percent of Asian Americans, 51 percent of Hispanics, 46 percent of H/PI, and 32 percent of Whites indicated the same. This study is one of only a few studies that focused on Asian American and H/PI youth.

Wackowski et al. (2007) conducted a cross-sectional study to examine the rates of menthol smoking and measures of nicotine dependence using data on 1,345 current established smokers in grade 9 – 12 who participated in the 2004 NYTS. This study found that approximately 46 percent of all current established cigarette smokers (e.g., those who smoked in the past 30 days and smoked at least 100 cigarettes during their lifetime) were menthol smokers. Overall, 21.7 percent of 9 – 12 grade students were current cigarette smokers and 13.8 percent were current established cigarette smokers. Prevalence of smoking significantly increased by grade among both current and current established smokers and differed by race or ethnicity, with prevalence being highest among White students. Approximately 24 percent of current established smokers indicated smoking a menthol exclusive brand (a brand that is only available in menthol, such as Newport (until 2010) or Kool) and 44 percent reported that they usually smoked menthol cigarettes. Of African American smokers, 88.4 percent reported that they regularly smoked menthol cigarettes, as compared to 54.2 percent Hispanic smokers, 49.7 percent of Asian American smokers, and 43.8 percent of White smokers who reported regularly smoking menthol cigarettes.

Hersey et al. (2006) analyzed data from the 2000 and 2002 NYTS on students in grades 6-12 in public and private schools at the time of the survey who reported to be current smokers (smoking cigarettes on one or more of the past 30 days) and who reported that they had a usual brand of cigarettes. This study reported that between 2000 and 2002, the percentage of smokers who regularly smoked menthol cigarettes increased significantly ($p<0.05$) from 40.0 percent to 47.4 percent - an increase of 18.5 percent. Menthol cigarette use significantly increased among middle school smokers (from 51.6% to 59.6%, $p<0.05$). Menthol cigarettes were most popular among younger and newer smokers. Overall, 51.8 percent of teens who had smoked for less than one year smoked menthol cigarettes, compared with 43.6 percent of those who had smoked for a year or more. For Hispanic and White youth, the prevalence of menthol cigarette use was higher among middle school students than among high school students. Among Hispanic youth, 62.9 percent of smokers in middle school, compared with 52.4 percent of smokers in high school, smoked menthol cigarettes. Among Whites, 53.1 percent of smokers in middle school, compared with 37.4 percent of smokers in high school, smoked menthol cigarettes. Among African American students, smokers in middle school (87.5%) and in high school (86.8%) smoked predominantly menthol cigarettes.

Hersey et al. (2010) analyzed data from the 2006 NYTS to examine the reliability of youth self-reported menthol cigarette use. They analyzed data from 4,738 students in grades 6-12 in the spring of 2006 who reported that they had smoked in the past 30 days, had a usual brand of cigarette, and could identify whether the usual brand was menthol or nonmenthol. The study found that among youth smokers who reported a usual brand, 51.7 percent of middle school smokers and 43.1 percent of high school smokers consistently reported that their usual brand was menthol. The proportion of middle school smokers whose usual brand was menthol was higher among those who smoked for one year or more (54.7%) than among those who smoked for less than a year (42.2%). Among high school youth, these percentages were similar for smokers who had smoked for less than and for more than one year (42.8% vs. 43.1%). This study also found that menthol cigarette use was very high among minority youth – 80.6 percent of African American middle school smokers and 84.8 percent of African American high school smokers reported that their usual brand was menthol. Among Asian Americans, a menthol brand was used by 57.4 percent of middle school smokers and 43.6 percent of high school smokers. Among Hispanics, 57.9 percent of middle school smokers and 56.4 percent of high school smokers reported that they smoked menthol cigarettes. In non-Hispanic Whites, the proportion of menthol smokers was higher among middle school students (43.1%) than among high school students (37.6%). Misclassification of menthol or nonmenthol cigarette use was up to 12 percent among new smokers (i.e., smoked < 6 cigarettes over lifetime; about 19 percent of smokers) compared to 2 percent among established smokers (who had smoked for at least 12 months).

*National Health Interview Survey – Cancer Control Supplement (NHIS – CCS)*

The NHIS-CCS had a nationally representative sample with information on smoking habits. The relatively small sample size limited subgroup analysis, and data may not have been representative of the population under 25 years old and over 64 years old due to the selection of the study population. There was also a potential for misclassification, as former smokers were defined as not currently smoking, which could have classified those who quit as recently as one week before as former smokers. There was also no description of how the predicted prevalence was calculated or what imputation method was used for assigning missing data on income. There was no validation or comparison between imputed and non-imputed data.

Cubbin et al. (2010) analyzed data from the 2005 NHIS – CCS. Among 7,688 former smokers and current everyday smokers who were 25-64 years old and provided information on the brand of cigarettes they used, the prevalence of menthol cigarette use was significantly higher in African American female and male current everyday smokers (77.9% and 69.7%, respectively) and former smokers (72.7% and 66.0%, respectively) compared with their Hispanic and White counterparts (14.6% and 35.6% in current smokers, respectively; 14.5% and 34.9% in former smokers, respectively).

Mendiondo et al. (2010) analyzed data from the 2005 NHIS – CCS survey. The study found that among 6,055 current menthol smokers, 55.6 percent were female (41.7% in 5,949 nonmenthol smokers), 33.1 percent were African American (3.8% in nonmenthol smokers), 20.8 percent resided in the Northeast (15.0% in nonmenthol smokers), 22.2 percent had less than a high school education (20.2% in nonmenthol smokers), 27.1 percent had an annual income of less than $20,000 (21.9% in nonmenthol smokers). Among former menthol smokers, 60.7 percent were female (39.9% in the nonmenthol group), and 19.1 percent were

African American (3.6% in the nonmenthol group).

Stahre et al. (2010) analyzed data from the 2005 NHIS – CCS (n = 31,428). They found that 42 percent of the study subjects reported being either a current (n = 6,511 or 21%) or former (n = 6,774 or 21%) smoker. Of 12,004 study subjects for which menthol cigarette status was known, approximately 26 percent of current smokers smoked menthol cigarettes and 22 percent of former smokers had used menthol. Overall, menthol smoking prevalence was significantly different by gender, region, race, marital status, and quantity of cigarettes smoked per day. African American smokers had the highest prevalence of menthol cigarette use (76% for current smokers; 63% for former smokers) compared with White and other racial groups (20% and 33% in current White and Asian American smokers, respectively; 21% and 30% in former White and Asian American smokers, respectively). More female smokers (33% for both current and former smokers) used menthol than male smokers did (22% for current smokers and 18% for former smokers). Participants 18-24 years old had the highest prevalence of menthol use for both current and former smokers (32% and 34%) compared with other age groups (23-28% for current smokers; 19-28% for former smokers). Among both current and former smokers, menthol smokers smoked fewer cigarettes per day (15 for current smokers and 17 for former smokers) compared with nonmenthol smokers (17 for current and 19 for former smokers).

*National Survey on Drug Use and Health (NSDUH)*

The NSDUH is an annual nationwide household survey with a nationally representative sample of population 12 years old or over. This study was of a nationally representative sample with a reasonable response rate of 75 percent. However, smoking status was based on self-report, and there was a small sample size for certain racial groups (Asian American and American Indian/Alaska Native).

O’Connor et al. (2005) analyzed data from the 2002 NSDUH and reported that Newport (exclusively menthol brand at time of study) was the dominant brand among African American smokers under age 26 years old. Among 12–17 year olds, 54.1 percent smoked Newport Full Flavor (FF) and 13.5 percent smoke Newport Lights, while among 18–25 year olds, 70.6 percent smoke Newport FF and 9.1 percent smoke Newport Lights. By contrast, only 36.7 percent of African American smokers over age 26 smoked Newport FF and 4.2 percent smoked Newport Lights. Since this study was reported in the form of a Letter to the Editor, details of the study were limited and there was no description of the study population.

Rock and associates (2010) analyzed combined data from the 2004 – 2008 NSDUH to assess menthol cigarette use among current smokers. Rock reported that 35.7 percent of current smokers 12 years old or over smoked menthol cigarettes. In this population, more than half of menthol smokers were females (52.2%) compared with 43.0 percent of nonmenthol smokers. About 29.4 percent of all menthol smokers were African American, which was almost 10 times the percentage of nonmenthol smokers who were African American (3.0%). For Hispanic and Asian American smokers, the percentages of menthol and nonmenthol smokers were approximately the same. White smokers represented more than half of the menthol smokers (54%). Approximately 71.2 percent of all menthol smokers were adults 26 years old and over, 23.0 percent were young adults 18-25 years old, and 5.8 percent were youth 12-17 years old compared with 77.5 percent, 19.2 percent, and 3.4 percent of all nonmenthol smokers of the same age groups, respectively.

*National Health and Nutrition Examination Survey (NHANES)*

FDA analyzed demographic characteristics of over 5,000 smokers participating in NHANES from 1999-2008. Unlike the previously discussed surveys, menthol use data were collected through barcode scanning of the participants' cigarette packs. Thus, there is no opportunity for misclassification. As has been reported previously, menthol cigarette use was more common in female smokers than male smokers and in African American smokers compared to White smokers.

*Conclusion*

Multiple large scale surveys and studies of nationally representative populations show consistency in the patterns of use of menthol cigarettes. The five studies that reported from CPS-TUS data found that menthol cigarette use was more common among smokers who were female, African American, had a lower education, and younger (Alexander et al., 2010; Fagan et al., 2010; Fernander et al., 2010; Lawrence et al., 2010; Trinidad et al., 2010). The four studies that reported from NYTS data found that menthol cigarette use was more common among smoking students who were African American and Hispanic, and that there was an inverse relationship by grade (Appleyard et al., 2001; Hersey et al., 2006; Hersey et al., 2010; Wachowski et al., 2007). The three studies that reported on data from the NHIS found that menthol cigarette use was more common among smokers who were female, African American and had lower education (Cubbin et al., 2010; Mendiondo et al., 2010; Stahre et al., 2010). The two studies that reported on NSDUH data found that menthol cigarette use was more common among smokers who were African American, female, and under age 26 (O'Connor et al., 2005; Rock et al., 2010). The FDA analysis of NHANES data found that menthol cigarette smokers were more likely to be female and African American. The varied nature of these studies and the large number of analyses performed on this data, which provide consistent findings, enable researchers to draw clear conclusions. Most of the surveys relied on self-reported data to categorize menthol and nonmenthol smokers. Use of such self-reported data are standard in the research field. Although studies that relied on self-report of menthol or nonmenthol use may have potential misclassifications, this is not necessarily a problem. As noted by Caraballo et al. (2011), it is likely that this type of bias is fairly constant over time. Data support that (1) a majority of African American smokers reported menthol cigarette use and other minority groups were more likely to smoke menthol cigarettes than White smokers, (2) younger smokers had the highest rate of smoking menthol cigarettes, (3) female smokers were more likely to smoke menthol cigarettes, and (4) menthol smokers were more likely to have lower education levels and lower incomes compared with nonmenthol smokers. From published studies and FDA analysis of the 1999–2008 NHANES data with nationally representative samples, the weight of evidence supports the conclusion that menthol in cigarettes is associated with particular patterns of smoking.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Alexander LA, Crawford T, Mendiondo MS | Occupational status, work-site cessation programs and policies and menthol smoking on quitting behaviors in US smokers. Addiction 105(suppl. 1):95–104. | 2010 | No funding source(s) provided. Authors are affiliated with the University of Kentucky | Cross-sectional survey (2006 Tobacco Use Supplement to the Current Population Survey) | Current smokers age 18 and older | N=30,176 | …there were no differences for menthol versus non-menthol smokers on quitting behaviors [odds ratio (OR) = 0.98; 95% confidence interval (CI) = 0.83, 1.15].<br><br>When occupational status and work-place smoking policies are controlled for, smokers of menthol cigarettes in the United States appear to have similar self-reported life-time rates of attempts to stop smoking to non-menthol smokers. |
| Appleyard J, Messeri P, Haviland ML. | Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. | 2001 | American Legacy Foundation | National Youth Tobacco Survey | Asian American and Hawaiian/ Pacific Islander youth | N=35,828.The schools response Rate was 90% and the student response rate was 93%, resulting in an overall response rate of 84%. | While many studies have documented the high prevalence of Menthol cigarette use among African Americans, NYTS 2000 data reveal that smoking mentholated cigarettes is also common among Asian American youth. Overall, 74% of African Americans and 58% of Asian Americans reported that their usual brand of cigarette is menthol brand. |
| Caraballo, RS & Asman, K | Epidemiology of menthol cigarette use in the United States. | 2011 | No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention | Review and secondary analyses of national surveys | NSDUH: adolescents aged 12-17 years old who smoked in the past month and adult smokers (aged 18 years or older) who smoked in the past month<br>NYTS: middle school (MS) and high school (HS) students with school year, past 30 | NSDUH: 9,595 adolescents; 62,010 adults<br>NYTS: 1,978 MS students and 6,163 HS students<br>MTF: 20,863 8th | Menthol cigarettes are disproportionately smoked by adolescents, blacks/African Americans, adult females, those living in the Northeast of the United States and those with family incomes lower than $50,000. Based on self-reports of menthol cigarette use, menthol cigarette use among smokers have increased from 2004 to 2008. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | day smoking, brand use, and menthol information. MTF: current smokers in 8th, 10th and 12th grade NHANES: 20 years and older who had Smoked and were non-Hispanic white, non-Hispanic black/African American, or Mexican American | graders; 30,722 10th graders; 40,914 12th Graders NHANES: 1571 individuals with UPC information | |
| Cubbin C, Soobader M-J, LeClere FB | The intersection of gender and race/ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. | 2010 | Research Network on Disparities | Cross-sectional national survey (2005 National Health Interview Survey and Cancer Control Supplement) | Black, Hispanic and white men and women, 25-64 years old | N= 7688 | After adjusting for age, income and education, black (compared with Hispanic and white) and female (compared with male) smokers were more likely to choose menthol cigarettes. There was only one statistically significant difference in age of initiation, cigarettes smoked per day, quit attempts or time since quitting between menthol and non-menthol smokers: white women who smoked menthol cigarettes reported longer cessation compared with those who smoked non-menthol cigarettes. |
| Fagan P, Moolchan ET et al. | Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. | 2010 | The National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current Population Surveys) | Civilian non-institutionalized daily smokers aged 18 years and above. | N=11,671 (menthol smokers) N=33,644 (nonmenthol smokers) N=958 (no usual type) | …among adults, daily menthol smokers consuming six to 10 cigarettes per day were more likely than non-menthol smokers consuming six to 10 cigarettes per day to smoke their cigarette within the first 5 minutes after waking. |
| Fernander A, Rayens ML, et al. | Are age of smoking initiation and purchasing | 2010 | No funding source(s) provided. Authors affiliated with the | Cross-sectional survey (2003 and 2006/07 | Civilian non-institutionalized individuals aged 18 | N= 16,294 (menthol smokers) | The multivariate logistic model only marginally revealed that age of smoking initiation predicted menthol smoking: findings are suggestive that |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | patterns association with menthol smoking? | | University of Kentucky | Tobacco Use Supplement to the Current Population Survey) | years and above. | N= 46,899 (non-menthol smokers) | the longer the delay of initiation the more likely that an individual smoked menthol cigarettes [odds ratio (OR) = 1.01; 95% confidence interval (CI): 1.00–1.01].<br><br>Menthol smokers in the United States are more likely to be female, younger, from ethnic minority groups, and to have a high school education |
| Giovino GA, et al. | Epidemiology of menthol cigarette use | 2004 | No funding source(s) provided. Authors affiliated with the Roswell Park Cancer Institute, Kaiser Permanente Medical Care Program, Substance Abuse and Mental Health Services Administration, University of Michigan, American Legacy Foundation, Centers for Disease Control and Prevention | Review article | Not applicable | Not applicable | The epidemiological literature on menthol cigarettes and cancer risk is inconclusive regarding whether these cigarettes confer a risk for cancer above that of nonmentholated varieties. Available data indicate that mentholated cigarettes are at least as dangerous as their nonmentholated counterparts. In addition, because mentholation improves the taste of cigarettes for a substantial segment of the smoking population and appears to mask disease symptoms, this additive may facilitate initiation or inhibit quitting. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Hersey JC, Ng SW, Nonnemaker JM, Mowery P, Thomas KY, Vilsaint MC, Allen JA, Haviland ML. | Are menthol cigarettes a starter product for youth? | 2006 | American Legacy Foundation and RTI International | 2000 and 2002 NYTS, School-based, national survey | Data from the 2000 NYTS and from the 2002 NYTS.The survey used a three-stage cluster sample design that oversampled African American, Hispanic, and Asian students. The NYTS was administered to | N=5,512 youth (2000 NYTS) and 3,202 youth (2002 NYTS) | Additionally, youth who smoked menthol cigarettes had significantly higher scores on a scale of nicotine dependence compared with nonmenthol smokers, controlling for demographic background and the length, frequency, and level of smoking.. |
| Hersey JC, Nonnemaker JM, Homsi G. | Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. | 2010 | American Legacy Foundation | Survey (2006 National Youth Tobacco Survey) | Middle and high school students who smoked in the past 30 days who reported that they had a usual brand of cigarette and who could identify whether the usual brand was menthol or nonmenthol. | N=1458 (menthol smokers) N=1710 (nonmenthol smokers) | A logistic regression model of dependence, controlling for background (i.e., school level, gender, and race/ethnicity) and smoking level (i.e., years, frequency, and level of smoking) found that smoking menthol cigarettes was significantly associated with reduced time to needing a cigarette among smokers with a regular brand (odds ratio [OR]: 1.86, p = .003) and among established smokers (OR: 2.06, p = .001). |
| Lawrence DL, Rose A et al. | National patterns and correlates of menthol cigarette use in the United States. | 2010 | National Cancer Institute | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current Population Survey) | Smokers at least 18 years old. | N=63,193 | Use of mentholated cigarettes was higher among women than among men.<br><br>Additional significant factors associated with mentholated cigarette smoking included being unmarried (never married: OR: 1.21, 99% CI: 1.09–1.34; divorced/separated: OR: 1.13, 99% CI: 1.03–1.23), being born in a US territory (OR: 2.01, 99% CI: 1.35–3.01), living in a non- |
| Mendiondo MS, Alexander LA, Crawford T | Health profile differences for menthol and non-menthol smokers: findings from the National Health Interview Survey. | 2010 | No funding source(s) provided. Authors affiliated with the University of Kentucky | Cross-sectional survey (2005 National Health Interview Survey and its cancer control supplement | civilian, non-institutionalized adults at least 18 years old | N=5949 | Overall, current menthol and non-menthol smokers have similar health profiles. However, menthol smokers reported smoking fewer cigarettes per day than their non-menthol counterparts. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| O'Connor RJ. | What brands are US smokers under 25 choosing? | 2005 | No funding source(s) provided. Authors affiliated with Roswell Park Cancer Center | Online Analysis | Data on the cigarette brand preferences of smokers in the 2002 US National Survey on Drug Use and Health from three age groups: 12–17, 18–25 years, and 26+ years. | 12–17 years (n = 2290), 18–25 years (n = 7321), 26+ years (n = 5238). | The youth market in the USA appears dominated by varieties of the major advertised brands; other products make up a more modest percentage of the market. Conversely, the adult market is much more diffuse, with the major varieties commanding smaller overall percentages of the market. Light varieties appear to be popular choices for younger smokers. Similar investigations in other countries could shed further light on younger smokers' brand choices, particularly in those countries that have banned descriptors such as ''Light'' and ''Mild''. |
| Rock VJ, Davis SP, Thorne SL, et al. | Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. | 2010 | No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention | Cross-sectional survey (2004–2008 National Survey on Drug Use and Health) | Current smokers age 12 and over | N=71,605 | Over half of menthol cigarette smokers were female (52.2%), and approximately 29.4% of all menthol smokers were Black, which was almost 10 times the percentage of nonmenthol smokers who were Black (3.0%, $p < .01$). Prevalence of past month menthol cigarette use was highest among current smokers aged 12–17 years (44.7%) and decreased as age group increased. |
| Stahre M, Okuyemi KS et al. | Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. | 2010 | Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development | Cross-sectional survey (2005 National Health Interview Survey (NHIS) Cancer Control Supplement) | Current or former smokers, age 18 and over | N= 6511 (smoker) N= 6774 (former smoker) | Overall menthol smoking prevalence was significantly different by sex, region of the United States, race, marital status and average number of cigarettes smoked per day for both current and former smokers and age for former smokers only.<br><br>For current and former smokers, non-menthol smokers reported a higher number of cigarettes smoked per day on average than menthol smokers.<br><br>Menthol smoking status was not associated with differences in utilization of quit aids. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

Patterns of Use: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Trinidad DR, Gilpin EA, Lee L, Pierce JP. | Do the majority of Asian-American and African-American smokers start as adults? | 2004 | Grant no. MRSGT 07-277-01 from the American Cancer Society, no. 15RT-0238 from the Tobacco-Related Disease Research Program of the University of California Office of the President and contract no.28XS017 from the National Cancer Institute; the Tobacco Research Network on Disparities funded by the National Cancer Institute and the American Legacy Foundation | Comparative | Adults aged 26 to 50 years. Asians/Pacific Islanders (A/PI), African Americans (AA), Hispanics/Latinos (H/L) and non-Hispanic whites (WH). | N=130,356 | Significant ethnic disparities in relation to when people start smoking, with the majority of A/PIs and AAs initiating as young adults. The findings suggest that prevention strategies should begin at a young age and continue throughout young adulthood, especially among ethnic minority populations. |
| U.S. Department of Health and Human Services | Preventing tobacco use among youth and young adults: a report of the Surgeon General | 2012 | U.S. Deparment of Health and Human Services | Review | Not applicable | Not applicable | [Not applicable] |
| Wackowski O, Delnevo CD. | Menthol cigarettes and indicators of tobacco dependence | 2007 | No funding source(s) provided. Authors are associated with the University of Medicine and | Survey | U.S. high school students, School-based, national survey | N=1345 current smokers in grades 9-12 | Menthol cigarette smoking was associated with two dependence measures and may be more addictive than regular cigarettes in young smokers. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

References


1. Alexander LA, Crawford T, Mendiondo MS (2010). Occupational status, work-site cessation programs and policies and menthol smoking on quitting behaviors in US smokers. Addiction 105(suppl. 1):95–104. [No funding source(s) provided. Authors are affiliated with the University of Kentucky]
2. Appleyard J, Messeri P, Haviland ML (2001) Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. Asian American & Pacific Islander Journal of Health 9**(**1):5-14. [Funded by the American Legacy Foundation]
3. Caraballo, RS & Asman, K (2011). Epidemiology of menthol cigarette use in the United States. Tobacco Induced Diseases, 9 (Suppl 1): S1. [No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention]
4. Cubbin C, Soobader M-J, LeClere FB (2010) The intersection of gender and race/ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. Addiction 105(suppl. 1):32–8. [Funded by Research Network on Disparities]
5. Fagan P, Moolchan ET et al. (2010) Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. Addiction 105(suppl. 1):55–74. [Funded by the National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center]
6. Fernander A, Rayens ML, et al. (2010) Are age of smoking initiation and purchasing patterns association with menthol smoking? Addiction 105(suppl. 1): 39–45. [No funding source(s) provided. Authors affiliated with the University of Kentucky]7. Giovino, GA, Sidney, S, Gfroerer, JC, O'Malley, PM, Allen, JA. et al. (2004) Epidemiology of menthol cigarette use. Nicotine and Tobacco Research 6 Suppl 1:S67-S81. [No funding source(s) provided. Authors affiliated with the Roswell Park Cancer Institute, Kaiser Permanente Medical Care Program, Substance Abuse and Mental Health Services Administration, University of Michigan, American Legacy Foundation, Centers for Disease Control and Prevention]
8. Hersey JC, Ng SW, et al (2006) Are menthol cigarettes a starter product for youth? Nicotine and Tobacco Research 8(3):403–13. [Funded by the American Legacy Foundation]
9. Hersey JC, Nonnemaker JM & Homsi G. (2010) Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. Nicotine and Tobacco Research 12(suppl. 2):S136-146. [Funded by the American Legacy Foundation]
10. Lawrence DL, Rose A et al. (2010) National patterns and correlates of menthol cigarette use in the United States. Addiction 105(suppl. 1):13–31. [Funded by the National Cancer Institute]
11. Mendiondo MS, Alexander LA, Crawford T (2010) Health profile differences for menthol and non-menthol smokers: findings from the National Health Interview Survey. Addiction 105(suppl. 1):124-40. [No funding source(s) provided. Authors affiliated with the University of Kentucky]
12. O'Connor RJ (2005) What brands are US smokers under 25 choosing? Tobacco Control 14:213-8. [No funding source(s) provided. Authors affiliated with Roswell Park Cancer Center]
13. Rock VJ, Davis SP, Thorne SL, et al. (2010) Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. Nicotine and Tobacco Research 12(suppl.

2):S117-24. [No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention]

14. Stahre M, Okuyemi KS et al. (2010) Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. Addiction 105(suppl. 1):75–83. [Funded by Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development]
15. Trinidad DR, Perez-Stable EJ, Messer K, et al. (2010) Menthol cigarettes and smoking cessation among racial/ethnic groups in the United States. Addiction 105:84-94. [Funded by grant no. MRSGT 07-277-01 from the American Cancer Society, no. 15RT-0238 from the Tobacco-Related Disease Research Program of the University of California Office of the President and contract no.28XS017 from the National Cancer Institute; the Tobacco Research Network on Disparities funded by the National Cancer Institute and the American Legacy Foundation]
16. U.S. Department of Health and Human Services (2012). Preventing tobacco use among youth and young adults – A report of the Surgeon General. Rockville, MD.
17. Wackowski O, Delnevo CD (2007) Menthol cigarettes and indicators of tobacco dependence among adolescents. Addictive Behaviors 32:1964–9. [No funding source(s) provided. Authors are associated with the University of Medicine and Dentistry of New Jersey]

## *E. Marketing and Consumer Perception of Risk*

Marketing plays a role in promoting consumer products, and touches each of us every day, whether we see a television commercial for children's cereal, a billboard for car insurance, or hear a radio ad for pet food. These ads influence consumer choices, and the tobacco industry uses proven marketing tools to market tobacco as well. In order to determine how marketing influences smokers, FDA examined data on trends in the marketing of menthol cigarettes. In addition, this chapter reviews consumer perceptions of menthol cigarettes. In particular, this chapter reviews marketing articles related to trends in brand preference and marketing strategies used to promote menthol cigarettes as well as consumer perceptions literature related to the risks and benefits of using menthol cigarettes, in an effort to determine what role, if any, marketing plays in the use of menthol cigarettes and the relationship between consumer perceptions and the use of menthol. Of particular interest is whether these relationships are present among subpopulations (e.g. youth, African Americans, Hispanics, women).

*Marketing*

<u>Brand Preference</u>

Understanding trends in brand preference allows for contextualization of use patterns, advertising strategies, beliefs, and the process of establishing brand loyalty. The data overwhelmingly support distinct trends in adolescent brand preference, with a much more heavily concentrated preference evident among adolescents than adults (Cummings et al, 1997, Pollay et al, 1996). The majority of teens report Marlboro as their preferred brand, followed by Newport and Camel (CDC, 1994; CDC, 1992; Cummings et al., 1997; Johnston et al., 1999; O'Connor, 2005). Newport's popularity among teens doubled from 1989-1996, from 8.3 percent to 16.4 percent (Johnston et al., 1999; Kaufman et al., 2004).

Research suggests adolescent brand preference is not a mere imitation of adult brand preference (Cummings et al., 1997; Pollay, 1996). Cummings et al. (1997) found that adult and adolescent brand preferences differ within communities, suggesting something other than modeling is influencing adolescent brand preference. Pollay et al. (1996) found that analysis of brand and behavior survey along with market share and ad expenditure data supported econometric studies that report teens' brand preference is three times more sensitive to cigarette ads than adults. This is further supported by teens overwhelming preference for the top three most heavily advertised brands (American Legacy Foundation, 2007; Arnett et al., 1998; CDC, 2009; CDC, 1992; Pollay et al., 1996). National surveys typically do not tease out sub-brand preference (e.g. Marlboro Menthol), which may cause difficulties in making an absolute judgment about menthol versus nonmenthol brand preference; menthol sub-brands make up only a small percentage of the market for Marlboro and Camel. Until 2010, Newport was an exclusively menthol brand. Thus, Marlboro and Camel are most often reported as nonmenthol brands and Newport as a menthol brand.

Evidence suggests differences in brand preference by age, race or ethnicity, and region. Brand loyalty begins in adolescence. The number of teens who report they do not have a brand preference declines dramatically with age (Johnston, et al., 1999). Data indicates that preference for certain nonmenthol cigarettes (Marlboro and Camel) neither changes with age (Mowry, 2004), nor rises in popularity (Johnston et al, 1999). Newport use suggests a different trajectory of preference. Data suggest that preference for Newport declines with age, with 22 percent of 8th graders reporting a preference for Newport and 13 percent of 12th graders reporting this preference (CDC, 1994; CDC et al., 1992; Johnston et al., 1999). O'Connor (2005) found Newport's popularity declines dramatically after age 26. According to the 2010 National Survey on Drug Use and Health, the decline in preference for Newport by age is found across races and ethnicities. Whereas 78.7 percent of African American smokers and 24.8 percent of Hispanic smokers 12-25 years old report using Newport cigarettes, only 48.4 percent of African American smokers and 13 percent of Hispanic smokers ages 26+ report using Newports. Newport preference among Caucasians declines from 11.4 percent in 12-25 year olds to 3.3 percent in smokers 26+ years old. Newport is overwhelmingly preferred by African Americans, with 41 percent of African American adults and 75 percent of African American youth reporting preference for Newport cigarettes (Cummings et al, 1987; Cummings, 1997; Johnston et al., 1999; O'Connor, 2005). Johnston et al. (1999) found a slight preference for the Newport brand among Hispanic youth. Additionally, some evidence suggests regional differences, with more cigarette smokers reporting a preference for Newport in the Northeast than in the West (OAS, 2003; CDC, 1994; Johnston et al., 1999). These regional differences in Newport use exist for African American, White, and Hispanic smokers. CDC reports from 1994 suggest regional preferences for Newport combined with a decrease in overall advertisement expenditures for Newport may have resulted from a heavier reliance on a regional marketing strategy than a national strategy. Differences in menthol versus nonmenthol brands by age, race, and region may suggest differences in marketing strategies, as described below.

Marketing Strategies

Similar to other consumer products, evidence indicates tobacco companies employ targeted marketing strategies to attract consumers to their brands. These strategies include using market research with target audiences to inform product placement and marketing, strategic placement of advertising, partnerships with relevant national and community organizations, and use of specific promotions to encourage use. Samji (2008) reviewed a collection of several thousand cigarette advertisements from 1920-1954 and that found these ads attempt to convey a health benefit through endorsements by physicians, with menthol advertising suggesting a therapeutic, soothing benefit. Anderson (2011) reviewed industry documents that further revealed cigarette marketing on a health platform conveying to consumers that menthol cigarettes were healthier than nonmenthol.

Research indicates tobacco companies with menthol brands use a marketing mix and concepts that target African Americans (Altman et al., 1991; Balback et al., 2003; Boley et al., 2010; Cummings et al., 1987; Glantz et al., 2006; Landrine et al., 2005; Laws et al., 2002; Sutton et al., 2004; White et al., 2006). This is reflected in advertising placement, with magazines with primarily African American readership containing more menthol advertisements than nonmenthol advertisements and more menthol advertisements than those magazines with primarily White readership (Balbach et al., 2003; Cummings et al., 1987; Landrine et al., 2005) and more outdoor menthol advertisements in African American neighborhoods than neighborhoods of other races/ethnicities (Altman et al., 1991; Henriksen et al., 2011; Laws et al., 2002; Seidenberg et al., 2010). A review of publicly available tobacco industry documents conducted by Yerger, Przewoznik, and Malone (2007) describes the tobacco industry’s use of free sampling, mobile vans, event sponsorships, and special inner-city sales programs to promote sales of menthol brands to African American communities. Anderson (2011) identified a similar pattern. An observational study conducted in Hawaii to examine the number of ads inside and outside of retail establishments found Kool, the most heavily used brand by middle schoolers, to have the most ads inside and outside retail establishments (Glantz et al., 2006). Industry documents and observational reviews suggest themes that reflect an urban, “cool” lifestyle have been used in advertising campaigns and product names to promote menthol cigarettes to the African American community (Gardiner, 2004: Sutton et al, 2004).

Connolly et al. (2011) found evidence of similar targeted marketing strategies in Japan which were used to increase the preference for menthol cigarettes among women. The study found that by 2000, half of all female smokers were smoking menthol cigarettes and that menthol use among adolescents was significantly higher than in the general population of smokers. While the Japanese National Health and Nutrition Survey did not measure cigarette use by brand and subbrand, evidence indicated that smoking rates increased significantly among the younger female cohort (20-29 years old) between 1989 and 2004, when menthol cigarettes were introduced into the Japanese market. The authors determined this rise in smoking among women was being driven in large part by the uptake in smoking by young girls—who, according to the youth smoking measure, are smoking primarily menthol cigarettes. The authors supported this data with illustrations from industry documents that detail marketing strategies to promote a lighter, more feminine cigarette to women in Japan. The marketing strategies appear to build on social and cultural norms and rely on brand extension strategies of already popular brands (e.g. Marlboro).

Researchers who reviewed publicly available tobacco industry documents reported evidence of tobacco companies conducting extensive market research with African Americans to better understand trends, attitudes, preferences, and behaviors and target their marketing strategies accordingly (Boley et al., 2010; Cruz et al., 2010; Gardiner, 2004; Johnson et al., 2008; Sutton et al., 2004). Johnson et al. (2008) and Gardiner (2004) also noted industry documents that suggest players in the tobacco industry formed strategic partnerships with national and community African American organizations to gain support for their menthol brands. Klausner's (2011) review of industry documents suggests this targeted marketing strategy occurred after manufacturers realized certain smokers, including African Americans, were disproportionately smoking menthol cigarettes. In the 1970s and 1980s, tobacco companies began using targeted marketing strategies to promote smoking behavior trends that were noted around this time. The studies of industry documents have limitations, though, that should be considered when evaluating their validity and reliability[1].

Mazis et al. (1992) conducted a study to examine the relationship between perceived age and attractiveness of models in tobacco advertisements in magazines. They found that models who were judged to be younger were rated as more attractive by participants. The authors noted that ads with models perceived as younger appeared more often in magazines with younger readerships. They also found that menthol ads featured models with a younger perceived age (25.7 years old) than those featured in nonmenthol ads (31.9 years old). The authors concluded, however, that given the limited number of ads with a clearly portrayed model, tobacco companies were probably not using younger models as a primary marketing strategy to attract youth.

White et al. (2006) found differences by brand in the use of promotional coupons as a marketing strategy, even when controlling for household income. They analyzed data from the 2002 California Tobacco Survey, including a question asking about how often the consumer took advantage of advertising promotions and about how often the consumer sees such promotions when purchasing cigarettes. The authors found that smokers of Newport and Kool cigarettes (both menthol brands) used coupons more often than those who purchased Marlboro and Camel cigarettes (both nonmenthol brands). Additionally, they found that African Americans who smoked menthol cigarettes (65%) used coupons more often than African Americans who smoked nonmenthol cigarettes (28%). The study also found that those who saw promotions more frequently were more likely to take advantage of them. This data suggest menthol smokers take advantage of price promotions more often than nonmenthol smokers. However, this study analyzed data only from California, so the results may not be representative of promotion use patterns in the rest of the United States.

Henrisken et al. (2011) examined variations in the price and availability of promotions of menthol and nonmenthol cigarettes as a function of neighborhood demographics. Researchers coded the presence of advertised promotions and lowest pack price in over 400 stores in 31 neighborhoods

[1] Information obtained from these documents provides isolated glimpses of industry data and communications. Unless a complete study with the raw data are available for review and analysis, conclusions derived from these documents are subjective and speculative. Information quoted directly may be most appropriately used as supportive material as long as the information is not taken out of context.

in California. Researchers found that 25 percent of the advertisements recorded were for menthol cigarettes. Menthol advertisements were particularly common in areas with higher proportions of African Americans and youth 10-17 years old. The proportion of stores that advertised promotions for Newport (menthol), Marlboro Menthol, and Marlboro (nonmenthol) were 27 percent, 51.4 percent, and 75 percent, respectively. When analyzed further, researchers found that for every 10 percent increase in the proportion of African American students in the neighborhood, the odds of a store advertising promotions for Newport were 1.5 times greater. Similarly, for every 10 percent increase in the proportion of youth 10-17 years old in the neighborhood, the odds of a store advertising promotions for Newport was 5.3 times greater. Although like others who have observed Newport are priced higher than Marlboro (nonmenthol), the authors reported that average price per pack for Newport appeared to be related to the racial makeup of neighborhoods, with the price of Newport decreasing $.12 for each 10 percent point increase in African American students. The amount of discount for Newport did not appear to be related to neighborhood demographics. No relationship between neighborhood demographics, promotions advertised, and/or price was found for Marlboro Menthol or Marlboro (nonmenthol).

Some data suggest differences in the influence of advertising receptivity on smoking behavior based on smoking status, gender, race or ethnicity, and age. Although there does not appear to be a validated measure of tobacco industry marketing exposure and receptivity, researchers define ad receptivity as the influence of tobacco marketing on an individual’s attitudes, preferences, and behaviors (Evans, 1995). In the case of tobacco advertising, one hypothesis suggests that an individual’s receptivity to advertising may predict initiation, preference, and continued use. Sargent et al. (2009) suggest the influence of advertising receptivity on initiation may vary by smoking status, whereby those who have not yet initiated smoking may be more influenced by smoking in movies than tobacco advertisements and promotions. Upon initiation, however, teens may become more receptive to tobacco advertising, and receptivity to tobacco marketing may further stimulate experimentation. Choi et al. (2002) also found that adolescents who were experimenters and were found to be highly receptive to advertising were 70 percent more likely to become established smokers at follow-up than those who were minimally receptive. Several studies included in the Lovato et al. (2003) review found gender differences in receptivity, whereby advertising receptivity was influential for girls but not boys. Research also suggests susceptible never smoking African Americans and Hispanics may be less likely to be receptive to tobacco advertising than never smoking White adolescents (Chen et al., 2002; West et al., 2007). Chen et al. (2002) only found a statistically significant relationship between receptivity and smoking for White and Hispanic youth. Evans (1995) found younger adolescents scored higher on measures of ad receptivity than older adolescents. Studies of advertising receptivity did not examine differences between menthol smokers and nonmenthol smokers nor were differences in receptivity to menthol versus nonmenthol advertisements studied.

*Consumer Perceptions*

Richter et al. (2006) conducted focus groups and found differences in perceived risk by race.

While White participants reported menthol cigarettes to be safer than nonmenthol cigarettes, African American participants believed there were no differences in risk between types of cigarettes. Hispanic participants were twice as likely as White participants to rank menthol cigarettes as safer than light cigarettes. African Americans reported the highest preference for menthol cigarettes, and Hispanic participants reported a slight preference. Researchers did not control for the type of cigarette smoked—menthol or nonmenthol—in the analysis. Richter (2008) held a follow up set of focus groups with African Americans in Atlanta and found the discussion around risk and harm to yield mixed results among the different focus groups. While some participants reported menthol cigarettes were less harsh and irritating to the body, others believed they were worse for the body and more addictive. During a ranking exercise conducted with several of the groups, one group ranked menthol cigarettes as less harsh than nonmenthol cigarettes. Additionally, during these group exercises participants reported taste as the primary driver behind their preference for menthol cigarettes and talked about the perceived "cool factor" they believed was promoting use among African Americans and youth. While focus groups provide useful formative and illustrative information, the qualitative nature of the data makes it impossible to draw causal conclusions or to generalize to a larger population.

Unlike Richter et al. (2006), Wackowski et al. (2010) found that African Americans surveyed in New Jersey were twice as likely as Whites to report menthol cigarettes as more risky than nonmenthol cigarettes, with young adults being three times as likely as adults to think menthol cigarettes were more risky. Among smokers and non-smokers surveyed, 70 percent reported menthol cigarettes were just as risky as nonmenthol cigarettes. Only 4 percent of all respondents and 2.4 percent of menthol smokers believed menthol cigarettes were less risky than nonmenthol cigarettes. Almost one-third of menthol smokers surveyed reported menthol cigarettes were more risky than nonmenthol cigarettes. Davis et al. (2010) found similar results from an analysis of the 2009 HealthStyles survey (n=4,556).

Allen et al. (2010) developed a scale to measure attitudes and beliefs about menthol cigarettes among African American smokers. Researchers identified five factors for the scale: medicinal effects, image, less harmful, tradition, and menthol taste or sensation. They piloted the scale on 720 African American smokers (57% menthol only, 15% nonmenthol only). Findings were mixed based on age, gender, and education. Older respondents had higher scores on medical effects, image, and less harmful. Men had higher scores on medical effects, image, and tradition, while women had higher scores on taste. Education was inversely associated with scores on the medicinal effects, image, less harmful, and tradition factors, with less educated subjects having higher scores.

Lee and Glantz (2011) suggest differences in consumer perception by age may be a related to exposure to early industry advertisements that promoted the health benefits of menthol. This would suggest that older smokers who were exposed to these messages may perceive menthol as less harmful than younger smokers were not exposed to such messages do. Additional research is needed to test this hypothesis.

*Conclusion*

Many of the studies on the marketing of menthol cigarettes and consumer perceptions of menthol cigarettes were cross-sectional or qualitative in nature and therefore a clear relationship cannot be drawn.

As seen in nonmenthol cigarettes and other consumer goods, marketing has a strong influence on consumer brand preference and use. The relationship between advertising expenditures and brand preference and the research supporting teen sensitivity to advertising illustrates this reality. Based on numerous studies (including American Legacy Foundation, 2007; Arnett et al., 1998; Altman et al., 1991; Balback et al., 2003; Boly et al., 2010; Connolly et al., 2011; Cummings et al., 1987; Cummings et al., 1997; Glantz et al., 2006; Johnston et al., 1999; Landrine et al., 2005; Laws et al., 2002; O'Connor, 2005; Pollay, 1996; Samaji, 2008; Sutton et al., 2004; White et al., 2006), it appears that a targeted marketing mix of price, promotion, product, and place promotes menthol cigarette use among youth and among African Americans in urban communities. It is likely, however, that factors in addition to marketing contribute to the preference and use of menthol cigarettes among consumers. From the available studies, the weight of evidence supports the conclusion that, like nonmenthol cigarettes, the marketing of menthol cigarettes is likely associated with brand preference. The marketing of menthol cigarettes is associated with menthol brand preference among adolescents and the African American community.

Overall, the results appear to be mixed in the perceived risk of menthol cigarettes. While the reviewed studies suggest that people may be more likely to report menthol cigarettes as less risky or just as risky as nonmenthol cigarettes, design limitations prevent researchers from drawing solid conclusions. Additionally, limited use of validated forms of measuring risk perceptions of menthol cigarettes suggests participants may vary in their ways of defining "risk" and "harm." None of the reviewed articles examined risk perceptions of menthol cigarettes among youth. Given the limited data reviewed and mixed results reported, the weight of evidence is not sufficient to support a conclusion that consumer perceptions are associated with the use of menthol cigarettes.

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Allen B Jr, Unger JB. | Sociocultural correlates of menthol cigarette smoking among adult African Americans in Los Angeles. | 2007 | The California Tobacco-Related Disease Research Program | Cross-sectional survey | Adult African Americans in Los Angeles, CA at least 18 years old, smoked at least 5 cigarettes/day for the past year | N=432 | Menthol smoking was most prevalent among women, 18–30-year-olds, and employed respondents. |
| Altman DG, Schooler C, Basil MD. | Alcohol and cigarette advertising on billboards. | 1991 | The Henry J. Kaiser Family Foundation | Neighborhood Census data | 901 billboards in San Francisco, CA | Not Applicable | Blacks and Hispanics were the target of the largest proportion of alcohol and cigarette billboard advertising; more tobacco advertisements per 1000 population in black neighborhoods than in other neighborhoods. [Not menthol specific] |
| American Legacy Foundation | Cigarette preferences among youth—Results from the 2006 Legacy Media Tracking Online. | 2007 | American Legacy Foundation | Survey | 13-18 year olds | N=3,567 | The role of mentholated cigarettes may also change if the court's order prohibiting the use of light and related descriptors is upheld. If light cigarettes are no longer sold, more youth may turn to mentholated cigarettes since menthol makes these cigarettes easier to smoke than regular cigarettes. Currently, 37% of youth smokers (and 81% of African-Americans) report usually smoking menthol cigarettes. Currently, 40% of youth smokers report usually smoking menthol cigarettes. Clearly, this type of cigarette has appeal among youth and may increase smoking uptake. |
| Anderson S | Marketing of menthol cigarettes and consumer perceptions: a review of tobacco industry documents. | 2011 | U.S. Department of Health and Human Services | Industry document review | Menthol smokers, including special populations | Not applicable | The tobacco industry knew consumers perceived menthol as healthier than non-menthol cigarettes, and this was the intent behind marketing. Marketing emphasizing menthol attracts consumers who may not otherwise progress to regular smoking, including young, inexperienced users and those who find 'regular' cigarettes undesirable. Such marketing may also appeal to health-concerned smokers who might otherwise quit. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Arnett JJ, Terhanian G. | Adolescents' responses to cigarette advertisements: links between exposure, liking, and the appeal of smoking. | 1998 | Funding source(s) not provided. Authors affiliated with the University of Missouri and the University of Pennsylvania | Questionnaire/ survey | Adolescents; grades 6-12 (ages 11-18 years) from seven schools in four states, 54% female, 76% white | N=534 | The results of the study are consistent with the view that certain cigarette advertisements enhance the appeal of smoking to many adolescents.<br>[not menthol specific] |
| Balbach ED, Gasior RJ, Barbeau EM. | R.J. Reynolds' targeting of African Americans: 1988-2000. | 2003 | American Cancer Society | 2 phases: systematic search of tobacco co. and documents and content analysis of the company's cigarette magazine advertising. | African Americans | Not Specified | Identified escape/fantasy and nightlife fun as two of the three primary images featured in the advertisements of menthol cigarettes to the Black/African American population. |
| Centers for Disease Control and Prevention | Comparison of the cigarette brand preferences of adult and teenaged smokers—United States, 1989, and 10 US communities, 1988 and 1990. | 1992 | Centers for Disease Control and Prevention | 2 surveys: Teenage Attitudes and Practices Survey (TAPS) and survey of selected COMMIT evaluation participations | TAPS: 12-18 year olds nationwide<br><br>COMMIT: adult smokers and 13-16 year olds from the 10 COMMIT communities | TAPS: 9,135 adolescents<br><br>COMMIT: 15,415 adults; 9,129 students | TAPS: Although Marlboro was the most popular brand among white and Hispanic adolescents, black adolescents preferred the mentholated brands of Newport, Kool, and Salem. Among 9th-grade students, Marlboro, Newport , and Camel were the most commonly purchased brands. In all regions, Marlboro was the most popular brand. Newport was second in the Northeast, and Camel was second in the West. Among white adolescents, Newport was more popular in the Northeast and the Midwest than in the South and the West.<br><br>COMMIT: Among 9th-grade smokers across all 10 communities, three cigarette brands -- Marlboro, Camel, and Newport -- were consistently preferred. Camel cigarettes were |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | most popular among teenaged smokers in western and midwestern communities. Newport cigarettes were most popular among teenaged smokers from communities in the Northeast. Newport was the most popular brand among black 9th-grade students and third most popular among white 9th-grade students. |
| Centers for Disease Control and Prevention | Changes in the cigarette brand preferences of adolescent smokers− United States, 1989-1993. | 1994 | Centers for Disease Control and Prevention | 2 Surveys: 1989 TAPS and 1993 TAPS | 12-18 year olds | 1989 TAPS: 9,135<br><br>1993 TAPS: 7,311 | Marlboro, Camel, and Newport were the most frequently purchased brands for 86% of the adolescents. Marlboro was the most commonly purchased brand for both male and female adolescents; the second most commonly purchased brand among males was Camel and among females was Newport. Marlboro was the most commonly purchased brand among white and Hispanic adolescents; black adolescents most frequently purchased Newport. Younger smokers (aged 12-15 years) were more likely than older smokers (aged 16-18 years) to buy Newport and less likely to buy Marlboro; purchasing frequency for Camel cigarettes was similar among all adolescents.<br><br>Among adolescents nationwide, Marlboro was the most commonly purchased brand. However, by region, Camel was most commonly purchased in the West, and Newport, in the Northeast.<br><br>From 1989 to 1993, substantial changes in brand preference occurred among adolescents. The percentage of adolescents purchasing Marlboro cigarettes decreased 8.7 percentage points (13% decrease), the percentage of |

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | adolescents purchasing Camel cigarettes increased 5.2 percentage points (64% increase), and the percentage purchasing Newport cigarettes increased 4.5 percentage points (55% increase). These changes did not completely correlate with changes in overall cigarette market share during 1989-1993. Increases in brand preference for Camel cigarettes were greatest among white adolescents and adolescents residing in the Midwest and West, and increases for Newport cigarettes were greatest among younger smokers and adolescents residing in the Northeast. |
| Centers for Disease Control and Prevention | Cigarette brand preference among middle and high school students who are established smokers—United States, 2004 and 2006. | 2009 | Centers for Disease Control and Prevention | 2 Surveys: 2004 and 2006 National Youth Tobacco Surveys | Adolescents in grades 6-12 | 2004: N=27,933<br><br>2006: N=27,038 | Marlboro was the preferred brand (43.3% and 52.3%, respectively), followed by Newport (26.4% and 21.4%, respectively). The use of Newport was significantly higher among blacks in middle school (59.7%) and high school (78.6%) compared with other racial/ethnic groups. Information on brand preferences and tobacco marketing strategies that are attractive to students can be used by tobacco control programs and community initiatives in the design of tobacco countermarketing campaigns. These countermarketing campaigns have been shown to be effective as part of a comprehensive tobacco control program to decrease the initiation of tobacco use among youths and young adults. [Not menthol specific] |
| Chen X, Cruz TB, Schuster DV, Unger JB, Johnson CA. | Receptivity to protobacco media and its impact on cigarette smoking among ethnic minority youth in | 2002 | Partially by funds from the University of California Tobacco-Related Disease Research Program, award number 6KT-0191 | Cross-sectional | Ethnic Minority youth (boys and girls), 12–17 years of age, in CA | N=20,332 | Results indicate that receptivity to protobacco media was lower among African Americans, Asian Americans, and Hispanics than among White youth. There was a consistent dose-response relationship between receptivity to protobacco media and 30-day cigarette smoking |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | California. | | | | | | across ethnic groups. Having a cigarette brand preference was associated with the highest risk for cigarette smoking, having a favorite tobacco ad showed the lowest risk, while having received or being willing to use tobacco promotional items was associated with a moderate risk. [Not menthol specific] |
| Choi WS, Ahluwalia JS, Harris KJ, Okuyemi K. | Progression to established smoking: the influence of tobacco marketing. | 2002 | Robert Wood Johnson Foundation, American Cancer Society, the Tobacco-Related Disease Research Program at the University of California, the National Cancer Institute | Data taken from longitudinal survey | Adolescents (12-17 years) in California. | N=965 | This study provides evidence that receptivity to tobacco advertising and promotions is an important factor in progressing from experimentation to established smoking among adolescents.<br>[Not menthol specific] |
| Connolly GN, Behm I, Osaki Y, et al. | The impact of menthol cigarettes on smoking initiation among non-smoking young females in Japan | 2011 | No funding source(s) provided. Authors affiliated with the Center for Global Tobacco Control, Harvard School of Public Health; Tottori University | Industry document review<br><br>Cross-sectional survey of Japanese adolescents<br><br>Japanese National Health and Nutrition Survey | Japanese females, including adolescents | Not reported | Japan provides an excellent case-study on the impact of the introduction and marketing of menthol brands to young women and initiation into smoking. Smoking prevalence in Japan has been declining among men for decades, but rates of smoking among women have recently increased. The internal tobacco documents demonstrate the intent of tobacco manufacturers to increase initiation among young females through development and marketing of menthol brands. Adolescent survey data provides evidence that the uptake of smoking among high school aged girls in Japan is largely via menthol brands. Adult survey data, though not segmented by brand type (e.g., menthol), indicates that the increased uptake of smoking among young girls has translated to rising smoking rates among young women as these cohorts age. The Japan experience suggests the importance of brand targeting as a vehicle to capitalize on social changes and encourage initiation and use among a historically non-smoking population. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Cruz TB, Wright LT, Crawford G. | The menthol marketing mix: targeted promotions for focus communities in the United States. | 2010 | No funding source(s) provided. Authors affiliated with University of Southern California, National African American Tobacco Prevention Network, Georgia Division of Public Health. Data were partially gathered while an author (Wright) was employed by Brown & Williamson Tobacco Corporation | Interview<br><br>Review of industry documents | Interview with former Brown and Williamson trade marketing manager<br><br>Industry review focused on menthol marketing strategies in urban communities | Not applicable | Tobacco companies recognize the growth potential for the menthol segment in these urban communities. They have higher levels of price discounts and signage, exert tight controls over the retail environment, and use hip-hop lifestyle to associate menthol products with urban nightlife, music, fame, and cultural edginess among younger smokers. |
| Cummings KM, Giovino G, Mendicino AJ. | Cigarette advertising and black-white differences in brand preference. | 1987 | The National Cancer Institute | Not Applicable | Two Populations: (1) patients seen at the Deaconness Family Medicine Center (FMC) located in Buffalo, NY. During the 4-month period of February to May 1984 (2) white and black smokers who called the Stop Smoking Hotline between August 1984 and June 1985 | FMC N=440<br>Hotline N=1199 | Magazines directed to blacks include a much greater proportion of ads for menthol cigarettes compared with magazines similar in content but directed to white readers. |
| Cummings KM, Hyland A, Pechacek TF, Orlandi M, Lynn WR. | Comparison of recent trends in adolescent and adult cigarette smoking behavior and brand preferences. | 1997 | National Cancer Institute; Robert Wood Johnson Foundation | 2 cross-sectional phone surveys (adults); and 2 surveys conducted at schools (adolescents) | Adolescent and adult smokers in 18 communities | Jan-May 1988 N=99348; Aug 1993-Jan 1994 N=79890; | No gender difference between males and females who smoked the menthol brand Newport™ or reported smoking menthol cigarettes in general. Cigarette brand use was more tightly concentrated among adolescents compared to adults, with young smokers most likely to use the most heavily marketed cigarette brands. |
| Davis SP, McClave- | Perceptions of menthol cigarette | 2010 | Centers for Disease Control and Prevention | Survey | U.S. adults and current smokers | N=4,556 | Close to half of adults (45.8%) believed that menthol cigarettes are just as harmful as |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Regan AK, Rock VJ, et al. | use among U.S. adults and adult smokers: Findings from the 2009 HealthStyles survey. | | | | | | nonmenthol cigarettes, and 40.9% of adults did not know whether menthol cigarettes are more or less harmful than nonmenthol cigarettes. Few adults (0.6%), including smokers, perceived menthol cigarettes to be less harmful than nonmenthol cigarettes. Blacks were more likely to believe that menthol cigarettes have health benefits when compared with Whites. Almost half of current smokers believed menthol cigarettes are equally addictive as nonmenthol cigarettes and 74.9% believed menthol and nonmenthol cigarettes are equally hard to quit. |
| Evans N, Farkas A, Gilipin E, Berry C, Pierce JP. | Influence of tobacco marketing and exposure to smokers on adolescent susceptibility to smoking. | 1995 | The California Department of Health Services; Robert Wood Johnson Foundation; the American Heart Association. | Survey | 1993 California Tobacco Survey of adolescent non-smokers | N=3536 | Tobacco marketing may be a stronger current influence in encouraging adolescents to initiate smoking than demographics, school performance, or exposure to other smokers in peers or family network. [Not menthol specific] |
| Gardiner PS. | The African Americanization of menthol cigarette use in the United States. | 2004 | Tobacco Related Disease Research Program at the University of California | Literature Review | African American Population | Not Applicable | Menthol targeting has changed little since the 1960s: African Americans continue to be bombarded with menthol slogans and advertisements. |
| Glanz K, Sutton NM, Jacob Arriola KR. | Operation storefront Hawaii: tobacco advertising and promotion in Hawaii stores. | 2006 | Master Tobacco Settlement through the Hawaii State Department of Health, Georgia Cancer Coalition Distinguished Scholar Award | Cross-sectional study of tobacco product store-based advertisements, including the number, location (indoor/outdoor; | Advertisements and promotions among 184 stores | N=3151 | Among just 184 stores, more than 3,000 ads and promotions were identified. Kool, which is a mentholated brand, was the most heavily advertised brand, consistent with earlier research that found this brand to be the most heavily smoked by middle school youth in Hawaii |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | proximity to candy, toys, school), size, and brand of the ads. Trained youth (ages 12–19 years). | | | |
| Henriksen, L, Schleicher, NC, Dauphinee, AL, Fortmann, SP. | Targeted advertising, promotion, and price for menthol cigarettes in California high school neighborhoods. | 2011 (e-pub ahead of print) | California's Tobacco-Related Disease Research Program, Grant #14RT-0103 | Observational | Tobacco retailers within .5 miles of schools who participated in the California Tobacco Survey | N=726 | In high school neighborhoods, targeted advertising exposes Blacks to more promotions and lower prices for the leading brand of menthol cigarettes. This evidence contradicts the manufacturer's claims that the availability of its promotions is not based on race/ethnicity. It also highlights the need for tobacco control policies that would limit disparities in exposure to retail marketing for cigarettes. |
| Johnson DM, Wine LA, Zack S, Zimmer E, Wang JH, Weitzel-O'Neill PA, Claflin V, Tercyak KP | Designing a tobacco counter-marketing campaign for African American youth. | 2008 | National Institutes of Health/National Cancer Institute grants U56CA101429, U56CA101563, and K07CA091831 | Qualitative | African American middle school-aged youth. | N=28 | High degree of industry commitment to recruiting and retaining young African American smokers and their preference for mentholated brands. |
| Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. | Cigarette brand preferences among adolescents. | 1999 | National Institute on Drug Abuse | Survey | American students in 8th, 10th, or 12th grade attending public or private secondary schools in the coterminous 48 states. | N=2,048 eighth graders, 2,708 tenth graders, and 2,335 twelfth graders | There are dramatic racial/ethnic differences in brand preferences among those who do smoke. Newport, a mentholated cigarette, predominates among African American teenage smokers to an even greater extent than Marlboro predominates among white teenage smokers. |
| Kaufman NJ, Castrucci BC, Mowery P, Gerlach KK, Emont S, | Changes in adolescent cigarette-brand preference, 1989 to 1996. | 2004 | No funding source(s) provided. Authors affiliated with the Robert Wood Johnson, Research Triangle Institute, White | Survey | 3 national samples of adolescents collected in 1989, 1993, and 1996. | N=17,287 | Brand preference among adolescents has been steadily concentrated among 3 brands. More attention may need to be focused on mentholated brands given the increase in Newport's market share. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Orleans CT. | | | Mountain Research Associates | | | | |
| Klausner, K. | Menthol cigarettes and smoking initiation: a tobacco industry perspective. | 2011 | No funding source(s) provided. Author affiliated with University of California, San Francisco | Industry document review | Not applicable | N=128 documents | The documents show that menthol is added to cigarettes in part because it is known to be an attractive feature to inexperienced smokers who perceive menthol cigarettes as less harsh and easier to smoke and because of their availability from friends and family. Second, the tobacco industry found that some youths smoke menthols because they perceive them to be less harmful than non-menthol cigarettes. A key product design issue concerns whether to increase brand menthol levels to appeal to the taste preferences of long-term menthol smokers or keep menthol levels lower to appeal to inexperienced smokers. Marketing studies showed that the companies carefully researched the menthol segment of the market in order to recruit younger smokers to their brands. The industry tracked menthol cigarette usage by age, gender and race to inform product development and marketing decisions. |
| Landrine H, Klonoff EA, Fernandez S, Hickman N, Kashima K, Parekh B, Thomas K, Brouillard CR, Zolezzi M, Jensen JA, Weslowski Z. | Cigarette advertising in Black, Latino, and White magazines, 1998-2002: an exploratory investigation. | 2005 | National Cancer Institute, Tobacco Related Disease Research Program at the University of California, the California Department of Health Services | Review | Analysis of digital photographs of cigarette ads appearing in Ebony (Black), People (White), and People in Spanish (Latino) for the 4.5-year period of January 1998 to August 2002. | N=274 advertisements | Black magazines were 9.8 times and Latino magazines 2.6 times more likely than White magazines to contain ads for menthol cigarettes... |
| Laws MB, Whitman J, | Tobacco availability and | 2002 | No funding source(s) provided. Authors | Survey | Retail businesses in the Boston area that sell | N=1676 | Mentholated brands were marketed most heavily in the predominantly African American |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Bowser DM, Krech L. | point of sale marketing in demographically contrasting districts of Massachusetts. | | affiliated with the Latin American Health Institute, Arias Foundation, Harvard School of Public Health | | tobacco products | | neighborhood, and disproportionately in the Latino neighborhoods. |
| Lee, YO, Glantz, SA. | Menthol: putting the pieces together. | 2011 | The National Cancer Institute grants CA-113710 and CA-87472 | Review | Not applicable | Not applicable | Tobacco companies shaped consumer perceptions of menthol cigarettes. Menthol is not just a flavouring agent. Cigarette companies use menthol's ability to mask irritation and provide sensory effects to make menthol cigarettes appeal to youth and health-concerned smokers, in part because menthol makes low-tar cigarettes more palatable. Consistent with targeted marketing, youths, women and African Americans disproportionately smoke menthols. There appear to be complex interactions with addictive effects of nicotine. The ubiquitous addition of menthol by tobacco companies to over 90% of all tobacco products, whether labelled 'menthol' or not, demonstrates that menthol is not simply a flavour or brand. Menthol imparts sensory characteristics to cigarettes and has a complex interaction with nicotine that affects smoking behaviour whether it is perceived or not, or whether cigarettes containing menthol are marketed as 'menthol' or not. Adding menthol increases fine particles in cigarette smoke, which have immediate adverse effects on the risk of heart attack. |
| Lovato C, Linn G, Stead LF, Best A. | Impact of tobacco advertising and promotion on increasing adolescent | 2003 | National Cancer Institute of Canada, Canada; Canadian Cancer Society, Canada; Centre for Behavioural Research and | Review | 9 Longitudinal studies that assessed individuals' smoking behaviour and exposure to advertising, | N=12,000 baseline nonsmokers. | Tobacco advertising and promotion increases the likelihood that adolescents will start to smoke.<br>[Not menthol specific] |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.
[Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | smoking behaviours. | | Program Evaluation, Canada | | receptivity or attitudes to tobacco advertising, or brand awareness at baseline, and assessed smoking behaviour at follow-ups. Participants were adolescents aged 18 or younger who were not regular smokers at baseline. | | |
| Mazis MB, Ringold DJ, Perry ES, Denman DW. | Perceived age and attractiveness of models in cigarette advertisements. | 1992 | The Center for Marketing Policy Research, American University, University of Baltimore | Sample Survey | Two quota samples of 280 and 281 people were recruited in a racially and economically diverse shopping mall in a suburban area of a large east-coast city. | N=561 | Cigarette ads with young persons were found to appear more often in magazines with younger audiences and for menthol brands. |
| O'Connor RJ. | What brands are US smokers under 25 choosing? | 2005 | No funding source(s) provided. Author affiliated with the Roswell Park Cancer Center | Online Analysis | Data on the cigarette brand preferences of smokers in the 2002 US National Survey on Drug Use and Health from three age groups: 12–17, 18–25 years, and 26+ years. | 12–17 years (n = 2290), 18–25 years (n = 7321), 26+ years (n = 5238). | The youth market in the USA appears dominated by varieties of the major advertised brands; other products make up a more modest percentage of the market. Conversely, the adult market is much more diffuse, with the major varieties commanding smaller overall percentages of the market. Light varieties appear to be popular choices for younger smokers. Similar investigations in other countries could shed further light on younger smokers' brand choices, particularly in those countries that have banned descriptors such as ''Light'' and ''Mild''. [Not menthol specific] |
| Office of Applied Studies. | Results from the 2005 National Survey on Drug Use and Health: National findings | 2006 | Department of Health and Human Services | Survey | Nationally representative sample of U.S. population ages 12 and older | N=68,308 | Marlboro was the cigarette brand used most often by past month cigarette smokers in all four geographic regions. Newport was second in prevalence in the Northeast, Midwest, and |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | South, while Camel was second in the West. |
| Pollay RW, Siddarth S, Siegel M, Haddix A, Merritt RK, Giovino GA, Eriksen MR. | The last straw? Cigarette advertising and realized market shares among youths and adults, 1979–1993. | 1996 | The Social Science and Humanities Research Council of Canada | Analysis | Market shares among adults and teenagers for five years between 1979 and 1993 (1979, 1986, 1989, 1992, 1993). | Based on information of 9 brands | Cigarette brand shares of advertising voice are found to be significantly related to realized market shares, with advertising sensitivity being about three times larger among teenagers than among adults.<br>[Not menthol specific] |
| Richter P, Beistle D, Pederson L, O'Hegarty M. | Small-group discussions on menthol cigarettes: listening to adult African American smokers in Atlanta, Georgia. | 2008 | Centers for Disease Control and Prevention | Focus Groups | Explored health risk perceptions in two studies using focus groups. In the first, Black/African American men and women (ages 45–64 years) who smoked menthol cigarettes participated in small-group discussions | N=54 | The majority of the participants agreed that menthol cigarettes were predominantly featured in Black publications, and that most cigarette advertising and marketing in their communities were for menthol brands, with minimal advertising of non-menthol brands. Some participants thought that tobacco companies targeted menthol cigarettes to Black/African American communities (and non-menthol cigarettes to White communities) and believed that advertising played a role in what brands were sold in an area |
| Richter PA, Pederson LL, O'Hegarty MM. | Young adult smoker risk perceptions of traditional cigarettes and nontraditional tobacco products. | 2006 | U.S. Department of Health and Human Services | Focus Groups | African American, non-Hispanic white, and Hispanic young adult current smokers between the ages of 18 and 22 years who had tried or who currently used NTPs (nontraditional tobacco products). | N=137 | In comparisons with menthol and regular cigarettes, most college and not-in-college participants chose the same risk or more harmful ratings, regardless of the order of presentation of the products. |
| Sargent JD, Gibson J, Heatherton TF. | Comparing the effects of entertainment | 2009 | National Cancer Institute and The American Legacy Foundation | Comparative, Multicenter | Northern New England adolescents aged 10-14 in 1999 | N=4524 | Separate roles for entertainment media and tobacco marketing on adolescent smoking. Both exposures deserve equal emphasis from a policy |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.
[Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | media and tobacco marketing on youth smoking. | | | | | | standpoint.<br>[Not menthol specific] |
| Seidenberg, AB, Caughey, RW, Rees, VW, Connolly, GN. | Storefront cigarette advertising differs by community demographic profile. | 2010 | American Legacy Foundation grant 6212 and National Cancer Institute grant 5 U01 CA114644 | Observational | Tobacco retailers in Brookline, MA (primarily Caucasian) and Dorchester, MA (primarily African American) | N=102 | The low-income/minority community had more tobacco retailers, and advertisements were more likely to be larger, promote menthol products, have a lower mean advertised price, and occur within 1000 feet of a school. |
| Sutton CD, Robinson RG. | The marketing of menthol cigarettes in the United States: populations, messages, and channels. | 2004 | No funding source(s) provided. Authors affiliated with the Onyx Group, the Centers for Disease Control and Prevention | Commentary | Tobacco industry documents related to specific populations including women, middle school youth, Asian/Pacific Islander immigrants, and African Americans | Not Applicable | Learning more about the messages and media used to promote menthol cigarette brands to target markets such as women, Blacks, and youth can be an invaluable aid in helping to decrease the uptake of menthol brands and in creating improved prevention and cessation strategies for at-risk communities and populations. [Not menthol specific] |
| Wackowski O, Delnevo CD, Lewis, MJ | Risk perceptions of menthol cigarettes compared with nonmenthol cigarettes among New Jersey adults. | 2010 | New Jersey Department of Health and Senior Services | Statewide random-digit-dial telephone survey | Data from the 2005 New Jersey Adult Tobacco Survey, oversampling young adults aged 18–24 years, smokers, and recent quitters | N=3062 | Overall, 70.1% (±2.4) of all survey respondents (including nonsmokers) reported that they perceived menthol cigarettes to have about the same risk as nonmenthol cigarettes.<br><br>Current smokers overall were significantly more likely than nonsmokers to believe menthol cigarettes were riskier than nonmenthol cigarettes |
| West JH, Romero RA, Trinidad DR. | Adolescent receptivity to tobacco marketing by racial/ethnic groups in California. | 2007 | the Tobacco Related Disease Research Program of the University of California, the National Cancer Institute, the California Department of Health Services | Survey | Adolescents | 5857 adolescents ages 12-17 years | There may be features of the American and Asian/Pacific cultures that are protective for receptivity to tobacco smoking among those who are susceptible smokers. Prevention strategies emphasizing such features for adolescents of other ethnicities may be beneficial in reducing smoking disparities.<br>[Not menthol specific] |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Marketing and Consumer Perception of Risk: Table of Referenced

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| White VM, White MM, Freeman K, Gilpin EA, Pierce JP | Cigarette promotional offers: who takes advantage? | 2006 | the Tobacco Related Disease Research Program of the University of California, California Department of Health Services | Population | Current smokers | N=4618 | With the exception of smokers intending to quit, cigarette promotional offers are effectively reaching most industry-targeted groups. Importantly, young adults, who have the greatest long-term customer potential, are responding. [Not menthol specific] |
| Yerger VB, Przewoznik J, Malone RE. | Racialized geography, corporate activity, and health disparities: tobacco industry targeting of inner cities. | 2007 | No funding source(s) provided. Authors affiliated with the University of California, San Fancisco and the University of Pennsylvania | Review | Inner cities containing predominately low-income African American residents | 400 internal tobacco industry documents | Tobacco industry's activities contributed to the racialized geography of today's tobacco-related health disparities.<br><br>[Not menthol specific] |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

References

1. Allen B., Cruz TB, Leonard E, et al. (2010) Development and validation of a scale to assess attitudes and beliefs about menthol cigarettes among African-American smokers. Evaluation and the Health Professions 33(4):414-436. [Funded by the Tobacco Related Disease Research Program at the University of California]
2. Altman DG, Schooler C, Basil MD (1991) Alcohol and cigarette advertising on billboards. Health Education Research 6(4):487–490. [Funded in part by Henry J. Kaiser Family Foundation]
3. American Legacy Foundation (2007). Cigarette preferences among youth—Results from the 2006 Legacy Media Tracking Online. First Look Report 17. http://www.legacyforhealth.org/4206.aspx
4. Anderson S (2011) Marketing of menthol cigarettes and consumer perceptions: a review of tobacco industry documents. Tobacco Control 20(suppl.2):ii20-ii28. [Funded by U.S. Department of Health and Human Services]
5. Arnett JJ, Terhanian G (1998) Adolescents' responses to cigarette advertisements: links between exposure, liking, and the appeal of smoking. Tobacco Control 7(2):129–133. [Funding source(s) not provided. Authors affiliated with the University of Missouri and the University of Pennsylvania]
6. Balbach ED, Gasior RJ, Barbeau EM (2003) R.J. Reynold's targeting of African Americans: 1988–2000. American Journal of Public Health 93:822–827. [Funded by the American Cancer Society]
7. Centers for Disease Control and Prevention (1992) Comparison of the cigarette brand preferences of adult and teenaged smokers—United States, 1989, and 10 US communities, 1988 and 1990. Morbidity and Mortality Weekly Report 41(10):169–73,179–81. http://www.cdc.gov/mmwr/preview/mmwrhtml/00016275.htm [Funded by the Centers for Disease Control and Prevention]
8. Centers for Disease Control and Prevention (1994) Changes in the cigarette brand preferences of adolescent smokers− United States, 1989-1993. Morbidity and Mortality Weekly Report 43:577-581. http://www.cdc.gov/mmwr/preview/mmwrhtml/00032326.htm [Funded by the Centers for Disease Control and Prevention]
9. Centers for Disease Control and Prevention (2009). Cigarette brand preference among middle and high school students who are established smokers—United States, 2004 and 2006. Morbidity and Mortality Weekly Report, 58(05): 112-115.
10. Chen X, Cruz TB, Schuster DV, et al. (2002) Receptivity to protobacco media and its impact on cigarette smoking among ethnic minority youth in California. Journal of Health Communication 7(2):95–111. [Funded in part by the Tobacco-Related Disease Research Program at the University of California]
11. Choi WS, Ahluwalia JS, Harris KJ, Okuyemi K (2002) Progression to established smoking: the influence of tobacco marketing. American Journal of Preventive Medicine 22(4):228–233. [Funded by the Robert Wood Johnson Foundation, American Cancer Society, the Tobacco-Related Disease Research Program at the University of California, the National Cancer Institute]
12. Connolly GN, Behm I, Osaki Y, et al. (2011) The impact of menthol cigarettes on smoking initiation among non-smoking young females in Japan. International Journal of

Environmental Research and Public Health 8(1):1-14 [No funding source(s) provided. Authors affiliated with the Center for Global Tobacco Control, Harvard School of Public Health; Tottori University]

13. Cruz TB, Wright LT, Crawford G (2010) The menthol marketing mix: targeted promotions for focus communities in the United States. Nicotine and Tobacco Research 2(suppl 2):S147-S153. [No funding source(s) provided. Authors affiliated with University of Southern California, National African American Tobacco Prevention Network, Georgia Division of Public Health. Data were partially gathered while an author (Wright) was employed by Brown & Williamson Tobacco Corporation]
14. Cummings KM, Hyland A, Pechacek TF, Orlandi M, Lynn WR (1997) Comparison of recent trends in adolescent and adult cigarette smoking behaviour and brand preferences. Tobacco Control 6(Suppl 2):S31-7. [Funded by the National Cancer Institute, Robert Wood Johnson Foundation]
15. Cummings KM, Giovino G, Mendicino AJ (1987) Cigarette advertising and Black-White differences in brand preference. Public Health Report 102(6):698–701. [Funded by the National Cancer Institute]
16. Davis SP, McClave-Regan AK, Rock VJ, et al.(2010) Perceptions of menthol cigarette use among U.S. adults and adult smokers: Findings from the 2009 HealthStyles survey. Nicotine and Tobacco Research 12(suppl 2);S125-35. [Funded by the Centers for Disease Control and Prevention]
17. Evans N, Farkas A, Gilpin E, et al. (1995) Influence of tobacco marketing and exposure to smokers on adolescent susceptibility to smoking. Journal of the National Cancer Institute 87(20):1538–1545. [Funded in part by the California Department of Health Services, Robert Wood Johnson Foundation, American Heart Association]
18. Gardiner PS (2004) The African Americanization of menthol cigarette use in the United States. Nicotine and Tobacco Research 6(suppl 1):S55–S65. [Funded by Tobacco Related Disease Research Program at the University of California]
19. Glanz K, Sutton NM, Arriola KRJ (2006) Operation storefront Hawaii: tobacco advertising and promotion in Hawaii stores. Journal of Health Communication 11(7):699–707. [Funded in part by Master Tobacco Settlement through the Hawaii State Department of Health, Georgia Cancer Coalition Distinguished Scholar Award]
20. Henriksen, L, Schleicher, NC, Dauphinee, AL, Fortmann, SP (2011). Targeted advertising, promotion, and price for menthol cigarettes in California high school neighborhoods. Nicotine and Tobacco Research. epub ahead of print. [Funded by California's Tobacco-Related Disease Research Program, Grant #14RT-0103]
21. Johnson DM, Wine LA, Zack S, et al. (2008) Designing a tobacco counter-marketing campaign for African American youth. Tobacco Induced Diseases 4(1):7. [Funded in part by National Cancer Institute, Lombardi Comprehensive Cancer Center at Georgetown University, University of the District of Columbia]
22. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE (1999) Cigarette brand preferences among adolescents. Monitoring the Future Occasional Paper No. 45, Ann Arbor, MI: Institute for Social Research. http://www.monitoringthefuture.org/pubs/occpapers/occ45.pdf [Funded by the National Institute on Drug Abuse]
23. Kaufman NJ, Castrucci BC, Mowery P, Gerlach KK, Emont S, Orleans TC (2004) Changes in adolescent cigarette-brand preference, 1989 to 1996. American Journal of

Health Behavior 28(1):54-62. [No funding source(s) provided. Authors affiliated with the Robert Wood Johnson, Research Triangle Institute, White Mountain Research Associates]
24. Klausner, K (2011). Menthol cigarettes and smoking initiation: a tobacco industry perspective. Tobacco Control 20(suppl 2): ii12-ii19. [No funding source(s) provided. Author affiliated with University of California, San Francisco]
25. Landrine H, Klonoff EA, Fernandez S, et al. (2005) Cigarette advertising in Black, Latino, and White magazines, 1998–2002: an exploratory investigation. Ethnicity and Disease 15(1):63–67. [Funded by the National Cancer Institute, Tobacco Related Disease Research Program at the University of California, the California Department of Health Services]
26. Laws MB, Whitman J, Bowser DM, et al. (2002) Tobacco availability and point of sale marketing in demographically contrasting districts of Massachusetts. Tobacco Control 11(suppl 2):S71–S73. [No funding source(s) provided. Authors affiliated with the Latin American Health Institute, Arias Foundation, Harvard School of Public Health]
27. Lee, YO, Glantz, SA (2011). Menthol: putting the pieces together. Tobacco Control 20(suppl 2): ii1-ii7. [Funding provided by The National Cancer Institute grants CA-113710 and CA-87472]
28. Lovato C, Linn G, Stead LF, Best A (2003) Impact of tobacco advertising and promotion on increasing adolescent smoking behaviours. Cochrane Database of Systematic Review (4):CD003439. [Funded by National Cancer Institute of Canada, Canada; Canadian Cancer Society, Canada; Centre for Behavioural Research and Program Evaluation, Canada]
29. Mazis MB, Ringold DJ, Perry ES, Denman DW (1992) Perceived age and attractiveness of models in cigarette advertisements. Journal of Financial Markets 56(1):22–37. [Funded in part by the Center for Marketing Policy Research, American University, University of Baltimore]
30. O'Connor RJ (2005) What brands are US smokers under 25 choosing? Tobacco Control 14:213-218. [No funding source(s) provided. Author affiliated with the Roswell Park Cancer Center]
31. Office of Applied Studies. (2002). *Results from the 2001 National Household Survey on Drug Abuse: Volume I. Summary of national findings* (DHHS Publication No. SMA 02–3758, NHSDA Series H–17). Rockville, MD: Substance Abuse and Mental Health Services Administration. [Funding provided by the Department of Health and Human Services]
32. Pollay RW, Siddarth S, Siegel M, et al. (1996) The last straw? Cigarette advertising and realized market shares among youths and adults, 1979–1993. Journal of Financial Markets 60:1–16. [Funded by the Social Science and Humanities Research Council of Canada]
33. Richter P, Beistel D, Pederson L, O'Hegarty M (2008) Small-group discussions on menthol cigarettes: listening to adult African American smokers in Atlanta, Georgia. Ethnicity and Health 13(2):171–182. [Funded by the Centers for Disease Control and Prevention]
34. Richter PA, Pederson LL, O'Hegarty MM (2006) Young adult smoker risk perceptions of traditional cigarettes and nontraditional tobacco products. American Journal of Health Behavior 30(3):302-12. [Funded by the Centers for Disease Control and Prevention]

35. Sargent JD, Gibson J, Heatherton TF (2009) Comparing the effects of entertainment media and tobacco marketing on youth smoking. Tobacco Control 18(1):47–53. [Funded by the National Cancer Institute, American Legacy Foundation]
36. Seidenberg, AB, Caughey, RW, Rees, VW, Connolly, GN (2010). Storefront cigarette advertising differs by community demographic profile. American Journal of Health Promotion 24(6): e26-e31. [Funded by American Legacy Foundation grant 6212 and National Cancer Institute grant 5 U01 CA114644]
37. Sutton D, Robinson RG (2004) The marketing of menthol cigarettes in the United States: populations, messages, and channels. Nicotine and Tobacco Research, 6 (suppl 1):S83–S91. [No funding source(s) provided. Authors affiliated with the Onyx Group, the Centers for Disease Control and Prevention]
38. Wackowski O, Delnevo CD, Lewis, MJ (2010) Risk perceptions of menthol cigarettes compared with nonmethol cigarettes among New Jersey adults. Nicotine and Tobacco Research 12(7): 786-790. [Funded by the New Jersey Department of Health and Senior Services]
39. West JH, Romero RA, Trinidad DR (2007) Adolescent receptivity to tobacco marketing by racial or ethnic groups in California. American Journal of Preventive Medicine 33(2):121–123. [Funded by the Tobacco Related Disease Research Program of the University of California, the National Cancer Institute, the California Department of Health Services]
40. White VM, White MM, Freeman K, et al. (2006) Cigarette promotional offers: who takes advantage? American Journal of Preventive Medicine 30(3):225–231. [Funded by the Tobacco Related Disease Research Program of the University of California, California Department of Health Services]
41. Yerger VB, Przewoznik J, Malone RE (2007) Racialized geography, corporate activity, and health disparities: tobacco industry targeting of inner cities. Journal of Health Care for the Poor and Underserved 18(suppl 4):S10–S38. [No funding source(s) provided. Authors affiliated with the University of California, San Fancisco and the University of Pennsylvania]

## *F. Initiation and Progression to Regular Use*

Close to 90 percent of adult smokers in the United States started to smoke before age 18 (Substance Abuse and Mental Health Services Administration, 2009; U.S. Department of Health and Human Services, 2012). Thus, youth and young adulthood appear to be critical developmental periods for initiation of cigarette smoking. Menthol cigarettes may have an impact on initiation rates and progression to regular use that differ from nonmenthol cigarettes. Since even a small increase in the rate of initiation of cigarette smoking may have a large impact on public health, assessing this possible impact is important. Although some assessments of initiation have included data on switching behavior (i.e. switching between menthol and nonmenthol preferences), this is not included in the current assessment due to difficulties in interpretation. This report assesses the available, though limited, data on the possible impact of menthol cigarettes on initiation of cigarette smoking and progression to regular use, and focuses primarily on smoking behavior by youth and young adults. Given that no large scale, carefully designed cohort study has been carried out to clearly delineate initiation dynamics (progression from experimentation to regular smoking), this assessment examines both age and period data estimates from many data sources.

*Differences in preference rates*

Appleyard et al. (2001) analyzed data from the 2000 National Youth Tobacco Survey (NYTS), using data from 35,828 middle and high school students from across the country for a cross-sectional survey of school-age children. They found that, among those surveyed who reported smoking in the past 30 days, 32 percent of White middle and high school students said their usual brand of cigarette was a menthol brand, as compared to higher values of Asian American (58%), Hawaiian/Pacific Islander (46%), African American (74%) and Hispanic (51%) middle and high school students who reported that they usually smoke menthol cigarettes. An overall number of youth who regularly smoke nonmenthol cigarettes was not provided. This study included a nationally representative population with a high response rate and adequate representation from most racial or ethnic groups. Participating students were from both public and private schools; however results may not generalize to students in non-traditional schools.

Hersey et al. (2006) analyzed data from over 1700 participants of the National Youth Tobacco Survey and found that, after adjusting for demographic differences, menthol use was more common among newer, younger smokers. Younger adolescents were more likely to smoke menthol cigarettes as compared to older adolescents, with both age groups increasing in menthol cigarette use from 2000 to 2002. In 2000, 52 percent of middle school smokers and 37 percent of high school smokers reported menthol cigarette use. In 2002, this percentage increased for both age groups (60% of middle school youth, 44% of high school youth). Rock et al. (2010) found similar results, and addressed the issue of misclassification of the kind of cigarettes smoked through a modification of the response options.

Lawrence et al. (2010), in a cross-sectional study of adults, analyzed data from the 2003 and 2006/2007 CPS-TUS. As with Appleyard et al. (2001), this study found that the prevalence of smoking menthol cigarettes was highest in participants 18-24 years old. Smokers in the 18-24 and 45-64 year old age groups were approximately 1.4 and 1.3 times as likely, respectively, to be menthol smokers as compared to smokers in the 65 years old or over age group. There was no significant difference between the 25-44-year age group and the 65 years age group (CI 1.07; 0.89-1.28). This suggested that smokers 65 years old or over tend to smoke menthol cigarettes at a lower rate than other age groups (Lawrence et al., 2010).

Hersey et al. (2010) analyzed data from the cross-sectional 2006 National Youth Tobacco Survey, a survey of over 27,000 students in grades 6-12. They found that youth (n=3281) who smoked in the past month were more likely to report smoking menthol cigarettes at rates inversely proportional to age. Of middle school students who reported smoking in the past month, over 50 percent reported smoking menthol cigarettes, whereas of high school students who reported smoking in the past month, 43 percent reported smoking menthol cigarettes. Differences exist in prevalence of menthol smoking depending on race and ethnicity, with African American youth reporting the highest prevalence (80.6% middle school smokers and 84.8% high school smokers), followed by both Hispanics (57.9% and 56.4% for middle and high school smokers) and Asian Americans (57.4% middle school smokers and 43.6% high school smokers). White youth smokers reported the lowest levels, but still higher than that seen in adults. Among current non-Hispanic White smokers who smoked in the past month, 43.1

percent and 37.6 percent for middle and high school smokers smoked menthol cigarettes. This study included a large nationally representative population with a high response rate (80.2%) and weighted estimates, used three menthol smoking status definitions to model the relationship between menthol cigarette use, and included a nicotine dependence measure to assess the robustness of the association.

Rock et al. (2010) analyzed data from the 2004-2008 NSDUH (n=71,605) and found that 35.7 percent of current smokers 12 years old or over smoked menthol cigarettes. Among smokers age 12-17, 71.9 percent of African American youth reported smoking menthol cigarettes, followed by 51.5 percent of Asian Americans, 47.0 percent of Hispanics, 41.0 percent of Whites, and 34.7 percent of American Indian/Alaska Natives. This pattern remained relatively consistent among 18-25 year olds, with a slight increase for African American smokers (85%). Among adult smokers 26 years old or over in the survey, the prevalence of current menthol use was only modestly lower (and still high) for African American smokers (82.2%), however rates were much lower for Hispanics (29.5%), Asian Americans (28.6%), American Indian/Alaska Natives (23%), and Whites (21.9%). From 2004 to 2008, menthol cigarette smoking among White smokers 12-17 years old increased from 40.3 percent to 46.0 percent. In addition, menthol cigarette use among individuals 18-25 years old increased for Hispanic (from 33.9% to 42.4%) and White (from 26.7% to 32.5%) smokers. Thus, not only were younger smokers more likely to be menthol smokers, but prevalence may be increasing.

Fernander et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS. They found that current smokers 18-24 years old were more likely to smoke menthol cigarettes. Odds ratios indicated that, relative to the 65+ year group, smokers who were 18-24 years old, 25-44 years old, and 45-65 years old were significantly more likely to be menthol smokers (66%, 20%, and 22%, respectively).

*First smoking experience*

Pletcher et al. (2006) analyzed data collected during the CARDIA study, which included data from 972 menthol and 563 nonmenthol smokers (18-30 years old). They found that there was no difference in age of first cigarette use when comparing menthol and nonmenthol smokers; both groups smoked their first cigarette at an average age of 16. This was a cohort study with a long follow up period. Although not nationally representative, there was a diverse group of participants. Participants were limited to adults 30 years old and younger, which was appropriate to assess smoking initiation.

Okuyemi et al. (2004) analyzed data from a cross-sectional survey of 480 African American smokers and asked about age of first cigarette use as part of the subjects' demographic and smoking characteristics. No significant differences were found; menthol smokers smoked their first cigarette on average at 15 years old, nonmenthol smokers at around 16 years old. Although there were more menthol smokers (n=407) than nonmenthol smokers (n=73), there was sufficient power to make statistically comparisons between these two groups.

Gandhi et al. (2009) analyzed data from 1,688 patients of a specialist smoking cessation service. No differences were found in the age at which menthol and nonmenthol smokers reported first using tobacco. For menthol smokers, “age first used tobacco” was an average of 14.87 years old; for nonmenthol smokers, “age first used tobacco” was an average of 15.21 years old. The study included comparable numbers of menthol (n=778) and nonmenthol (n=910) smokers, however generalizability may be limited because of the use of a non-nationally representative community sample and the inclusion of only those who were seeking smoking cessation treatment.

*Progression to regular smoking*

Hyland et al. (2002) analyzed data (n=13,268) from the Community Intervention Trial for Smoking Cessation (COMMIT), a telephone tobacco use survey in 1988 with re-interviews in 1993. When “age started smoking” of menthol smokers was compared with nonmenthol smokers, there were no significant differences. This study used 11 matched pairs of communities (10 in the United States and one in Canada), which decreased confounding by pairing controls with similar groups, and had a large sample size. However, there was a lack of definition of “age started smoking”, so it is unknown if this refers to first experience or to onset of regular smoking. Generalizability may be limited due to the use of a community based sample that was not nationally representative.

Okuyemi et al. (2004) surveyed a cross-section of 480 inner-city African American smokers and examined the relationship between menthol smoking and smoking cessation. This survey examined sociodemographics, smoking characteristics, and smoking cessation experiences of participants and compared menthol smokers (n=407) to nonmenthol smokers (n=73). No differences were seen in age of onset of regular smoking. The inclusion of only African American smokers is both a strength and a limitation of the study. It limits generalizability but also eliminates the effect of disproportionate subgroup size (see Fagan et al., 2010 and Fernander et al., 2010). Although the sample sizes were small, there was sufficient power to make comparisons.

Okuyemi et al. (2007) conducted a randomized, double-blind, placebo-controlled clinical trial looking at African American “light” smokers (n=755). “Light” refers to a low number of cpd smoked, and does not refer to the cigarettes themselves. In this case, a light smoker is defined as one who smoked 10 or fewer cpd. No differences were found in “age started smoking regularly” between menthol and nonmenthol smokers. The study included a large number of participants, however, the majority (81.7%) was self-identified menthol smokers. Despite this uneven distribution, there appears to be sufficient statistical power to compare these groups. The inclusion of only African American smokers of 10 or fewer cpd limits the generalizability of the findings (see Fagan et al., 2010 and Fernander et al., 2010).

Fagan et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS to study progression to regular smoking. The study compared the age of onset of “fairly regular smoking” of menthol and nonmenthol smokers. Smokers were defined as those who had smoked at least 100 cigarettes, however no formal definition for “smoking fairly regularly” was given. Covariates included age, race or ethnicity, marital status, and socioeconomic variables, as well as total years smoked daily and smoking status 12 months ago. Since African Americans typically initiate smoking at later ages (Finkenauer et al., 2009), it was important to include race or ethnicity as a covariate. Menthol smokers started smoking regularly at a later age. When investigating the age of onset to regular smoking, menthol smokers were less likely to start before 15 years old as compared to nonmenthol smokers or smokers with no usual type. Although there were no significant differences in the 15-17 year old groups, menthol smokers were more likely to report 18 years old or more as the age of onset of regular smoking. The tabular data had uneven racial or ethnic representations with more White smokers identifying as nonmenthol smokers and more African Americans identifying as menthol smokers. The study had a large sample size with nationally representative data.

Like Fagan et al. (2010), Fernander et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS to study progression to regular smoking. They also assessed the age of onset of regular smoking by asking respondents, who had smoked at least 100 cigarettes, at what age they first started “smoking fairly regularly.” Like the results from Fagan et al. (2010), menthol smokers started smoking regularly at a later age. The CPS-TUS data set contains an uneven distribution of racial or ethnic subpopulations in the cell sizes, with more White smokers identifying as nonmenthol smokers and more African Americans identifying as menthol smokers. Hispanics and other minorities were more likely to smoke menthols, and African Americans tend to start smoking later, which can complicate the interpretation of what drives a later onset of progression to regular smoking in menthol smokers (see Okuyemi et al., 2004 and 2007).

Like Fagan et al. (2010) and Fernander et al. (2010), Lawrence et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS. A significant association exists between use of menthol cigarettes and the age of onset of regular smoking among women, but not among men. That is, women who reported smoking menthol cigarettes were more likely to report having an earlier onset of regular smoking. Importantly, however, this was limited to smokers in the 45-64 year old age group as compared to the 65 and over age group.

Cubbin et al. (2010) analyzed cross-sectional, nationally representative data in the United States from the 2005 NHIS – CCS (n = 31,428 18 years old and over). Among current smokers (identified as having smoked at least 100 cigarettes and currently smoking some days or everyday), Cubbin et al. compared the “age of initiation” of menthol and nonmenthol smokers and found no significant differences between menthol and nonmenthol smokers on this measure. All analyses were adjusted for age, income, and education levels, and stratified by gender and race or ethnicity. Readers likely assume that the researchers are using data from the “How old were you when you FIRST started to smoke fairly regularly?” question because there is no question that uses ‘age of initiation’ language. In addition, no indication of whether someone started out as a menthol or nonmenthol smoker is provided. Among both menthol and nonmenthol smokers, White smokers have been shown to initiate regular smoking one and a half to three years earlier than non-Whites (Cubbins et al., 2010).

Stahre et al. (2010) also analyzed data from the 2005 NHIS – CCS, which examined current smokers (n=6511) and former smokers (n=6774). No significant difference existed in the average age of first smoking regularly. Menthol smokers reported an average age of 19.6 and nonmenthol smokers reported an average age of 19.7.

Among a set of secondary data analyses conducted in 2010 that have not been peer-reviewed, one study included an analyis related to initiation. The Nonnemaker secondary data analysis used a measure of progression that was based on several measures, including a transition from smoking less than 100 cigarettes to smoking more than 100 cigarettes, a transition from smoking on less than 20 days per month to smoking 20 or more days per month, and a transition from nondaily smoking to daily smoking. Survey data were collected over three consecutive school years (2000-2001, 2001-2002, 2002-2003). Middle and high school students who initiated to menthol cigarettes during the first or second year of data collection were more likely to report being daily smokers at the third year of data collection. Racial or ethnic subpopulations were unevenly distributed, but the analysis accounted for baseline characteristics. Although this analysis pulled from a large sample, this study lacked appropriate controls for socioeconomic status, and the point estimates for other (non-progression) covariates were somewhat implausible due to small sample size.

*Industry documents research*

Two studies examined publicly available tobacco industry documents. Although utility of these kinds of studies may be limited due to unknown details related to the original data, they can be useful in providing some insight into tobacco industry communications, plans, and research. Kreslake et al. published two articles that reviewed such documents on the topic of initiation of smoking behavior. The documents mainly focused on the possible palliative effect of menthol on smoking; menthol appears to moderate or alleviate negative sensory experiences that often accompany a first-smoking experience (Kreslake et al., 2008a). Indeed, Kreslake et al. (2008b) also found an internal Brown and Williamson memo stating that "Kool's menthol level may be considered too high for new smokers, and that a successful 'starter' cigarette would need to include a low tobacco taste, low impact and irritation, low tobacco aftertaste and low menthol content." Although these are single examples, they indicate tobacco industry knowledge and acceptance that menthol provides a mechanism through which new smokers are able to more successfully initiate smoking.

*Conclusion*

In all peer-reviewed articles, data were collected through self-report. Although this could be associated with recall bias or misclassification, self-report is the standard of this research field and not considered detrimental to the study results. The data do not support the claim that a substantial number of adult respondents intentionally under-report tobacco use (Everhart et al, 2009; Yeager & Krosnick, 2010). Furthermore, as noted by Caraballo et al. (2011), while evidence exists of some self-report bias in reporting menthol or nonmenthol cigarette use, especially among adolescents, this is not necessarily problematic since it is likely that this type of bias is fairly constant over time.

There is no indication that menthol smokers first experience cigarette smoking any earlier or later than nonmenthol smokers (Pletcher et al., 2006; Okuyemi et al., 2004; Gandhi et al., 2009). However, data regarding age of onset of regular smoking are mixed. Six studies found no difference (Hyland et al., 2002; Okuyemi et al., 2004; Okuyemi et al., 2007; Cubbin et al., 2010; Stahre et al., 2010; Lawrence et al., 2010 – males only), two found that menthol smokers began regular smoking at a later age (Fagan et al., 2010; Fernander et al., 2010), and two found that menthol smokers began regular smoking at an earlier age (Lawrence et al., 2010 – females only; Nonnemaker secondary data analysis). Data that appear to indicate that menthol smokers start smoking later than nonmenthol smokers are difficult to interpret because differences may be driven by racial or ethnic differences. Evidence exists of significant racial or ethnic differences in early experiences with smoking and transitioning to regular smoking, with African Americans experimenting and transitioning later than White smokers (Finkenauer et al., 2009). Age of smoking initiation may also be dependent on the ethnic background in which the smokers grow up (Baron-Epel & Haviv-Messika, 2004). Although there were no consistent differences in the onset of regular smoking, the non-peer-reviewed Nonnemaker secondary data analysis indicated that those who start smoking with menthol cigarettes were more likely to progress to regular smoking.

Prevalence data from cross sectional studies make a case for the involvement of menthol in the initiation process; all six studies found that youth/younger smokers were more likely to smoke menthol cigarettes as compared to older smokers (Appleyard et al., 2001; Hersey et al., 2006; Lawrence et al., 2010; Hersey et al., 2010; Rock et al., 2010; Fernander et al., 2010). Although cohort effects could be a factor in these differences, the consistency of findings across datasets gathered from different years suggests that this is not the case. When the logical connections between and among cohorts are considered in several articles, the suggestion of greater influence on initiation dynamics grows. Younger, newer smokers prefer menthol at levels far above that of the general population, a finding that is generally consistent across racial or ethnic groups. The data that support the finding that those of younger age have greater menthol preference are consistent. This suggests that as smokers grow older, menthol preferences change. Additionally, while this is not a direct measure of individual initiation, it tracks very well to the ages that initiation typically occurs. Given that the general adult smoking population smokes menthol cigarettes at rates lower than the younger age groups, the type of cigarette chosen does not appear to be purely based on availability through parents or other adults, which suggests that younger smokers may intentionally seek out menthol cigarettes. This could be for a variety of reasons, some of which have been discussed in publicly available internal tobacco industry documents, including effects directly related to menthol (e.g., soothing or cooling effects) or for social reasons and marketing. However, as stated previously, since the studies addressing differences in menthol or nonmenthol in prevalence are all fairly recent (within the past 10 years), it is possible that these differences may be due to cohort effects. Despite this caveat, from the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased initiation and progression to regular use of cigarette smoking.

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Appleyard J, Messeri P, Haviland ML. | Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. | 2001 | American Legacy Foundation) | National Youth Tobacco Survey | Asian American and Hawaiian/ Pacific Islander youth | N=35,828.The schools response Rate was 90% and the student response rate was 93%, resulting in an overall response rate of 84%. | While many studies have documented the high prevalence of Menthol cigarette use among African Americans, NYTS 2000 data reveal that smoking mentholated cigarettes is also common among Asian American youth. Overall, 74% of African Americans and 58% of Asian Americans reported that their usual brand of cigarette is menthol brand. |
| Baron-Epel O, Haviv-Messika A. | Factors associated with age of smoking initiation in adult populations from different ethnic backgrounds. | 2004 | No funding source(s) provided. Authors affiliated with the University of Haifa and the Israel Center for Disease Control | Cross-sectional national (Israel) survey | Households with at least one resident 21+ years old | 4248 Jews, 858 Arabs and 915 Immigrants (856 from the former Soviet) | Age of smoking initiation is dependent on the ethnic background in which the smokers grow up, however, the influence of the father smoking seems to be similar in all population groups.<br><br>[Not menthol specific] |
| Caraballo, RS & Asman, K | Epidemiology of menthol cigarette use in the United States. | 2011 | No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention | Review and secondary analyses of national surveys | NSDUH: adolescents aged 12-17 years old who smoked in the past month and adult smokers (aged 18 years or older) who smoked in the past month<br>NYTS: middle school (MS) and high school (HS) students with school year, past 30 day smoking, brand use, and menthol information.<br>MTF: current smokers in 8$^{th}$, 10$^{th}$ and 12$^{th}$ | NSDUH: 9,595 adolescents; 62,010 adults<br>NYTS: 1,978 MS students and 6,163 HS students<br>MTF: 20,863 8th graders; 30,722 10th graders; 40,914 12th Graders | Menthol cigarettes are disproportionately smoked by adolescents, blacks/African Americans, adult females, those living in the Northeast of the United States and those with family incomes lower than $50,000. Based on self-reports of menthol cigarette use, menthol cigarette use among smokers have increased from 2004 to 2008. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | grade<br>NHANES: 20 years and older who had Smoked and were non-Hispanic white, non-Hispanic black/African American, or Mexican American | NHANES: 1571 individuals with UPC information | |
| Cubbin C, Soobader M-J, LeClere FB. | The intersection of gender and race/ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. | 2010 | Research Network on Disparities | Cross-sectional national survey (2005 National Health Interview Survey and Cancer Control Supplement) | Black, Hispanic and white men and women, 25-64 years old | N= 7688 | After adjusting for age, income and education, black (compared with Hispanic and white) and female (compared with male) smokers were more likely to choose menthol cigarettes. There was only one statistically significant difference in age of initiation, cigarettes smoked per day, quit attempts or time since quitting between menthol and non-menthol smokers: white women who smoked menthol cigarettes reported longer cessation compared with those who smoked non-menthol cigarettes. |
| Everhart J, Ferketich AK, Browning K et al. | Acculturation and misclassification of tobacco use status amont Hispanic men and women in the United States. | 2009 | Summer Research Opportunities Program at the Ohio State University | Survey (1999 – 2002 National Health and Nutrition Examination Surveys) | Self-identified "Mexican American" or "other Hispanic" and were at least 20 years old. | N=9965 (wave 1999-2000)<br>N=11,039 (wave 2001-2002) | A gender-specific association between misclassification and acculturation was found. Among males (n=1,175), the prevalence estimates of misclassification were 4.8%, 1.8%, and 2.2% for low, medium, and highly acculturated males, respectively ($p < .02$). Among females (n=1,345), the prevalence estimates of misclassification were 0.8%, 2.0%, and 4.9% for low, medium, and highly acculturated females, respectively ($p < .03$). [not menthol specific] |
| Fagan P, Moolchan ET et al. | Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with | 2010 | The National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current | Civilian non-institutionalized daily smokers aged 18 years and above. | N=11,671 (menthol smokers)<br>N=33,644 (nonmenthol smokers) | …among adults, daily menthol smokers consuming six to 10 cigarettes per day were more likely than non-menthol smokers consuming six to 10 cigarettes per day to smoke their cigarette within the first 5 minutes after waking. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | similar consumptive patterns. | | | Population Surveys) | | N=958 (no usual type) | |
| Fernander A, Rayens ML et al. | Are age of smoking initiation and purchasing patterns association with menthol smoking? | 2010 | No funding source(s) provided. Authors affiliated with the University of Kentucky | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplement to the Current Population Survey) | Civilian non-institutionalized individuals aged 18 years and above. | N= 16,294 (menthol smokers) N= 46,899 (non-menthol smokers) | The multivariate logistic model only marginally revealed that age of smoking initiation predicted menthol smoking: findings are suggestive that the longer the delay of initiation the more likely that an individual smoked menthol cigarettes [odds ratio (OR) = 1.01; 95% confidence interval (CI): 1.00–1.01].<br><br>Menthol smokers in the United States are more likely to be female, younger, from ethnic minority groups, and to have a high school education |
| Finkenauer R, Pomerleau CS, Snedecor SM, Pomerleau OF. | Differences in factors relating to smoking initiation. | 2009 | NIH grants DA017640 and R01 DA006529 | Research study | Regular daily smokers (≥ 5 cpd for at least 5 years) between 25 and 65 years old | N=203 | Ninety percent of African American smokers consumed menthol cigarettes, as opposed to 25% of Caucasian smokers. |
| Gandhi KK, Foulds J, Steinberg MB, Lu SE, Williams JM. | Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic. | 2009 | The New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health] | Retrospective Cohort/ Population Studies | Specialized smoking cessation outpatient clinic in New Jersey: patients who set a quit date and attempted to quit smoking, between 1 January 2001 and 30 June 2005; African American, Latinos, Whites | N=1688 (787 Menthol, 910 Nonmenthol) | This study found lower short-term (4-week follow-up) quit rates among AA and Latino menthol smokers as compared with non-menthol smokers within the same racial / ethnic subgroups. |
| Hersey JC, Ng SW, Nonnemaker JM, Mowery P, Thomas KY, Vilsaint MC, | Are menthol cigarettes a starter product for youth? | | American Legacy Foundation | 2000 and 2002 NYTS, School-based, national survey | Data from the 2000 NYTS and from the 2002 NYTS.The survey used a three-stage cluster sample design that oversampled | N=5,512 youth (2000 NYTS) and 3,202 youth (2002 NYTS) | Additionally, youth who smoked menthol cigarettes had significantly higher scores on a scale of nicotine dependence compared with nonmenthol smokers, controlling for demographic background and the length, frequency, and level of smoking. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Allen JA, Haviland ML. | | | | | African American, Hispanic, and Asian students. The NYTS was administered to 35,828 students in grades 6 through 12 in spring 2000 and to 26,149 students in spring 2002. The | | |
| Hersey JC, Nonnemaker JM, Homsi G. | Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. | 2010 | American Legacy Foundation and RTI International | Survey (2006 National Youth Tobacco Survey) | Middle and high school students who smoked in the past 30 days who reported that they had a usual brand of cigarette and who could identify whether the usual brand was menthol or nonmenthol. | N=1458 (menthol smokers) N=1710 (nonmenthol smokers) | A logistic regression model of dependence, controlling for background (i.e., school level, gender, and race/ethnicity) and smoking level (i.e., years, frequency, and level of smoking) found that smoking menthol cigarettes was significantly associated with reduced time to needing a cigarette among smokers with a regular brand (odds ratio [OR]: 1.86, p = .003) and among established smokers (OR: 2.06, p = .001). |
| Hyland A, Garten S, Giovino GA, Cummings KM. | Mentholated cigarettes and smoking cessation: findings from COMMIT. | 2002 | The National Cancer Institute grant CA016056-26 | Telephone survey | COMMIT study: Baseline smokers who reported whether their current cigarette brand or not in 1988, and had a known smoking status in 1993. | N=13,268 (3,184 menthol, 10084 non-menthol) | No clear associations were observed between menthol cigarette use and indicators of nicotine dependence, even after controlling for race/ethnicity and other demographics.. |
| Kreslake JM, Wayne GF, Alpert HR, Koh HK, Connolly GN. | Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. | 2008 | American Legacy Foundation grant 6212 and the National Cancer Institute grant RO1 CA87477-07 | Review | Tobacco industry documents from 1985-2007, describing menthol product development, results of laboratory testing of US menthol brands, market research reports, and the 2006 National Survey on Drug Use | N=580 documents | Tobacco companies manipulate the sensory characteristics of cigarettes, including menthol content, thereby facilitating smoking initiation and nicotine dependence. Menthol brands that have used this strategy have been the most successful in attracting youth and young adult smokers and have grown in popularity. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | and Health Results. | | |
| Kreslake JM, Wayne GF, Connolly GN. | The menthol smoker: tobacco industry research on consumer sensory perception of menthol cigarettes and its role in smoking behavior. | 2008 | National Cancer Institute Grant R01 CA87477-07 and American Legacy Foundation Grant 6212 | Review | Internal tobacco industry documents ranging in date from 1965-2000. | N=440 documents | Two unique types of menthol smoker emerged from this analysis: those who cannot tolerate the harshness and irritation associated with smoking nonmenthol cigarettes, and those who seek out the specific menthol flavor and associated physical sensation. |
| Lawrence DL, Rose A et al. | National patterns and correlates of menthol cigarette use in the United States. | 2010 | National Cancer Institute | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current Population Survey) | Smokers at least 18 years old. | N=63,193 | Use of mentholated cigarettes was higher among women than among men.<br><br>Additional significant factors associated with mentholated cigarette smoking included being unmarried (never married: OR: 1.21, 99% CI: 1.09–1.34; divorced/separated: OR: 1.13, 99% CI: 1.03–1.23), being born in a US territory (OR: 2.01, 99% CI: 1.35–3.01), living in a non-metropolitan area (OR: 0.87, 99% CI: 0.80–0.96), being unemployed (OR: 1.24, 99% CI: 1.06–1.44) and lower levels of education. |
| Okuyemi KS, Ebersole-Robinson M, Nazir N, Ahluwalia JS. | African-American menthol and nonmenthol smokers: differences in smoking and cessation experiences. | 2004 | Grants from the National Institutes of Health (K08 CA90334) and the Cancer Research Foundation of America | Cross sectional surbey | African-American smokers at an inner-city health center. Menthol smokers (n = 407) were compared to nonmenthol smokers (n = 73) in these characteristics. | N=480 | Based on the consistency of the direction of the three measures of cessation success, the authors suggested that Black/African American individuals who smoke menthol cigarettes may be less likely to be successful in their quit attempts. |
| Okuyemi KS, Faseru B, Sanderson Cox L, Bronars CA, | Relationship between menthol cigarettes and smoking cessation | 2007 | National Cancer Institute at the National Institutes of Health grant R01 CA091912 | Randomized Controlled Trial | African American light smokers | N=755 | Among African American light smokers, use of menthol cigarettes is associated with lower smoking cessation rates. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Ahluwalia JS. | among African American light smokers. | | | | | | |
| Pletcher MJ, Hulley BJ, Houston T, Kiefe CI, Benowitz N, Sidney S. | Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. | 2006 | Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute | Multi-center U.S. cohort study (CARDIA) | African American and European American smokers aged 18 to 30 years and healthy at the time of enrollment in 1985 | 1544 (non-menthol smokers (n = 563) and menthol smokers (n = 972)) | Menthol and nonmenthol cigarettes seem to be equally harmful per cigarette smoked in terms of atherosclerosis and pulmonary function decline, but menthol cigarettes may be harder to quit smoking. |
| Rock VJ, Davis SP, Thorne SL, et al. | Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. | 2010 | No funding source(s) provided. Authors affiliated with Centers for Disease Control and Prevention and RTI International | Cross-sectional survey (2004–2008 National Survey on Drug Use and Health) | Current smokers age 12 and over | N=71,605 | Over half of menthol cigarette smokers were female (52.2%), and approximately 29.4% of all menthol smokers were Black, which was almost 10 times the percentage of nonmenthol smokers who were Black (3.0%, p < .01). Prevalence of past month menthol cigarette use was highest among current smokers aged 12–17 years (44.7%) and decreased as age group increased. |
| Stahre M, Okuyemi KS et al. | Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. | 2010 | Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development | Cross-sectional survey (2005 National Health Interview Survey (NHIS) Cancer Control Supplement) | Current or former smokers, age 18 and over | N= 6511 (smoker) N= 6774 (former smoker) | Overall menthol smoking prevalence was significantly different by sex, region of the United States, race, marital status and average number of cigarettes smoked per day for both current and former smokers and age for former smokers only.<br><br>For current and former smokers, non-menthol smokers reported a higher number of cigarettes smoked per day on average than menthol smokers. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Smoking Initiation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | | Menthol smoking status was not associated with differences in utilization of quit aids. |
| U.S. Department of Health and Human Services. | Preventing Tobacco Use Among Young People: A Report of the Surgeon General. | 1994 | Centers for Disease Control and Prevention | Review | Not applicable | Not applicable | [Not applicable] |
| U.S. Department of Health and Human Services | Preventing tobacco use among youth and young adults – A report of the Surgeon General. Rockville, MD. | 2012 | U.S. Department of Health and Human Services | Review | Not applicable | Not applicable | [Not applicable] |
| Yeager DS & Krosnick JA | The validity of self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. | 2010 | No funding source(s) provided. Authors affiliated with Stanford University | Study based on National Health and Nutrition Examination Survey (multiple waves) | Adult smokers age 20 and over | N=21,414 | These analyses of NHANES data collected between 2001 and 2008 suggest that if any nicotine product users under-reported this behavior, the proportion of people who did so was exceedingly small.<br><br>[Not menthol specific] |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

References


1. Appleyard J, Messeri P, Haviland ML (2001) Smoking among Asian American and Hawaiian/Pacific Islander youth: data from the 2000 National Youth Tobacco Survey. Asian American & Pacific Islander Journal of Health 9(1):5-14. [Funded by the American Legacy Foundation]
2. Baron-Epel O, Haviv-Messika A. (2004) Factors associated with age of smoking initiation in adult populations from different ethnic backgrounds. European Journal of Public Health 14(3):301-5. [No funding source(s) provided. Authors affiliated with the University of Haifa and the Israel Center for Disease Control]
3. Caraballo, RS & Asman, K (2011). Epidemiology of menthol cigarette use in the United States. Tobacco Induced Diseases, 9 (Suppl 1): S1. [No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention]
4. Cubbin C, Soobader M-J, LeClere FB (2010) The intersection of gender and race or ethnicity in smoking behaviors among menthol and non-menthol smokers in the United States. Addiction 105(suppl. 1):32–8. [Funded by Research Network on Disparities]
5. Everhart J, Ferketich AK, Browning K et al (2009) Acculturation and misclassification of tobacco use status amont Hispanic men and women in the United States. Nicotine and Tobacco Research 11(3): 240-247. [Funding provided by the Summer Research Opportunities Program at the Ohio State University].
6. Fagan P, Moolchan ET et al. (2010) Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. Addiction 105(suppl. 1):55–74. [Funded by the National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center]
7. Fernander A, Rayens ML et al. (2010) Are age of smoking initiation and purchasing patterns association with menthol smoking? Addiction 105(suppl. 1): 39–45. [No funding source(s) provided. Authors affiliated with the University of Kentucky]
8. Finkenauer R, Pomerleau CS, Snedecor SM, Pomerleau OF (2009) Differences in factors relating to smoking initiation. Addictive Behaviors 34(12):1056-9. [Funded by NIH grants DA017640 and R01 DA006529]
9. Gandhi KK, Foulds J, Steinberg MB, et al. (2009) Lower quit rates among African American and Latino menthol smokers at a tobacco treatment clinic. International Journal of Clinical Practice 63:360–367. [Funded by the New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health]
10. Hersey JC, Ng SW, Nonnemaker JM, et al. (2006) Are menthol cigarettes a starter product for youth? Nicotine and Tobacco Research 8:403–13. [Funded by the American Legacy Foundation]
11. Hersey JC, Nonnemaker JM, Homsi G. (2010) Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. Nicotine and Tobacco Research 12(suppl 2):S136-46. [Funded by the American Legacy Foundation and RTI International]
12. Hyland A, Garten S, Cummings KM (2002) Menthol cigarettes and smoking cessation: findings from COMMIT (Community Intervention Trial for Smoking Cessation).

Tobacco Control 11(2):135–9. [Funded by the National Cancer Institute Grant CA016056-26]

13. Kreslake JM, Wayne GF, et al. (2008a) Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. American Journal of Public Health 98(9):1685–92. [Funded by National Cancer Institute Grant R01 CA87477-07 and American Legacy Foundation Grant 6212]
14. Kreslake JM, Wayne GF, Connolly GN (2008b) The menthol smoker: Tobacco industry research on consumer sensory perception of menthol cigarettes and its role in smoking behavior. Nicotine and Tobacco Research, 10(4):705–715. [Funded by National Cancer Institute grant R01 CA87477-07 and American Legacy Foundation Grant 6212]
15. Lawrence DL, Rose A et al. (2010) National patterns and correlates of menthol cigarette use in the United States. Addiction 105(suppl. 1):13–31. [Funded by the National Cancer Institute]
16. Okuyemi KS, Ebersole-Robinson M, Nazir N, et al. (2004) African-American menthol and non-menthol smokers: differences in smoking and cessation experiences. Journal of the National Medical Association, 96(9):1208–11. [Funded by grants from the National Institutes of Health (K07 CA90334) and the Cancer Research Foundation of America]
17. Okuyemi KS, Faseru B, Cox LS, et al. (2007) Relationship between menthol cigarettes and smoking cessation among African American light smokers. Addiction 102(12):1979–86. [Funded by National Institutes of Health grant R01 CA091912]
18. Pletcher MJ, Hulley BJ, Houston T, et al. (2006) Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Archives of Internal Medicine 166(17):1915–22. [Funded by contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute]
19. Rock VJ, Davis SP, Thorne SL, et al. (2010) Menthol cigarette use among racial and ethnic groups in the United States, 2004-2008. Nicotine and Tobacco Research 12(suppl 2):S117-24. [No funding source(s) provided. Authors affiliated with Centers for Disease Control and Prevention and RTI International]
20. Stahre M, Okuyemi KS et al. (2010) Racial or ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. Addiction 105(suppl. 1):75–83. [Funded by Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development]
21. Substance Abuse and Mental Health Services Administration. Results from the 2008 National Survey on Drug Use and Health: national findings. Rockville, MD: US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration; 2009. [Funded by the US Department of Health and Human Services]
22. U.S. Department of Health and Human Services (2012). Preventing tobacco use among youth and young adults – A report of the Surgeon General. Rockville, MD.
23. Yeager DS & Krosnick JA (2010) The validity of self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. Medical Care 48(12): 1128-1132. [No funding source(s) provided. Authors affiliated with Stanford University]

## G. Dependence

Nicotine dependence is the primary driver of continued tobacco use and may affect the overall adverse health impact of smoking (e.g., failure of quit attempts). Researchers have used peer-reviewed literature, data from the Altria TES, and menthol secondary data analyses to evaluate the impact of nicotine dependence. This assessment includes primary measures that have historically been used to assess nicotine dependence: time to first cigarette (TTFC), cpd, the Fagerström Test for Nicotine Dependence (FTND; a composite measure), and craving. Night waking to smoke has also emerged as a reliable indicator of strength of dependence and is therefore included in this assessment. This assessment also includes other scales of nicotine dependence and craving if there were direct menthol versus nonmenthol assessments, particularly if they were used to assess dependence in youth. Although relapse to smoking has been used as an indicator of strength of dependence, those studies are included in the assessment of the literature on cessation later in this report.

*Time to First Cigarette (TTFC)*

Baker et al. (2007) used data from four placebo-controlled smoking cessation trials and one international epidemiologic study to determine the relationships between cessation success and each of the following: FTND (Heatherton et al., 1991), the Heaviness of Smoking Index (Kozlowski et al., 1994), the Nicotine Dependence Syndrome Scale (Shiffman et al., 2004), and the Wisconsin Inventory of Smoking Dependence Motives (Piper et al., 2004). TTFC in the morning had the strongest predictive validity of all of the questions on the FTND and had greater validity than any other single measure. TTFC is therefore considered to be the best single measure of assessing nicotine dependence.

Fagan et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS to examine the relationship between menthol and nicotine dependence, including TTFC. All analyses were adjusted for age, income and education levels, and stratified by gender and race or ethnicity. This large (n= 46,273) cross-sectional survey found that moderate menthol smokers (6-10 cpd) were 22 percent more likely to have less than five minutes TTFC compared to nonmenthol smokers. For light smokers (≤ 5 cpd) or heavy smokers (11+ cpd), there were no differences associated with menthol in TTFC.

Collins and Moolchan (2006) analyzed data from a telephone survey of 572 adolescent smokers who participated in a treatment study. TTFC reported by menthol smokers was compared with nonmenthol smokers. Statistical analysis revealed a significant difference in TTFC in the five minutes or less groups, with the menthol groups significantly higher than nonmenthol groups (45% versus 29%), but no significant differences between the 6-30 minutes, 31-60 minutes, or 60 or more minuntes groups. The majority of smokers surveyed were menthol smokers (n=531) with no additional racial or ethnic breakdowns by menthol or nonmenthol preference. Since the participants were adolescents recruited from a single urban community and who were seeking treatment to stop smoking, generalizability may be limited to other populations of smokers. Results may not hold true across communities, to adults, or to smokers who are not seeking treatment to stop smoking.

Bover et al. (2008) analyzed data from 2,312 cessation treatment-seeking smokers. They compared TTFC after waking reported by 1,048 menthol smokers with that reported by 1,226 nonmenthol smokers and found that smokers who wake at night to smoke had a significantly shorter time before smoking their first cigarette after waking in the morning. While a direct comparison of menthol to nonmenthol smokers and TTFC was not made, a majority of menthol smokers (57.9%) as compared to nonmenthol smokers (45.4%) woke at night to smoke. This suggests that menthol smokers may also be more likely to have a shorter TTFC. Generalizability may be limited by the use of a local population of smokers seeking treatment to stop smoking.

FDA's independent analysis of Altria TES data showed significantly higher nicotine dependence scores for TTFC (p=0.0374) for menthol smokers using an ordinal response model adjusting for number of cigarettes smoked, number of years smoked, total puff volume, and SES or demographic characteristics. FDA did not include a tar delivery content (TDC) category in its statistical model. FDA did not want to include this in its model because models with TDC assume that a menthol user would necessarily switch to a nonmenthol brand in the same TDC if menthol brands were no longer available.

Hyland et al. (2002) conducted a large, community-based cohort study to evaluate the associations between menthol use and future nicotine dependence using data collected in the COMMIT study. Hyland found no differences in TTFC, however the two shortest intervals that are typically used with TTFC (≤5 minutes and 6-10 minutes) were combined. From other studies, the five minutes or less time period appears to be the most sensitive to differences, thus the comparison of the results of this study to others is limited.

Okuyemi et al. (2003) analyzed data from 600 African American smokers enrolled in a clinical trial for smoking cessation. Menthol smokers (n=471) reported smoking their first cigarette within 30 minutes of waking significantly more often than nonmenthol smokers (n= 129) (81.7% compared to 69.8%). This study cannot be directly compared with other TTFC data because the TTFC bins were combined, losing all of the fastest time intervals. Data from this randomized clinical trial were self-reported and may have limited generalizability due to the inclusion of only African Americans and an individual community sample. Furthermore, as with Hyland et al. (2002), the lack of the five minutes or less time period, which appears to be the most sensitive to differences, limits the comparison to other studies.

Muscat et al. (2009) analyzed data from a community-based cross-sectional study of 525 African American and White hospital-based, older smokers. TTFC was separated into only two broad categories. Analysis of data collected from this study found no differences in either the 30 minutes or less or the more than 30 minutes groups. As with Hyland et al. (2002) and Okuyemi et al. (2003), the lack of the five minutes or less time period, which appears to be the most sensitive to differences, limits the interpretation of the results of this study.

Lawrence et al. (2010) analyzed data from the 2003 and 2006/2007 CPS-TUS and compared menthol (n=16,294) and nonmenthol smokers' (n=46,899) responses to a question asking if they had smoked a cigarette within their first 30 minutes of waking. Lawrence et al. (2010) found no significant difference in the responses between the two groups. As with Hyland et al. (2002), Okuyemi et al. (2003), and Muscat et al. (2009), the lack of the five minutes or less time period, which appears to be the most sensitive to differences, limits the comparison of the results of this study to other studies.

Through non-peer-reviewed secondary data analyses using the same dataset that was used previously (Muscat et al., 2009), Muscat categorized TTFC into four categories (<15 minutes, 15-30 minutes, 31-60 minutes and >60 minutes). After adjusting for race, sex and BMI, no significant differences existed between menthol and nonmenthol smokers for TTFC. Since the previous differences have been in the five minutes or less timeframe, caution should be exercised with interpreting these results. This analysis is somewhat limited by its small sample size, and it may be difficult to generalize from its results due to the use of a community sample.

Through secondary data analyses that have not been peer-reviewed, Hyland and Kasza analyzed data from the International Tobacco Control Four Country Survey, with data from the United States, United Kingdom, Canada and Australia. Data were collected from 7,532 individuals in the United States between 2002 and 2008. This study had a large and nationally representative sample population. After adjustment for demographic and smoking behavior variables, menthol smokers reported fewer minutes to first cigarette compared to nonmenthol smokers. Additionally, the strength of this relationship differed between racial or ethnic groups, with Hispanic respondents (particularly men), experiencing the greatest difference in TTFC. Hispanic nonmenthol smokers had an average TTFC of nearly three hours, while Hispanic menthol smokers had an average time of slightly over one hour. The "minutes to first cigarette" (equivalent to TTFC) was, on average, an hour or more, with a median of about 20 minutes.
This average is well beyond those of the previously discussed studies. This may have been influenced by a liberal definition of a smoker as someone who smokes at least one cpd, with approximately 12 percent of included smokers smoking fewer than five cpd. The authors suggest that the inclusion of these light smokers influenced the distribution, which could also limit this study's generalizability.

*Cigarettes per day (cpd)*

Historically, cpd has been used as an indicator of nicotine dependence, however changing policies such as smoke-free workplaces, smoking restrictions in and around public buildings and restaurant and bar smoking restrictions have made this an increasingly problematic and less-reliable indicator. These issues are exaggerated when evaluating youth smokers because adolescents are subject to greater social restrictions on smoking than adults (e.g., school and household rules, age restrictions for legal purchase). Nevertheless, given the historical record of use of cpd as an index of nicotine dependence, it is included in this discussion.

Okuyemi et al. (2003) analyzed data from 600 African American smokers who were enrolled in a clinical trial for smoking cessation. They compared cpd for menthol smokers (n=471) with cpd reported by nonmenthol smokers (n= 129). There was no difference in cpd; both groups smoked an average of 18 cpd. Although helpful in addressing issues of menthol use in this population, results cannot be generalized to menthol smokers from other racial or ethnic groups. Generalizability is also limited due to the use of a single community.

Okuyemi et al. (2004) analyzed data from a cross-sectional survey of 480 African American smokers at an inner-city health center. Menthol smokers (n=407) were compared to nonmenthol smokers (n=73). Both menthol and nonmenthol smokers smoked, on average, 10 cpd. Although there were more menthol smokers than nonmenthol smokers, there was sufficient power to make this comparison. The use of a single racial or ethnic group eliminates race or ethnicity as a possible confounder but limits the conclusions to only smokers who are African American and live in urban communities. Although helpful in addressing issues of menthol use in this population, results cannot be generalized to menthol smokers from other racial or ethnic groups.

Collins and Moolchan (2006) analyzed data from telephone interviews of 572 adolescent menthol and nonmenthol smokers who were recruited to participate in a treatment study. Analysis with independent t-tests revealed no significant difference, with both menthol and nonmenthol smokers smoking 11-12 cpd. The majority of smokers were menthol smokers (n=531) with no additional racial or ethnic breakdowns by menthol or nonmenthol preference. Data were not stratified by race or ethnicity. Generalizability may be limited due to the local sample and use of treatment-seekers. The limit to adolescence increased sensitivity to this group, but findings may not generalize to adults.

Pletcher et al. (2006) analyzed data from the CARDIA study, a longitudinal study of risk factors for coronary artery disease, including 972 menthol smokers and 563 nonmenthol smokers. Menthol smokers smoked significantly fewer cpd as compared to nonmenthol smokers (10 and 15 cpd, respectively). Although there were reasonable numbers of menthol and nonmenthol smokers, the majority of menthol smokers were African American while the majority of nonmenthol smokers were White. Since there was no adjustment for race or ethnicity, this difference could be due to racial/ethnic factors rather than menthol use.

Gandhi et al. (2009) evaluated the relationship between menthol cigarette smoking and short-term and long-term smoking cessation rates among 1,688 patients attending a tobacco treatment clinic. This retrospective clinical trial cohort study found that African American and Latino menthol smokers smoked fewer cpd than nonmenthol smokers, however there were no differences among White smokers.

Fagan et al. (2010) analyzed data from daily current smokers who were at least 18 years old and participated in the 2003 and 2005/2007 CPS-TUS. Covariates included age, race or ethnicity, marital status, and socioeconomic variables, as well as total years smoking daily and smoking status 12 months ago. This large (n= 46,273) cross-sectional, nationally representative survey found that menthol smokers smoked fewer cpd (mean=13.05) compared with nonmenthol smokers (mean = 15.01).

Lawrence et al. (2010) also analyzed data from the 2003 and 2005/2007 CPS-TUS. This large (n= 63,193) cross-sectional, nationally representative survey found that adult current smokers of less than 10 cpd were more likely to be menthol smokers than nonmenthol smokers (52% as compared to 42%), while smokers of 20 or more cpd were more likely to be nonmenthol smokers compared to menthol smokers (44% as compared to 34%).

Stahre et al. (2010) analyzed data from the 2005 NHIS-CCS, a nationally representative household survey. Among current smokers (n=6511), menthol smokers reported smoking significantly fewer cpd as compared to nonmenthol smokers (14.6 and 17.5, respectively). There was no adjustment for race or ethnicity, which limits the conclusions that can be drawn since the majority of menthol smokers were non-White while the majority of nonmenthol smokers were White.

As part of the secondary data analyses conducted in 2010 that were not peer-reviewed, Hyland and Kasza analyzed data from adult smokers who were interviewed in the United States as part of the International Tobacco Control Four Country Survey (ITC-4). Researchers collected data from 7,532 individuals between 2002 and 2008, including cpd data, but did not provide statistical results. Menthol smokers smoked 18.7 cpd and nonmenthol smokers smoked 16.5 cpd. A strength of this data set is that the sample size was generally larger than many of the other post- hoc analyses of similar measures and outcomes.

*Scales of nicotine dependence (e.g., FTND)*

The FTND is an aggregate of several measures of dependence including measures of cigarette craving, as well as the previously discussed time to first cigarette and number of cpd smoked. Use of the FTND score may be limited because cpd accounts for 30 percent of the total FTND score, which, as previously discussed, may not be as reliable a measure of nicotine dependence due to the influence of smoking policies and restrictions.

Okuyemi et al. (2004) analyzed data from 480 African American smokers at an inner-city health center. There was no significant difference in FTND scores. The restriction to African Americans eliminates racial or ethnic variability, however the majority of smokers were menthol smokers (n=407), leaving only a small number of nonmenthol smokers (n=73).

Collins and Moolchan (2006) analyzed data from telephone interviews with 572 White and African American adolescent smokers in a treatment study. There were no differences in the FTND scores of menthol and nonmenthol smokers. The majority of smokers were menthol smokers (n=531), with no additional racial or ethnic breakdowns by menthol or nonmenthol preference. Generalizability may be limited due to the local sample and use of treatment-seekers. The limit to adolescence increases sensitivity to this group, but findings may not generalize to adults.

Muscat et al. (2009) conducted a community-based cross-sectional study (n=525) and compared FTND scores of menthol and nonmenthol smokers. No significant differences existed in either those with a low to medium FTND score or those with a high FTND score. There was good distribution by race or ethnicity across menthol and nonmenthol groups. However, generalizability may be limited due to the community sample.

Hersey et al. (2010) analyzed data from the cross-sectional 2006 NYTS, a survey of over 27,000 students in grades 6-12 in public and private schools. After controlling for demographic background and the length, frequency, and level of smoking, Hersey concluded that young smokers who smoked menthol cigarettes had significantly higher scores on a scale of nicotine dependence compared with nonmenthol smokers. This study included a large nationally representative population with a high response rate (80.2%) and weighted estimates. Three menthol smoking status definitions were used to model the relationship between menthol cigarette use and nicotine dependence measure to test the robustness of the association. Data were not stratified by race or ethnicity.

FDA's independent analysis of the Altria TES data showed significantly higher nicotine dependence scores for FTND (p=0.0437) for menthol smokers using an ordinal response model adjusting for cpd, number of years smoked, total puff volume, and SES or demographic characteristics. In FDA's analysis, tar delivery content (TDC) category was not included in the statistical model. FDA did not want to include this in its model because models with TDC assume that a menthol user would necessarily switch to a nonmenthol brand in the same TDC if menthol brands were no longer available.

As part of the secondary data analyses conducted in 2010 that were not peer-reviewed, two analyses used scales geared toward youth. Nonnemaker analyzed a school-based study of students 12-18 years old that collected longitudinal cohort data once a year for three years. The Nonnemaker secondary data analysis used an aggregate of four measures:

1) The average score for the response to two survey questions: "How soon after you wake up do you usually smoke your first cigarette on weekdays?" and "How soon after you wake up do you usually smoke your first cigarette during the weekend?"
2) The score for responses to the survey question "If you are sick with a bad cold or sore throat, do you smoke cigarettes?"
3) The score for the response to the survey question "How true is this statement for you? When I go without a smoke for a few hours, I experience cravings?"
4) The score for response to the survey question "How true is this statement for you? I sometimes have strong cravings for cigarettes where it feels like I'm in the grip of a force that I can't control?"

Nonnemaker found that middle and high school students who initiated to menthol cigarettes reported higher dependence at the third yearly assessment compared to those who initiated to nonmenthol cigarettes (consistent with students who were more likely to be a daily smoker). Nonnemaker also found that those who switched from menthol to nonmenthol reported a higher level of dependence than those who smoked nonmenthol across the yearly assessments. In this study the majority of menthol smokers were White. Although this analysis pulled from a large sample, this study did not control for socioeconomic status, and point estimates for the other covariates in the model were somewhat implausible due to the small sample size (e.g., the odds ratio for becoming an established smoker for African Americans was 0.23). In addition, researchers included youth who reported initiation in the final wave in an expanded analysis in order to increase sample size, even though these smokers are not followed for smoking progression or menthol use change over time.

The Hersey analysis is a second non-peer-reviewed secondary data analysis that used a dependence scale geared toward youth. Using data from a Legacy for Health-supported national survey of 5511 youth, which included responses to the Nicotine Dependence Scale for Adolescents, Hersey found that, among youth who smoked for less than one year, smoking menthol cigarettes was associated with significantly higher nicotine dependence. Data did not appear to be stratified by race or ethnicity.

*Craving*

Wackowski & Delnevo (2007) examined rates of menthol smoking and measures of nicotine dependence among 1,345 current established smokers in grades 9-12 who participated in the

2004 NYTS, a nationally representative survey of public and private school students. Logistic regression was used to generate an adjusted odds ratio for menthol smoking for four measures of nicotine dependence, controlling for demographic characteristics and smoking patterns. Approximately 46 percent of current established cigarette smokers in the study were menthol smokers. Menthol smokers had 2.6 and 1.6 greater odds than nonmenthol smokers for reporting that they could go for less than one hour before feeling like they needed a cigarette and that they experienced cravings after not smoking for a while, respectively. This study found that high school menthol smokers were more likely to report symptoms of dependence compared to high school nonmenthol smokers, even when controlling for race, age, and cigarette consumption. The responses to one question (how long before needing a cigarette) had a strong association with menthol use. Although not specifically TTFC, this question resembles this measure. When considering this NYTS question to be a proxy for the "time to first cigarette" question, the results of this study are consistent with previous studies that found adult menthol smokers were more likely to have their first cigarette within a shorter time period than nonmenthol smokers (Ahijevych & Parsley, 1999; Okuyemi et al., 2003; Collins and Moolchan, 2006).

Hersey et al. (2010) analyzed data from the cross-sectional 2006 NYTS, a survey of over 27,000 students in grades 6-12 in public and private schools that garnered a response rate 80.2 percent in a three stage cluster sample design that oversampled African American, Hispanic, and Asian American students.After controlling for demographic background and the length, frequency, and level of smoking, the odds of needing a cigarette within one hour after smoking was greater in menthol smokers than nonmenthol smokers in new youth smokers and in established youth smokers. The need for a cigarette within one hour after smoking was significantly associated with being a likely menthol smoker in both the youth smoker and established youth smoker groups (86% and 106% more likely, respectively). This large, nationally representative sample used two menthol smoking status definitions (including self-description as a menthol smoker and reporting of brand) to model the relationship between menthol cigarette use and nicotine dependence in order to test the robustness of the association. In addition, data were not stratified by race or ethnicity.

*Night waking to smoke*

Night waking to smoke has emerged as a reliable indicator of nicotine dependence. It is strongly associated with several measures associated with nicotine dependence, including TTFC (Bover et al., 2008) and risk for relapse to smoking (Scharf et al., 2008; Foulds et al., 2006). Bover et al. (2008) examined data from 2,312 cigarette smokers who sought treatment at a specialist tobacco dependence clinic. Waking at night to smoke was reported as a "yes" or "no," with no information about the number of wakings. Significantly more menthol smokers (58%) reported waking at night to smoke as compared to nonmenthol smokers (45%). This was a large study, but generalizability may be limited due to the treatment-seeking sample.

Gandhi et al. (2009) conducted a retrospective cohort analysis of 1,688 patients who attempted to quit smoking. Waking at night to smoke was reported as a "yes" or "no," with no information about the number of wakings. Significantly more menthol smokers (55.3%) reported waking at night to smoke as compared to nonmenthol smokers (44.9%). As above, this was a large study, but generalizability may be limited due to the treatment-seeking sample.

*Conclusion*

In all peer-reviewed articles, researchers collected data through self-report. Although this could be associated with recall bias or misclassification, self-report is the standard of this research field and not considered detrimental to the study results. The data do not support the claim that a substantial number of adult respondents intentionally under-report tobacco use (Everhart et al, 2009; Yeager & Krosnick, 2010). Furthermore, as noted by Caraballo et al. (2011), although evidence exists that there is some self-report bias in reporting menthol or nonmenthol cigarette use, especially among adolescents, this is not necessarily problematic since it is likely that this type of bias is fairly constant over time.

Cpd and FTND, two measures that have historically been used to assess nicotine dependence, find no consistent effect of menthol. Three studies failed to find any differences in cpd (Okutemi et al., 2003; Okuyemi et al., 2004; Collins and Moolchan, 2006), two studies found that menthol smokers smoked fewer cpd (Pletcher et al., 2006; Fagan et al., 2010), and one study found mixed results that varied by racial/ethnic group (Gandhi et al., 2009). Three studies failed to find any differences in FTND score (Okuyemi et al., 2004; Collins and Moolchan, 2006; Muscat et al., 2009) and one study found that menthol smokers scored higher than nonmenthol smokers (FDA analysis of Atria TES). However, as previously discussed, there are questions concerning the applicability of cpd and FTND measures to the current smoking situation in adults. There is even greater concern when applied to youth, as they smoke fewer cigarettes than established adult smokers and have greater social limitations on when/where they can smoke. In contrast there is consistent evidence that menthol smokers are more likely to smoke their first cigarette within 5 min of waking (Fagan et al., 2010; Collins and Moolchan et al., 2006; Bover et al., 2008; FDA analysis of Altria TES; Okuyemi et al., 2003; Hyland and Kasza secondary data analysis), indicating more severe dependence. Those studies that failed to find a difference in TTFC collapse the fastest timeframes, with either smoking within ten minutes (Hyland et al., 2992) or smoking within 30 minutes (Muscat et al., 2009; Lawrence et al., 2010; Muscat secondary data analysis) as their shortest option. As with TTFC, other measures of dependence consistently indicate that menthol smokers are more dependent as compared to nonmenthol smokers. This includes studies that use non-FTND scales of dependence (Hersey et al., 2010; Nonnemaker secondary data analysis; Hersey secondary data analysis), as well as measures of craving (Wachowski and Delnevo, 2007; Hersey et al., 2010) and waking at night to smoke (Bover et al., 2008; Gandhi et al., 2009). These studies consistently found that menthol smokers were more dependent. Based on the findings of TTFC, non-FTND scales of dependence, craving measures, and waking at night to smoke, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with increased dependence.

## Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Ahijevych K, Parsley LA. | Smoke constituent exposure and stage of change in black and white women cigarette smokers. | 1999 | American Lung Association Research Grant; General Clinical Research Center M01 RR00034 | Two-factor design | Black and White Women | N=95 total women (48 black with 27 smoking menthol cigarettes, and 47 white with 22 smoking menthol cigarettes) | Black women had significantly higher beliefs about the negative aspects of smoking than did White women; menthol smokers had a shorter time to first cigarette, indicating greater nicotine dependence. |
| Baker TB, Piper ME, McCarthy DE, et al. | Time to first cigarette in the morning as an index of ability to quit smoking: implications for nicotine dependence. | 2007 | National Institutes of Health | Data derived from four clinical trials and an epidemiology study | Data derived from smokers of three large clinical trials (including two with focused, real-time process measures) conducted in Madison and Milwaukee, WI, one clinical trial conducted in New Haven, CT, and one large international epidemiologic study. | N=463 (electronic diary study) N=608 (pharmacotherapy) N=410 (quitline) N=385 (naltrexone) N=9,058 (epi) | Results showed that much of the predictive validity of the FTND could be attributed to its first item, time to first cigarette in the morning, and this item had greater validity than any other single measure.<br><br>[not menthol specific] |
| Bover MT, Foulds J, Steinberg MB, Richardson D, Marcella SW. | Waking at night to smoke as a marker for tobacco dependence: patient characteristics and relationship to treatment outcome. | 2008 | The New Jersey Department of Health and Senior Services as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey and the Robert Wood Johnson Foundation | Not Specified | This study took place at the Tobacco Dependence Program (TDP) at University of Medicine and Dentistry of New Jersey (UMDNJ)-School of Public Health. The TDP operates a tobacco dependence clinic in New Brunswick, New | N=2312 consecutive eligible cigarette smokers who sought treatment at a specialist tobacco-dependence clinic declared a | Night-smoking was associated with a number of other patient characteristics, including African-American race or Hispanic ethnicity, having smoking-related medical symptoms, having been treated for a behavioural health problem, smoking mentholated cigarettes, smoking within 30 min of waking in the morning, increased cigarettes smoked per day, and not having private health insurance. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | Jersey, USA and provides tobacco-dependence treatment, including a combination of therapeutic support (individual and group counseling) and withdrawal symptom management (including use of Food and Drug Administration-approved smoking cessation medications). | Target Quit Date, provided baseline information at assessment, and were then followed-up 4 and 26 weeks after their target quit date. | |
| Caraballo, RS & Asman, K | Epidemiology of menthol cigarette use in the United States. | 2011 | No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention. | Review and secondary analyses of national surveys | NSDUH: adolescents aged 12-17 years old who smoked in the past month and adult smokers (aged 18 years or older) who smoked in the past month<br>NYTS: middle school (MS) and high school (HS) students with school year, past 30 day smoking, brand use, and menthol information.<br>MTF: current smokers in 8th, 10th and 12th grade<br>NHANES: 20 years and older who had Smoked and were non-Hispanic white, non-Hispanic black/African | NSDUH: 9,595 adolescents; 62,010 adults<br>NYTS: 1,978 MS students and 6,163 HS students<br>MTF: 20,863 8th graders; 30,722 10th graders; 40,914 12th Graders<br>NHANES: 1571 individuals with UPC information | Menthol cigarettes are disproportionately smoked by adolescents, blacks/African Americans, adult females, those living in the Northeast of the United States and those with family incomes lower than $50,000. Based on self-reports of menthol cigarette use, menthol cigarette use among smokers have increased from 2004 to 2008. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | American, or Mexican American | | |
| Collins CC, Moolchan ET. | Shorter time to first cigarette of the day in menthol adolescent cigarette smokers. | 2006 | National Institute on Drug Abuse, Intramural Research Program | Survey | Adolescent smokers recruited for a cessation treatment study, telephone survey | N=572 | Adolescent menthol cigarette smokers had shorter TTF cigarette of the day when compared to non-menthol adolescent cigarette smokers, despite a lack of group differences in FTND scores or smoking rates (CPD). |
| Everhart J, Ferketich AK, Browning K et al. | Acculturation and misclassification of tobacco use status amont Hispanic men and women in the United States. | 2009 | Summer Research Opportunities Program at the Ohio State University | Cross-sectional survey (1999 – 2002 National Health and Nutrition Examination Surveys) | Self-identified "Mexican American" or "other Hispanic" and were at least 20 years old. | N=9965 (wave 1999-2000) N=11,039 (wave 2001-2002) | A gender-specific association between misclassification and acculturation was found. Among males (n=1,175), the prevalence estimates of misclassification were 4.8%, 1.8%, and 2.2% for low, medium, and highly acculturated males, respectively (p< .02). Among females (n=1,345), the prevalence estimates of misclassification were 0.8%, 2.0%, and 4.9% for low, medium, and highly acculturated females, respectively (p< .03). [not menthol specific] |
| Fagan P, Moolchan ET et al. | Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. | 2010 | The National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current Population Surveys) | Civilian non-institutionalized daily smokers aged 18 years and above. | N=11,671 (menthol smokers) N=33,644 (nonmenthol smokers) N=958 (no usual type) | …among adults, daily menthol smokers consuming six to 10 cigarettes per day were more likely than non-menthol smokers consuming six to 10 cigarettes per day to smoke their cigarette within the first 5 minutes after waking. |
| Foulds J, Gandhi KK, Steinberg MB, Richardson DL, Williams JM, Burke MV, Rhoads GG. | Factors associated with quitting smoking at a tobacco treatment dependence treatment clinic. | 2006 | The New Jersey Department of Health and Senior Services, as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey, The Robert Wood Johnson Foundation, the | Cohort | first 1021 patients who attempted to quit tobacco at a specialist tobacco dependence treatment outpatient clinic based at the Tobacco Dependence Program at the University of | N=1021 | Forty-one percent of the patienta smoked menthol cigarettes. They were less likely to achieve abstinence in univariate analyses, and this item remained in the model predicting 4-week outcome. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | National Institute on Drug Abuse, and the American Legacy Foundation | | Medicine and Dentistry of New Jersey-School of Public Health | | |
| Gandhi KK, Foulds J, Steinberg MB, Lu SE, Williams JM. | Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic. | 2009 | New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health | Retrospective Cohort/ Population Studies | Specialized smoking cessation outpatient clinic in New Jersey: patients who set a quit date and attempted to quit smoking, between 1 January 2001 and 30 June 2005; African American, Latinos, Whites | N=1688 (787 Menthol, 910 Nonmenthol) | This study found lower short-term (4-week follow-up) quit rates among AA and Latino menthol smokers as compared with non-menthol smokers within the same racial / ethnic subgroups. |
| Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. | The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. | 1991 | No funding source(s) provided. Authors affiliated with Harvard University, Pennsylvania State University, Addiction Research Foundation, Ontario, and Pharmacia Leo Therapeutics AB, Sweden | Study | Smokers visiting the Ontario Science Centre | N=254 | We found that the nicotine rating item and the inhalation item were unrelated to any of our biochemical measures and these two items were primary contributors to psychometric deficiencies in the PTQ. We also found that a revised scoring of time to the first cigarette of the day (TTP) and number of cigarettes smoked per day (CPD) improved the scale.<br><br>[not menthol specific] |
| Hersey JC, Nonnemaker JM, Homsi G. | Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. | 2010 | American Legacy Foundation and RTI International | Survey (2006 National Youth Tobacco Survey) | Middle and high school students who smoked in the past 30 days who reported that they had a usual brand of cigarette and who could identify whether the usual brand was menthol or nonmenthol. | N=1458 (menthol smokers) N=1710 (nonmenthol smokers) | A logistic regression model of dependence, controlling for background (i.e., school level, gender, and race/ethnicity) and smoking level (i.e., years, frequency, and level of smoking) found that smoking menthol cigarettes was significantly associated with reduced time to needing a cigarette among smokers with a regular brand (odds ratio [OR]: 1.86, p = .003) and among established smokers (OR: 2.06, p = .001). |
| Hyland A, | Mentholated | 2002 | The National Cancer | Telephone | COMMIT study: | N=13,268 | No clear associations were observed between |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Garten S, Giovino GA, Cummings KM. | cigarettes and smoking cessation: findings from COMMIT. | | Institute grant CA016056-26 | survey | Baseline smokers who reported whether their current cigarette brand or not in 1988, and had a known smoking status in 1993. | (3,184 menthol, 10084 non-menthol) | menthol cigarette use and indicators of nicotine dependence, even after controlling for race/ethnicity and other demographics.. |
| Kozlowski LT, Porter CQ, Orleans CT, Pope MA, Heatherton T. | Predicting smoking cessation with self-reported measures of nicotine dependence: FTQ, FTND, and HSI. | 1994 | No funding source(s) provided. Authors affiliated with Pennsylvania State University | Experiment (two independent studies) | Smokers seeking treatment at the Ontario Lung Association | N=932 (study 1) N=1877 (study 2) | All tests made statistically reliable predictions of smoking cessation.<br><br>…samples of high scoring smokers will not be well differentiated from the mid-range to the high-end of the scores.<br><br>[not menthol specific] |
| Lawrence DL, Rose A et al. | National patterns and correlates of menthol cigarette use in the United States. | 2010 | National Cancer Institute | Cross-sectional survey (2003 and 2006/07 Tobacco Use Supplements to the Current Population Survey) | Smokers at least 18 years old. | N=63,193 | Use of mentholated cigarettes was higher among women than among men.<br><br>Additional significant factors associated with mentholated cigarette smoking included being unmarried (never married: OR: 1.21, 99% CI: 1.09–1.34; divorced/separated: OR: 1.13, 99% CI: 1.03–1.23), being born in a US territory (OR: 2.01, 99% CI: 1.35–3.01), living in a non-metropolitan area (OR: 0.87, 99% CI: 0.80–0.96), being unemployed (OR: 1.24, 99% CI: 1.06–1.44) and lower levels of education. |
| Muscat JE, Chen G, Knipe A, Stellman SD, Lazarus P, Richie JP Jr. | Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation. | 2009 | No funding source(s) provided. Authors associated with Pennsylvania State College of Medicine | Community-based cross-sectional | Black and White adult smokers | N=525 | Data indicate that menthol is not associated with a higher exposure to tobacco smoke carcinogens, but the findings on nicotine dependence are inconclusive. Menthol may not be more hazardous than other cigarette formulations for most smokers, although it cannot be ruled out at this time that some menthol smokers are possibly at increased risk for lung cancer because of selective inhibition of UDP-glucuronosyl transferase enzymes. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Okuyemi KS, Ahluwalia JS, Ebersole-Robinson M, Catley D, Mayo MS, Resnicow K. | Does menthol attenuate the effect of bupropion among African American smokers? | 2003 | National Cancer Institute grants (R01 CA77856, K07 CA90334, R24 CA95835-01) | Randomized Controlled Trial | African American smokers enrolled in a clinical trial that assessed the efficacy of sustained-release bupropion for smoking cessation. Menthol (n = 471) and non-menthol (n = 129) smokers were compared on smoking-related characteristics and abstinence rates at 6 weeks and 6 months. | N=600 | African American menthol smokers had lower smoking cessation rates after 6 weeks of treatment with bupropion-SR than African-American non menthol smokers, thereby putting menthol smokers at greater risk from the health effects of smoking. Lower overall cessation rates among African Americans menthol smokers may partially explain ethnic differences in smoking-related disease risks. |
| Okuyemi KS, Ebersole-Robinson M, Nazir N, Ahluwalia JS. | African-American menthol and nonmenthol smokers: differences in smoking and cessation experiences. | 2004 | The National Institutes of Health (K07 CA90334) and the Cancer Research Foundation of America | Cross sectional survey | African-American smokers at an inner-city health center. Menthol smokers (n = 407) were compared to nonmenthol smokers (n = 73) in these characteristics. | N=480 | Based on the consistency of the direction of the three measures of cessation success, the authors suggested that Black/African American individuals who smoke menthol cigarettes may be less likely to be successful in their quit attempts. |
| Piper ME, Piasecki TM, Federman EB, Bolt DM, Smith SS, Fiore MC, Baker TB. | A multiple motives approach to tobacco dependence: the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68). | 2004 | National Institutes of Health and a grant from the University of Missouri Research Board | Survey | Adults (18+) from Madison and Milwaukee, WI | N=775 | Data collected from a large sample of smokers (N r775) indicated that all 13 subscales of the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68) have acceptable internal consistency, are differentially present across levels of smoking heaviness, and have a multidimensional structure.<br><br>[not menthol specific] |
| Pletcher MJ, Hulley BJ, Houston T, | Menthol cigarettes, smoking | 2006 | Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, | Multi-center U.S. cohort study | African American and European American smokers aged 18 to 30 | 1544 (non-menthol smokers (n = | Menthol and nonmenthol cigarettes seem to be equally harmful per cigarette smoked in terms of atherosclerosis and pulmonary function decline, |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Kiefe CI, Benowitz N, Sidney S. | cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. | | and N01-HC-95095 from the National Heart, Lung, and Blood Institute | (CARDIA) | years and healthy at the time of enrollment in 1985 | 563) and menthol smokers (n = 972)) | but menthol cigarettes may be harder to quit smoking. |
| Scharf DM, Dunbar MS, Shiffman S. | Smoking during the night: prevalence and smoker characteristics. | 2008 | Social Sciences and Humanities Research Council of Canada and National Institute on Drug Abuse | Treatment study | Heavy smokers enrolled in one of three smoking cessation studies | N=691 | Night smoking is common, is associated with nicotine dependence, and it represents additional risk for cessation failure.<br><br>[not menthol specific] |
| Shiffman S, Waters A, Hickcox M. | The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. | 2004 | National Institutes on Health, GlaxoSmithKline and GlaxoSmithKline Consumer Healthcare | Factor analysis of three independent studies | Smokers participating in a smoking cessation study | N=317 (study 1) N=802 (study 2) N=93 (study 3) | …the NDSS presents a valid multidimensional assessment of nicotine dependence that may expand on current measure.<br><br>[not menthol specific] |
| Stahre M, Okuyemi KS et al. | Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. | 2010 | Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development | Cross-sectional survey (2005 National Health Interview Survey (NHIS) Cancer Control Supplement) | Current or former smokers, age 18 and over | N= 6511 (smoker) N= 6774 (former smoker) | Overall menthol smoking prevalence was significantly different by sex, region of the United States, race, marital status and average number of cigarettes smoked per day for both current and former smokers and age for former smokers only.<br><br>For current and former smokers, non-menthol smokers reported a higher number of cigarettes smoked per day on average than menthol smokers.<br><br>Menthol smoking status was not associated with differences in utilization of quit aids. |
| Yeager DS & | The validity of | 2010 | No funding source(s) | Study based on | Adult smokers age 20 | N=21,414 | These analyses of NHANES data collected |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Dependence: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Krosnick JA | self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. | | provided. Authors affiliated with Stanford University | National Health and Nutrition Examination Survey (multiple waves) | and over | | between 2001 and 2008 suggest that if any nicotine product users under-reported this behavior, the proportion of people who did so was exceedingly small.<br><br>[not menthol specific] |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions.
[Bracketed notes added by FDA]

References


1. Ahijevych K, Parsley LA (1999) Smoke constituent exposure and stage of change in Black and White women cigarette smokers. Addictive Behaviors 24:115-120. [Funding provided by an American Lung Association Research Grant, and General Clinical Research Center M01 RR00034]
2. Baker TB, Piper ME, McCarthy DE, et al. (2007) Time to first cigarette in the morning as an index of ability to quit smoking: implications for nicotine dependence. Nicotine and Tobacco Research 4:S555-70. [Funding provided by a grant through the National Institutes of Health]
3. Bover MT, Foulds J, Steinberg MB, et al. (2008) Waking at night to smoke as a marker for tobacco dependence: patient characteristics and relationship to treatment outcome. International Journal of Clinical Practice 62:182-190. [Funding provided by a grant from the New Jersey Department of Health and Senior Services as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey and the Robert Wood Johnson Foundation]
4. Caraballo, RS & Asman, K (2011). Epidemiology of menthol cigarette use in the United States. Tobacco Induced Diseases, 9 (Suppl 1): S1. [No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention]
5. Collins CC, Moolchan ET (2006) Shorter time to first cigarette of the day in menthol adolescent cigarette smokers. Addictive Behaviors 31:1460-4. [Funded by the National Institute on Drug Abuse, Intramural Research Program]
6. Everhart J, Ferketich AK, Browning K et al (2009) Acculturation and misclassification of tobacco use status amont Hispanic men and women in the United States. Nicotine and Tobacco Research 11(3): 240-247. [Funding provided by the Summer Research Opportunities Program at the Ohio State University].
7. Fagan P, Moolchan ET, et al. (2010) Nicotine dependence and quitting behaviors among menthol and nonmenthol smokers with similar consumptive patterns. Addiction 105(suppl. 1):55-74. [Funded by the National Cancer Institute, Virginia Commonwealth University and the Massey Cancer Center]
8. Foulds JF, Gandhi KK, Steinberg MB, et al. (2006) Factors associated with quitting smoking at a tobacco treatment dependence treatment clinic. American Journal of Health Behavior 30(4):400–12. [Funding provided by The New Jersey Department of Health and Senior Services, as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey, The Robert Wood Johnson Foundation, the National Institute on Drug Abuse, and the American Legacy Foundation]
9. Gandhi KK, Foulds J, Steinberg MB, et al. (2009) Lower quit rates among African American and Latino menthol smokers at a tobacco treatment clinic. International Journal of Clinical Practice 63:360–7. [Funded by New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health]
10. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. (1991) The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. British Journal of Addiction 86(9):1119-27. [No funding source(s) provided. Authors affiliated

with Harvard University, Pennsylvania State University, Addiction Research Foundation, Ontario, and Pharmacia Leo Therapeutics AB, Sweden]

11. Hersey JC, Nonnemaker JM, Homsi G (2010) Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. Nicotine and Tobacco Research 12(suppl 2):S136-46. [Funded by the American Legacy Foundation and RTI International]
12. Hyland A, Garten S, Cummings KM (2002) Mentholated cigarettes and smoking cessation: findings from COMMIT (Community Intervention Trial for Smoking Cessation). Tobacco Control 11(2):135–9. [Funded by the National Cancer Institute]
13. Kozlowski LT, Porter CQ, Orleans CT, Pope MA, Heatherton T. (1994) Predicting smoking cessation with self-reported measures of nicotine dependence: FTQ, FTND, and HSI. Drug Alcohol Dependence 34(3):211-6. [No funding source(s) provided. Authors affiliated with Penn State University]
14. Lawrence DL, Rose A et al. (2010) National patterns and correlates of mentholated cigarette use in the United States. Addiction 105(suppl 1):13–31. [Funded by the National Cancer Institute]
15. Muscat JE, Chen G, Knipe A, et al. (2009) Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation. Cancer Epidemiology, Biomarkers, and Prevention 18:35–41. [No funding source(s) provided. Authors associated with Pennsylvania State College of Medicine]
16. Okuyemi KS, Ahluwalia JS, Ebersole-Robinson M, et al. (2003) Does menthol attenuate the effect of bupropion among African American smokers? Addiction 98(10):1387–1393. [Funded by the National Cancer Institute grants (R01 CA77856, K07 CA90334, R24 CA95835-01)]
17. Okuyemi KS, Ebersole-Robinson M, Nazir N, et al. (2004) African-American menthol and nonmenthol smokers: differences in smoking and cessation experiences. Journal of the National Medical Association 96(9):1208–11. [Funded by the National Institutes of Health (K07 CA90334) and the Cancer Research Foundation of America]
18. Piper ME, Piasecki TM, Federman EB, Bolt DM, Smith SS, Fiore MC, Baker TB (2004). A multiple motives approach to tobacco dependence: the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68). Journal of Consulting and Clinical Psychology 72(2):139-54. [Funded by National Institutes of Health and a grant from the University of Missouri Research Board]
19. Pletcher MJ, Hulley BJ, Houston T, et al. (2006) Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Archives of Internal Medicine 166(17):1915–22. [Funded by contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute]
20. Scharf DM, Dunbar MS, Shiffman S (2008) Smoking during the night: prevalence and smoker characteristics. Nicotine & Tobacco Research 10(1):167-78. [Funded by Social Sciences and Humanities Research Council of Canada and National Institute on Drug Abuse]
21. Shiffman S, Waters A, Hickcox M (2004) The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. Nicotine & Tobacco Research 6(2):327-48. [Funded by the National Institutes on Health, GlaxoSmithKline and GlaxoSmithKline Consumer Healthcare]

22. Stahre M, Okuyemi KS, et al. (2010) Racial or ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. Addiction 105(suppl 1):75–83. [Funded by Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development]
23. Yeager DS & Krosnick JA (2010) The validity of self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. Medical Care 48(12): 1128-1132. [No funding source(s) provided. Authors affiliated with Stanford University]

## H. Cessation

Quitting smoking, even at later ages, can result in a significant reduction in disease risk and years of life lost (Doll et al., 2004). Therefore, any impact of menthol in cigarettes on smoking cessation has the potential to have a substantial impact on public health. This section evaluated the science comparing cessation success in menthol smokers and nonmenthol smokers. Articles that assessed differences in intention to quit, feelings regarding the likelihood of being able to quit, or the number of quit attempts without reference to cessation success are not a direct assessment of cessation and are not included. Additionally, studies of only former smokers or only current smokers are not included, as there is no relative measure of cessation success.

*Cohort studies*

Hyland et al. (2002) conducted a large community-based cohort study to evaluate the association between menthol use and smoking cessation using data collected in the COMMIT study. The COMMIT study was a randomized community-based intervention trial identified by telephone survey for smoking cessation in 11 matched pairs of communities. The study population included 13,268 current smokers (25-64 years old) at baseline (1988). Researchers collected self- reported menthol cigarette use by brand type at baseline. The cessation outcome was defined as no smoking in the last six months. The study indicated that 24 percent of the overall population smoked menthol cigarettes (23% Whites and 57% African Americans). Baseline menthol cigarette use was not associated with quitting in 1993 (RR (95% CI): 1 (0.90-1.11)) in overall and race or ethnicity subgroups. This longitudinal study had a large community-based cohort sample with a strong definition of smoking cessation (six months abstinence at five years). The analysis was adjusted for demographics, nicotine dependence (e.g., TTFC), and smoking/quitting history. Since dependence may be an intermediate variable affecting cessation success, it is possible that the analyses were over-adjusted, which may result in a dilution of an association. In addition, there was a high loss to follow-up rate over five years (34% from baseline 1988 to 1993).

Pletcher et al. (2006) evaluated the associations between menthol cigarette use and smoking cessation behavior, coronary calcification, and changes in pulmonary function test among 1,544 current smokers who were participants in CARDIA. CARDIA is a population-based cohort study of risk factors for coronary artery diseases among healthy 18-30 years old African Americans and Whites. Smoking cessation behavior (including current smoking status, recent quit attempts, and cessation if recent quit attempt), sustained smoking cessation, and documented relapse were collected. Sustained smoking cessation was defined as no current smoking in the past two times examined. After adjusting for demographic and social factors, menthol smokers had statistically significant increased risk of relapse (OR (95% CI): 1.89 (1.17-3.05), p=0.009) as compared to nonmenthol smokers. Researchers identified a trend toward lower cessation in menthol smokers, however this did not reach statistical significance (OR (95% CI): 0.71 (0.49-1.02), p=0.06). The statistical analyses were robust, with repeated measures for outcomes such as quit attempts and cessation after quit attempts and longitudinal assessment for sustained smoking cessation. This large study had long-term follow up, and menthol status was collected at multiple time points. The sample population was diverse, though not nationally representative. Generalizability may be limited since the study included only young African American and White adults 18-30 years old at entry (mean age: 25 years). Statistical power was limited in subgroup analysis (e.g., White menthol smokers, African American nonmenthol smokers).

Blot et al. (2011) conducted a nested case-control study among 440 incident lung cancer cases and 2,213 controls enrolled in the Southern Community Cohort Study between 2002 and 2009. Researchers prospectively determined quitting smoking through computation of quit rates from the follow-up interviews for patients who were current smokers at entry into the cohort. Thus, a quitter was defined as a former smoker, but there was no measure of duration of quitting. After adjusting for demographic variables, there was no difference in the prevalence of having quit smoking between menthol and nonmenthol smoking African Americans (OR (95% CI): 1.03 (0.96-1.11)). However, among Whites, menthol smokers were more likely to have quit as compared to their nonmenthol-smoking counterparts (OR(95% CI): 1.55 (1.41-1.70)). Although there was a reasonable follow up period of over four years, full follow up was lacking for about 40 percent of the subjects. Cessation was biochemically verified via assessment of serum cotinine levels. Although multiple sites were used, generalizability may be limited since the sample was not nationally representative.

Okuyemi et al. **(**2003) evaluated the association between menthol cigarette smoking and cessation using data collected for a randomized clinical trial that assessed the efficacy of the medication bupropion-SR (treated for seven weeks) for smoking cessation. The study consisted of 600 African American smokers enrolled in an inner-city health center (≥ 18 years, ≥10 cpd) (471 menthol and 129 nonmenthol smokers). Compared to nonmenthol smokers, menthol smokers were less likely to be abstinent at six weeks (41.5% and 28.3%, respectively, p=0.006). However, the seven-day point prevalence abstinence rates at six weeks was not different between menthol and nonmenthol smokers who received placebo (20.5% for menthol vs. 23.3% for nonmenthol, p=0.63). Among the treatment group, menthol smokers had significantly lower abstinence rates than nonmenthol smokers at six weeks (36.2% vs. 60.3%, p<0.01). Thus it appears that the menthol smokers did not get the same benefit from the medication as the nonmenthol smokers did. The association between smoking cessation and menthol also differed by age. Among smokers 49 years old or younger, 24.9 percent of the menthol smokers were abstinent compared to 44.4 percent for nonmenthol smokers (p<0.01) but no difference was seen in smokers 50 years old or over. Nonmenthol smokers were twice as likely to quit smoking as menthol smokers (OR (95% CI): 2 (1.03-3.95)) among smokers who were 49 years old or younger at six weeks, but not in smokers who were 50 years old or over after controlling for treatment. The age-specific logistic regression results did not explicitly mention which factors were controlled. In the methods section, the author mentioned treatment was controlled in logistic regressions but it is not clear whether other factors such as sex, cpd, and duration of smoking were retained and adjusted in the stepwise regression. Generalizability may be limited since the sample consisted of those seeking treatment and was not nationally representative. The self-reported seven-day point prevalence cessation rates were biochemically confirmed.

Using the same dataset as Okuyemi et al. (2003), Harris et al. (2004) analyzed the predictors of seven-day cessation in a clinical trial cohort among 600 African Americans who randomly received the cessation medication bupropion SR or placebo for seven weeks and were followed for 27 weeks. Self-reported menthol use was one of the 21 baseline variables examined for the prediction of smoking cessation. The study outcome was biochemically-confirmed self-reported seven-day point prevalence abstinence at week seven, the end of the treatment phase. The study indicated that menthol smokers were less likely to quit smoking after 7 weeks of treatment compared to nonmenthol smokers (28.3% vs. 41.5%, p=0.0062) using a Chi square test (unadjusted); the effect was not present when researchers adjusted the analysis for demographic factors and factors related to dependence. Since dependence may be an intermediate variable affecting cessation success, it is possible that the analyses were over-adjusted, which resulted in a dilution of the association.Researchers used biochemical verification of self-reported cessation outcomes. Generalizability may be limited since the sample consisted of those seeking treatment and was not nationally representative.

Gandhi et al. (2009) evaluated the relationship between menthol cigarette smoking and short-term (4 weeks) and long-term (6 months) smoking cessation among 1,688 patients attending a tobacco treatment clinic in New Jersey. The outcome was a biochemically-verified seven-day point prevalence abstinence rate. The study demonstrated that African American and Latino menthol smokers had significantly lower odds of quitting (OR (95% CI): 0.32 (0.16-0.62) for African Americans; 0.43 (0.1-0.9) for Latinos) as compared to their nonmenthol counterparts at four weeks of follow-up. Researchers observed a similar trend at the six-month follow-up. No significant differences existed in the cessation rates of White menthol and nonmenthol smokers. Researchers adjusted analyses for demographic and dependence variables (e.g., TTFC, waking at night to smoke). Since dependence may be an intermediate variable affecting cessation success, it is possible that the analyses were over-adjusted, which may result in a dilution of association(s). Although this was a large study, there was a high loss to follow up at six months (approximately 42%). Since all those who were lost were included as cessation failures (i.e. still smoking), overall quit rates may be underestimated. Although seven-day point prevalence was biochemically verified, these data were incomplete or not clearly described for all subjects; half of the sample was followed up in person (carbon monoxide verification) but half were followed up via phone contact (no carbon monoxide verification). Generalizability may be limited since the sample consisted of those seeking treatment and was not nationally representative.

Foulds et al. (2006) evaluated factors associated with successful quitting using a sample of 1,021 patients at a free tobacco treatment clinic. Researchers evaluated abstinence at four-week and six-month follow-ups, and biochemically verified self-reported cessation. At the four-week follow up, data showed a trend toward menthol smokers having worse cessation outcomes, however this failed to reach significance (p=0.053). No differences existed at the six-month follow up. Analyses were adjusted for treatment, but other adjustments were unclear, and they may have been overadjusted (e.g., adjusted for dependence variables). This large, longitudinal study had a sample that mimics the U.S. population, however generalizability may be limited since the sample consisted of people seeking smoking cessation treatment.

Murray et al. (2007) investigated the health effect of menthol cigarette smoking among 5887 smokers 35-60 years old with mild to moderate airway obstruction who were selected to participate in a smoking cessation program and were followed for 11 years using the data from the Lung Health Study. In addition to disease-specific mortality, the outcomes included smoking cessation assessments that included the percentages of sustained quitters, of intermittent smokers and of continued smokers. Researchers assessed self-reported menthol cigarette use at baseline and annual follow-up visits for five years. The study indicated no significant difference existed between menthol use and the percentage of quitters during five years of follow-up, after controlling for age, sex, baseline cpd, FEV1% predicted, randomization group assignment, race, and years of education. Although this large clinical trial cohort study had a long follow up period (14 years), the researchers maintained an excellent follow-up rate (94% at five years and 83% 11 years after enrollment). Menthol preference was assessed annually for five years. The smoking cessation definition was fairly strict: sustained quitters were defined as those who were biochemically-confirmed quitters at five annual visits and who recalled no month in which they smoked more than one cpd at any annual visit. Although this was a national survey, the generalizability may be limited due to an under representation of African Americans and due to the inclusion solely of smokers with mild or moderate airway obstruction who received smoking cessation treatment.

Cropsey et al. (2009) analyzed the relationship between race, menthol cigarette use, and smoking cessation rates using data from a smoking cessation intervention trial among 233 female prisoner smokers (≥ 18 years old) . This 12-month clinical trial cohort assessed cigarette type (menthol or nonmenthol) after the subjects entered the intervention. Researchers verified outcomes using seven-day point prevalence abstinence at multiple time points. Menthol cigarette use was not associated with differences in smoking cessation rates. This is a small study of women only, with a very small number of White menthol smokers (approximately 6%). Cessation was biochemically verified. Menthol use was only assessed while in prison, however use patterns may have changed (e.g., differences in brand availability). Despite being a controlled sample, there was a high loss to follow-up. Any generalizability potential is limited.

*Cross-Sectional Studies*

Fu et al. (2008) conducted a cross-sectional survey to evaluate the association between menthol cigarette use and smoking cessation among 1,343 older smokers involved in an aided quit attempt. They used data from a multi-center randomized clinical smoking cessation trial that evaluated the effectiveness of phone call intervention versus usual care. Self-reported menthol use was assessed at the six-month survey post randomization to treatment group. The outcome was self-reported seven-day point prevalence smoking abstinence. The study indicated that smoking menthol cigarettes was not associated with smoking cessation among these older smokers (OR (95% CI): 1.31 (0.95-1.82)). Analyses were adjusted for demographic variables, test site, and TTFC. Since dependence may be an intermediate variable affecting cessation, it is possible that the analyses were over-adjusted. Cessation was also self-reported with no biochemical verification. There was a low response rate at the six-month follow up survey, with a loss of 25 percent. Generalizability may be limited since the sample was composed of those seeking treatment, mostly older males (77% > 50 years old), and not nationally representative.

Muscat et al. (2002) conducted a cross-sectional study to analyze the associations between smoking status and menthol cigarette use among 19,545 current and former African American and White smokers (3,005 menthol and 16,540 nonmenthol) using data collected in a case-control study designed for characterizing tobacco-related cancers. The study was conducted in several hospitals in New York, Pennsylvania, and the District of Columbia between 1981 and 1999. Menthol status was self-reported based on last brand cigarette smoked. The primary outcome was self-reported smoking status (current vs. quit), which may be subject to misclassification. Menthol smoking was not associated with current versus quitting status (prevalence odds ratio (95% CI): 1.1 (0.8-1.4) in African Americans and 1.1 (1.0-1.3) in Whites).The odds ratios appear to have been rounded to the nearest tenth, which makes some of the findings difficult to interpret. Interpretation of some study results was questionable. For example, the authors stated that smokers of menthol cigarettes were significantly more likely to have been former smokers (African Americans), while the data shown in Table 1 indicated that menthol smokers were more likely to be current smokers (70.4% menthol smokers were current smokers vs. 64.3% nonmenthol smokers were current smokers ($p < 0.01$)). Although the sample size was reasonable, the study period spanned 18 years. The definition of an ex-smoker (someone who did not smoke at least one cigarette every day for the past 12 months) was weak and may lead to misclassification. Generalizability may be limited since the sample consisted of older, hospitalized patients, and was not nationally representative. More importantly, the utility of the findings of this study are limited due to significant methodological flaws.

Gundersen et al. (2009) analyzed the association between menthol smoking and cessation among a nationally representative sample of adult current and former smokers (n=7,815) using the 2005 National Health Interview Survey (NHIS). Self-reported menthol use was based on the usual brand of cigarettes smoked in the past 12 months for current smokers or 12 months prior to quitting for former smokers. A former smoker was defined as having smoked 100 or more cigarettes in a lifetime but now "not smoking at all." African Americans and Hispanics were combined under a category labeled "non-White.". The study indicated that non-White menthol smokers were significantly less likely to have quit smoking compared to nonmenthol smoking counterparts (odds ratio (95% CI): 0.55 (0.43-0.71)). The odds ratios (95% CI) were 0.78 (0.56-1.09) for African Americans and 0.61 (0.39-0.97) for Hispanics. White menthol smokers, in contrast, were more likely to have quit ($p<0.05$), with an odds ratio of 1.17 (1-1.36).

Stahre et al. (2010) examined the relationship between menthol smoking, the population quit ratio, and utilization of smoking cession aid among 6,511 current and 6,774 former smokers who participated in the 2005 NHIS-CCS. Researchers collected data on the menthol status of the participants' usual brand. The quit ratio was defined as the total number of former smokers divided by the total number of ever smokers, whereas quitters were defined as people who reported quitting within the previous 12 months. The quit ratio for African American menthol smokers was significantly lower than their nonmenthol counterparts (34% vs. 49%, $p < 0.001$). No significant difference was found in other racial groups including Whites, Asian Americans, American Indian/Alaska Natives and Hispanics. The NHIS sample was large and nationally representative. It is unknown whether smoking cessation lasted for a short time (e.g., one day) or continued long-term (e.g., months).

Levy et al. (2011) evaluated data from the 2003 and 2006-2007 CPS-TUS. This large, nationally representative survey included data from 34,260 individuals in the 2003 survey and 31,250 individuals in the 2006-2007 survey. The likelihood of quitting was 3.5% lower for quitting in the past year and 6% lower for quitting in the past 5 years in menthol compared with nonmenthol smokers. Although the CPS-TUS is a nationally representative dataset, there are limitations with this study, including data transformation, and calculation of prevalence differences. Thus, it may be difficult to interpret the data as presented or draw conclusions from this study.

Given the limitations of Levy et al. (2011), FDA performed independent analyses of the 2006/2007 CPS-TUS dataset. FDA assessed data related to cessation among smokers and former smokers who had last smoked less than five years ago. Menthol smokers had a lower prevalence of cessation as compared to nonmenthol smokers for smokers overall (OR = 0.87, 95% CI = 0.82-0.93), and among whites (OR = 0.87, 95% CI = 0.80-0.94), but not among African Americans (OR = 0.84, 95% CI = 0.65-1.08) or Hispanics (OR = 0.98, 95% CI = 0.74-1.29). The association with lower cessation for menthol smokers was more pronounced among males (OR = 0.83, 95% CI = 0.75-0.93) than among females (OR = 0.93, 95% CI = 0.85-1.02).

*Conclusion*

In all studies available for evaluation, the use of or preference for a menthol brand was based solely on self-report. Although this could be associated with misclassification, self-report is the standard of this research field and not considered detrimental to the study results. Furthermore, Caraballo et al. (2011) noted that while evidence exists of some self-report bias in reporting menthol or nonmenthol cigarette use, especially among adolescents, this is not necessarily problematic since it is likely that this type of bias is fairly constant over time.

Of the nine cohort studies reviewed, three studies (Hyland et al., 2002; Cropsey et al. 2009; Murray et al., 2007) failed to find any differences in the cessation or relapse rates of menthol versus non-menthol smokers. However, one of those studies may have over-adjusted their analyses (Hyland et al., 2002) and the generalizability of another was extremely limited due to the use of prisoners (Cropsey et al., 2009). A fourth study (Blot et al., 2011) found no difference between African American smokers but that White menthol smokers were more likely to have quit. Of the remaining five cohort studies, four found worse cessation outcomes for menthol smokers as compared to their nonmenthol counterparts (Pletcher et al., 2006; Okuyemi et al., 2003; Harris et al., 2004), and one had a trend towards menthol smokers having worse outcomes (Foulds et al., 2006).

Of the six reviewed cross sectional studies, two (Fu et al., 2008; Muscat et al., 2002) failed to find significant differences between menthol and non-menthol smokers. Of these, the utility of one (Muscat et al., 2002) was found to be extremely limited due to severe methodological flaws. Of the remaining four studies, three found that menthol smokers had worse cessation outcomes as compared to their nonmenthol smoking counterparts, while one (Gundersen et al., 2009), found that African-American and Latino menthol smokers had worse cessation outcomes as compared to their nonmenthol smoking counterparts while the reverse was true for White smokers.

Several of the studies that found no significant association between menthol and cessation success may have overadjusted their analyses by including adjustments for dependence factors such as

TTFC. Since dependence may be an intermediate factor impacting cessation success, it may not be appropriate to control for the level of dependence. This is consistent with the observation that menthol smokers appear to be more nicotine dependent as compared to nonmenthol smokers. Furthermore, the data regarding African American menthol smokers are fairly consistent; they are less likely to be successful in quitting smoking as compared to their nonmenthol counterparts. Although there is a suggestion that White menthol smokers may have greater quitting success, this is not consistent, even using large nationally representative datasets. From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is likely associated with reduced success in smoking cessation, especially among African American menthol smokers.

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Blot WJ, Cohen SS, Aldrich M, McLaughlin JK, Hargreaves MK, Signorello LB. | Lung cancer risk among smokers of menthol cigarettes. | 2011 | The National Cancer Institute | Prospective | 12,373 smokers who participated in a follow up of the Southern Community Cohort Study | 440 incident lung cancer case patients and 2213 matched control subjects | During an average of 4.3 years of follow-up, 21% of participants smoking at baseline had quit, with menthol and nonmenthol smokers having equal odds of quitting (OR = 1.02, 95% CI = 0.89 to 1.16). |
| Caraballo, RS & Asman, K. | Epidemiology of menthol cigarette use in the United States. | 2011 | No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention | Review and secondary analyses of national surveys | NSDUH: adolescents aged 12-17 years old who smoked in the past month and adult smokers (aged 18 years or older) who smoked in the past month<br>NYTS: middle school (MS) and high school (HS) students with school year, past 30 day smoking, brand use, and menthol information.<br>MTF: current smokers in 8th, 10th and 12th grade<br>NHANES: 20 years and older who had Smoked and were non-Hispanic white, non-Hispanic black/African American, or Mexican American | NSDUH: 9,595 adolescents; 62,010 adults<br>NYTS: 1,978 MS students and 6,163 HS students<br>MTF: 20,863 8th graders; 30,722 10th graders; 40,914 12th Graders<br>NHANES: 1571 individuals with UPC information | Menthol cigarettes are disproportionately smoked by adolescents, blacks/African Americans, adult females, those living in the Northeast of the United States and those with family incomes lower than $50,000. Based on self-reports of menthol cigarette use, menthol cigarette use among smokers have increased from 2004 to 2008. |
| Cropsey KL, Weaver MF, Eldridge GD, Villalobos GC, | Differential success rates in racial groups: results of a clinical | 2009 | National Institute on Drug Abuse (grant K23DA15774 ) | Original study = randomizied control trial. Extracted data | White and Black female prisoners, aged ≥18, smoking at least 5 cpd. | N=233 cases<br>N= 289 controls | Smoking mentholated cigarettes was not associated with these differences in quit rates. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Best AM, Stitzer ML. | trial of smoking cessation among female prisoners. | | | using case control design | | | |
| Doll R, Peto R, Boreham J et al. | Mortality in relation to smoking: 50 years' observation on male British doctors. | 2004 | Medical Research Council, the British Heart Foundation, and Cancer Research UK | Prospective study starting in 1951 | British doctors | N=34,439 | The excess mortality associated with smoking chiefly involved vascular, neoplastic, and respiratory diseases that can be caused by smoking.<br><br>[Not menthol specific] |
| Foulds J, Gandhi KK, Steinberg MB, Richardson DL, Williams JM, Burke MV, Rhoads GG. | Factors associated with quitting smoking at a tobacco treatment dependence treatment clinic. | 2006 | The New Jersey Department of Health and Senior Services, as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey, The Robert Wood Johnson Foundation, the National Institute on Drug Abuse, and the American Legacy Foundation | Cohort | first 1021 patients who attempted to quit tobacco at a specialist tobacco dependence treatment outpatient clinic based at the Tobacco Dependence Program at the University of Medicine and Dentistry of New Jersey-School of Public Health | N=1021 | Forty-one percent of the patients smoked menthol cigarettes. They were less likely to achieve abstinence in univariate analyses, and this item remained in the model predicting 4-week outcome. |
| Foulds J, Hooper MW, Pletcher MJ, Okuyemi KS. | Do smokers of menthol cigarettes find it harder to quit smoking? | 2010 | No funding source(s) provided. Authors affiliated with Pennsylvania State College of Medicine, University of Miami, University of California, San Francisco, University of Minnesota | Review | Ten published, peer-reviewed studies | Not Applicable | Half of the studies found evidence that menthol smoking is associated with lower odds of cessation, while the other half found no such effects. The pattern of results in these studies suggest that the association between smoking menthol cigarettes and difficulty quitting is stronger in (a) racial/ethnic minority populations, (b) younger smokers, and (c) studies carried out after 1999. |
| Fu SS, Kodl MM, Joseph AM, Hatsukami DK, Johnson EO, Breslau N, | Racial/Ethnic disparities in the use of nicotine replacement therapy and quit | 2008 | Veterans Affairs Health Services Research and Development research career development award and Veterans Affairs | Large, randomized intervention study | Adults ages 25 -44 years from 3 metropolitan areas in the Midwest were randomly sampled | N=27,031 baseline total; Caucasian (n= 7,907), | No association between adult use of menthol cigarettes and cessation success |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Wu B, Bierut L. | ratios in lifetime smokers ages 25 to 44 years. | | Health Services Research and Development postdoctoral research fellowship; National Cancer Institute and University of Minnesota Transdisciplinary Tobacco Use Research Center | | using Health Maintenance Organization membership lists in Detroit, MI and Minneapolis, MN and a driver's license registry in St. Louis, MO; sample was limited to lifetime smokers (individuals who had ever smoked >100 cigarettes). | African American (n= 955), Latino (n= 246), and Asian (n=108) race/ethnicity. Lifetime smokers who were multiracial or of other race (n=387) were excluded | |
| Gandhi KK, Foulds J, Steinberg MB, Lu SE, Williams JM. | Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic. | 2009 | New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health | Retrospective Cohort/ Population Studies | Specialized smoking cessation outpatient clinic in New Jersey: patients who set a quit date and attempted to quit smoking, between 1 January 2001 and 30 June 2005; African American, Latinos, Whites | N=1688 (787 Menthol, 910 Nonmenthol) | This study found lower short-term (4-week follow-up) quit rates among AA and Latino menthol smokers as compared with non-menthol smokers within the same racial / ethnic subgroups. |
| Gundersen DA, Delnevo CD, Wackowski O. | Exploring the relationship between race/ethnicity, menthol smoking, and cessation, in a nationally representative | 2009 | No funding source(s) provided. Authors affiliated with University of Medicine and Dentistry of New Jersey | Retrospective analysis of cross-sectional study | Sample of those who indicated that they do not currently use other tobacco products and have made a quit attempt.. | N=7815 | Menthol smoking can lead to poorer cessation outcomes, but only for non-white smokers. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | sample of adults. | | | | | | |
| Harris KJ, Okuyemi KS, Catley D, Mayo MS, Ge B, Ahluwalia JS. | Predictors of smoking cessation among African-Americans enrolled in a randomized controlled trial of bupropion. | 2004 | Grants RO1 CA77856, K07 CA87714, R24 CA95835 and K07 CA90334 from the National Cancer Institute | Double-blind placebo-controlled, randomized trial | 1,498 smokers in a mid-western city who identified themselves as black or African-American were screened, and 981 were eligible and invited to participate. | N=600 | Other than bupropion treatment, the strongest predictors for success included not smoking menthol cigarettes |
| Hyland A, Garten S, Giovino GA, Cummings KM. | Mentholated cigarettes and smoking cessation: findings from COMMIT. | 2002 | The National Cancer Institute grant CA016056-26 | Telephone survey | COMMIT study: Baseline smokers who reported whether their current cigarette brand or not in 1988, and had a known smoking status in 1993. | N=13,268 (3,184 menthol, 10084 non-menthol) | No clear associations were observed between menthol cigarette use and indicators of nicotine dependence, even after controlling for race/ethnicity and other demographics.. |
| Levy DT, Blackman K, Tauras J, Chaloupka F, Villanti A, Niaura R, Vallone DM, Abrams DB. | Quit attempts and quit rates among menthol and nonmenthol smokers in the United States | 2011 | Legacy | Tobacco Use Supplement to the Current Population Survey | Participants (18+ yo) who responded to 2003 and 2006–2007 waves | N=34260 for 2003 wave N=31250 for 2007 wave | Menthol smokers are more likely to make quit attempts, but are less successful at staying quit. |
| Murray RP, Connett JE, Skeans MA, Tashkin DP. | Menthol cigarettes and health risks in Lung Health Study data. | 2007 | Grant HR 46002 from the Division of Lung Disease; National Heart, Lung, and Blood Institute; National Institutes of Health | Randomized Controlled Trial | Adult smokers in a clinical trial of smoking cessation and ipratropium in the prevention of chronic obstructive pulmonary disease. | N=5,887 | We conclude that our data contain no evidence that mentholation of cigarettes increases the hazards of smoking. |
| Muscat JE, Richie JP Jr, | Mentholated cigarettes and | 2002 | US Public Health Service grants CA-32617, CA- | Cohort/ Population | Hospital between 1981 and 1999: 19 545 | N=19,545 subjects, | The risk of quitting was not associated with cigarette menthol flavour. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Stellman SD. | smoking habits in whites and blacks. | | 68384 and CA-17613 | | subjects. Eleven per cent of subjects were black, including 16 540 (84.6%) smokers of non-mentholated cigarettes and 3005 (15.4%) smokers of mentholated cigarettes; Current smokers vs Former smoker; Among blacks, no difference in heavy smoking of menthol vs non-menthol. | 11% of subjects were black, including 16,540 (84.6%) smokers of non-mentholated cigarettes and 3005 (15.4%) smokers of mentholated. | |
| Okuyemi KS, Ahluwalia JS, Ebersole-Robinson M, Catley D, Mayo MS, Resnicow K. | Does menthol attenuate the effect of bupropion among African American smokers? | 2003 | National Cancer Institute grants R01 CA77856, K07 CA90334, R24 CA95835-01 | Randomized Controlled Trial | African American smokers enrolled in a clinical trial that assessed the efficacy of sustained-release bupropion for smoking cessation. Menthol (n = 471) and non-menthol (n = 129) smokers were compared on smoking-related characteristics and abstinence rates at 6 weeks and 6 months. | N=600 | African American menthol smokers had lower smoking cessation rates after 6 weeks of treatment with bupropion-SR than African-American non menthol smokers, thereby putting menthol smokers at greater risk from the health effects of smoking. Lower overall cessation rates among African Americans menthol smokers may partially explain ethnic differences in smoking-related disease risks. |
| Pletcher MJ, Hulley BJ, Houston T, Kiefe CI, Benowitz N, Sidney S. | Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery | 2006 | Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute | Multi-center U.S. cohort study (CARDIA) | African American and European American smokers aged 18 to 30 years and healthy at the time of enrollment in 1985 | 1544 (non-menthol smokers (n = 563) and menthol smokers (n = 972)) | Menthol and nonmenthol cigarettes seem to be equally harmful per cigarette smoked in terms of atherosclerosis and pulmonary function decline, but menthol cigarettes may be harder to quit smoking. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Cessation: Table of Referenced Sources

| Author Name(s) | Article Title | Year Pub. | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | Risk Development in Young Adults (CARDIA) Study. | | | | | | |
| Stahre M, Okuyemi KS et al. | Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. | 2010 | Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development | 2005 National Health Interview Survey (NHIS) Cancer Control Supplement | 18+ yo for which menthol cigarette status was known. | N=12,004 | Menthol cigarette smoking is associated negatively with successful smoking cessation among African Americans |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

References

1. Blot WJ, Cohen SS, Aldrich M, McLaughlin JK, Hargreaves MK, Signorello LB (2011) Lung cancer risk among smokers of menthol cigarettes. Journal of the National Cancer Institute 103:810-6. [Funded by National Cancer Institute]
2. Caraballo, RS & Asman, K (2011). Epidemiology of menthol cigarette use in the United States. Tobacco Induced Diseases, 9 (Suppl 1): S1. [No funding source(s) provided. Authors affiliated with the Centers for Disease Control and Prevention]
3. Cropsey KL, Weaver MF, Eldridge GD, et al (2009) Differential success rates in racial groups: results of a clinical trial of smoking cessation among female prisoners. Nicotine and Tobacco Research 11(6):690–7. [Funded by National Institute on Drug Abuse grant K23 DA15774]
4. Doll R, Peto R, Boreham J et al. (2004) Mortality in relation to smoking: 50 years' observation on male British doctors. British Medical Journal 26;328(7455):1519. [Funded by the Medical Research Council, the British Heart Foundation, and Cancer Research UK]
5. Foulds JF, Gandhi KK, Steinberg MB, et al. (2006) Factors associated with quitting smoking at a tobacco treatment dependence treatment clinic. American Journal of Health Behavior 30(4):400–12. [Funding provided by grant from the New Jersey Department of Health and Senior Services, as part of New Jersey's Comprehensive Tobacco Control Program; the Cancer Institute of New Jersey, The Robert Wood Johnson Foundation, the National Institute on Drug Abuse, and the American Legacy Foundation]
6. Foulds J, Hooper MW, Pletcher MJ, Okuyemi KS (2010) Do smokers of menthol cigarettes find it harder to quit smoking? Nicotine and Tobacco Research 12(suppl 2): S102-9. [No funding source(s) provided. Authors affiliated with Pennsylania State College of Medicine, University of Miami, University of California, San Francisco, University of Minnesota]
7. Fu SS, Kodl MM, Joseph AM, et al (2008) Racial or ethnic disparities in the use of nicotine replacement therapy and quit ratios in lifetime smokers ages 25 to 44 years. Cancer Epidemiology, Biomarkers, and Prevention 17(7):1640–1647. [Funded by Veterans Affairs Health Services Research and Development research career development award and Veterans Affairs Health Services Research and Development postdoctoral research fellowship; National Cancer Institute and University of Minnesota Transdisciplinary Tobacco Use Research Center]
8. Gandhi KK, Foulds J, Steinberg MB, et al. (2009) Lower quit rates among African American and Latino menthol smokers at a tobacco treatment clinic. International Journal of Clinical Practice 63:360–367. [Funded by New Jersey Department of Health and Senior Services, the Cancer Institute of New Jersey, the Robert Wood Johnson Foundation, National Institute on Drug Abuse, the American Legacy Foundation and the National Institute on Mental Health]
9. Gundersen DA, Delnevo CD, Wackowski O (2009) Exploring the relationship between race or ethnicity, menthol smoking, and cessation, in a nationally representative sample of adults. Preventive Medicine 49(6):553-7. [No funding source(s) provided. Authors affiliated with University of Medicine and Dentistry of New Jersey]
10. Harris KJ, Okuyemi KS, Catley D, et al (2004) Predictors of smoking cessation among African-Americans enrolled in a randomized controlled trial of bupropion. Preventive Medicine 38(4):498–502. [Funded by Grants RO1 CA77856, K07 CA87714, R24 CA95835 and K07 CA90334 from the National Cancer Institute]

11. Hyland A, Garten S, Giovino, GA, Cummings KM (2002) Mentholated cigarettes and smoking cessation: findings from COMMIT (Community Intervention Trial for Smoking Cessation). Tobacco Control 11(2):135–9. [Funded by The National Cancer Institute grant CA016056-26]
12. Levy DT, Blackman K, Tauras J, Chaloupka F, Villanti A, Niaura R, Vallone DM, Abrams DB (2011) Quit attempts and quit rates among menthol and nonmenthol smokers in the United States. American Journal of Public Health, 101: 1241-1247. [Funded by Legacy]
13. Murray RP, Connett JE, Skeans MA, Tashkin, DP (2007) Menthol cigarettes and health risks in Lung Health Study data. Nicotine and Tobacco Research, 9(1):101–7. [Funded by Grant HR 46002 from the Division of Lung Disease; National Heart, Lung, and Blood Institute; National Institutes of Health]
14. Muscat JE, Richie JP Jr, et al (2002) Mentholated cigarettes and smoking habits in Whites and Blacks. Tobacco Control 11(4):368–71. [Funded by US Public Health Service grants CA-32617, CA-68384 and CA-17613]
15. Okuyemi KS, Ahluwalia JS, Ebersole-Robinson M, et al. (2003) Does menthol attenuate the effect of bupropion among African American smokers? Addiction 98(10):1387–1393. [Funded by National Cancer Institute grants R01 CA77856, K07 CA90334, R24 CA95835-01]
16. Pletcher MJ, Hulley BJ, Houston T, et al. (2006) Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Archives of Internal Medicine 166(17):1915–22. [Funded by Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-
95095 from the National Heart, Lung, and Blood Institute]
17. Stahre M, Okuyemi KS et al. (2010) Racial or ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. Addiction 105(suppl. 1):75–83. [Funded by Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development and Health Services Research and Development]

## *I. Disease Risk*

Data are clear that smoking tobacco results in an increased risk of disease for smokers, and research has identified causal links between smoking tobacco and risk for lung cancer, esophageal and oropharyngeal cancers, cardiovascular disease and respiratory outcomes, and many others. As part of FDA's analyses, scientists investigated case studies related to menthol and nonmenthol cigarette smoking and the above specific disease risks to determine if menthol affects disease risk for users.

*Lung cancer*

Kabat and Hebert (1991) conducted a hospital-based, case-control study among current smokers in eight hospitals located in four U.S. cities. They found no difference in lung cancer risk between menthol smokers (short-term 1-14 years or long-term ≥15 years) and nonmenthol smokers (males: OR (95% CI) 0.98 (0.70-1.38) and 1.14 (0.82-1.59); females, 0.76 (0.53-1.16) and 0.82 (0.52-1.28) for menthol ≥ 15 years and menthol 1-14 years respectively). Researchers detected no association in stratified analysis by histological types of lung cancer after controlling for cpd, duration of smoking, inhalation, race, education, age, and BMI. This appears to be the first epidemiologic study that evaluated the associations between menthol cigarette use and lung cancer risk. The racial or ethnic composition of this study was comparable to White and African Americans in the general population. Generalizability may be limited due to the relatively low prevalence of menthol use by African American participants as compared to the general African American smoking population. Most of the participants were at least 50 years old, however since lung cancer typically does not occur at younger ages, this is not considered a weakness. There is limited power for stratified analysis by histological type (e.g., large cell carcinoma), and the hospital-based controls may have had conditions potentially related to smoking (including colon and breast cancer), which may reduce an association. Menthol cigarette use status was determined by specifically asking about specific brands of cigarettes, which may reduce the potential for misclassification.

Sidney et al. (1995) conducted a cohort study among 11,761 Northern California Kaiser Permanente Insurers current smokers 30-89 years old who had smoked for at least 20 years. The study found that the prevalence of menthol cigarette use was highest among African American smokers, followed by Asian American and White smokers. Menthol smokers were younger and more likely to be females than nonmenthol smokers. Menthol smokers had a statistically significantly higher lung cancer risk than nonmenthol smokers among men (RR (95% CI): 1.45 (1.03-2.02)), but not among women (0.75 (0.51-1.11)). Relative risks were calculated adjusting for age, sex, race, education, cpd, and duration of smoking; the multivariate model did not adjust for other potential factors, such as family history of lung cancer. After more than eight years of follow up, researchers noted a loss of about 25 percent due to members terminating the insurance program which may lead to selection bias. Generalizability may be limited since the difference was only seen in men, and the participant pool was limited to Northern California Kaiser Permanente Insurerers customers only, a pool that was not nationally representative.

Carpenter et al. (1999) examined the association between menthol cigarette use and lung cancer using data from a population based case-control study that evaluated genetic markers for lung cancer risk in Los Angeles County, California. The subjects were current and former smokers 40-84 years old. The study found no difference in lung cancer risk between menthol and nonmenthol smokers (OR(95% CI): 1.04 (0.62, 1.75)). The study also found no difference in lung cancer risk between menthol smokers and nonmenthol smokers by race. The analysis adjusted for matching factors, total pack-years, and years since quitting. Due to the low response rate of controls (731:3193) the remaining controls may not be representative of the general population from which the cases were drawn. Generalizability is limited, as the African American sample reported smoking menthol cigarettes at rates lower than the national estimate.

Brooks et al. (2003) conducted a hospital-based case-control study using data collected in the Slone Epidemiology Center Case-Control Surveillance Study in the eastern United States. The analysis was restricted to subjects 40-74 years old who had smoked for at least 20 years, had no history of cancer, and were interviewed between 1981 and 2000. Analyses were adjusted for demographic factors and smoke-related factors (e.g., duration of smoking, cpd, years since quitting, proportion of years smoking filtered cigarettes, etc.). The study found no difference in lung cancer risk between long-term menthol smokers and nonmenthol smokers (OR (95% CI): 0.97 (0.70-1.34)). Risks also did not differ by race or sex. Menthol status was characterized by brand and dose of exposure (i.e. duration of menthol cigarette use). Due to differences in how cases and controls were identified, researchers adjusted the data for the time of interview to account for bias. The study was restricted to long-term smokers to minimize the potential for selection bias for controls, however this may limit generalizability. A significant amount of missing data makes establishing exposures difficult; brand information could be identified in 60 percent of total duration of smoking. Most lung cancer patients were discovered at a time when menthol cigarettes were not popular so menthol status was not known for many patients. The authors assumed these cases smoked nonmenthol cigarettes. However, this may result in misclassification of the exposure and bias the estimates. A possible selection bias may exist in cases since the study included lung cancer cases in patients who were diagnosed with lung cancer 12 months before their current admission instead of only newly diagnosed patients. Thus, the cases may include long-time survivors who may not have general characteristics for all lung cancer patients. The controls were hospitalized for diseases determined to be unrelated to cigarette smoking, however diagnoses could include breast and colon cancers, which may be related to smoking. Data collection was limited to the brand most recently smoked (or currently smoking) and also the brand reportedly smoked the longest. Data from both questions were only obtained from 17 percent of the subjects, so researchers included subjects who could provide brand information for at least 60 percent of the total duration of smoking.

Stellman et al. (2003) reported results from a hospital-based, case-control study that was conducted between 1984 and 1998. The study found no associations between menthol cigarette use status and lung cancer risk among current smokers for white males (OR (95% CI): 0.83 (0.63-1.09)), African American males (1.34 (0.79-2.29)), white females (0.61 (0.44-1.06)), and African American females (0.79 (0.41-1.54)). Odds ratios were adjusted for age at diagnosis, pack-years of smoking, education years, and BMI. The study did not report odds ratios for current smokers overall, by sex, or by race. The hospital-based controls may have had conditions related to smoking that would reduce the association. Generalizability is limited, as subjects were hospitalized and not nationally representative.

Murray et al. (2007) investigated the health effects of menthol cigarette smoking among 5,887 adult smokers 35-60 years old with mild to moderate airway obstruction who participated in a smoking cessation program as part of the Lung Health Study. This long-term cohort study had annual assessments for five years. Menthol cigarette use was not significantly associated with mortality caused by coronary heart disease, cardiovascular disease, lung cancer (hazard ratio (95% CI):0.96 (0.70-1.32)), and any causes during 14 years of follow-up. Researchers adjusted estimates for age, sex, race, years of education, cpd, and predicted respiratory volume (FEV1% predicted), and randomization group assignment. Menthol status was checked annually. Generalizability may be limited as the sample was not nationally representative.

Etzel et al. (2008) analyzed results from a case-control study of African American smokers in the Houston area to identify lung cancer risk factors to be included in a lung cancer risk prediction model. The study did not find statistically significant differences in lung cancer risk between menthol and nonmenthol smokers in the case-control data, although the risk estimates trended toward being lower for current smokers (OR 0.69 (0.46-1.03)) and ever smokers (0.81 (0.60- 1.09)), but not for former smokers 0.99 (0.62-1.56)). Menthol cigarette use was not retained in the final multivariable epidemiologic risk model for African Americans. The sample is not nationally representative. This novel model of lung cancer risk prevention has not yet been validated by others in the field.

Blot et al. (2011) conducted a nested case-control study among 440 incident lung cancer cases and 2,213 controls enrolled in the Southern Community Cohort Study between 2002 and 2009. Researchers matched cases and controls on age, sex, and race, and they adjusted estimates for pack-years of smoking, educational attainment, household income, use of other tobacco products, health insurance coverage, close family history of lung cancer, and BMI. The risk of lung cancer incidence for both current smokers and former smokers was substantially higher than for nonsmokers. In a multivariate analysis adjusted for pack-years of smoking, there was a statistically significant association between menthol smoking and lower lung cancer risks for incidence (OR 0.65 (0.47-0.90)) and mortality (HR 0.69 (0.49-0.95)) among current menthol smokers compared to current nonmenthol smokers. The study also found statistically significant lower incidence risks for menthol smoking among current female smokers (OR 0.43 (0.24-0.75)) and current African American smokers (OR 0.52 (0.34-0.78), but not among current male smokers (OR 0.77 (0.49-1.23)) and current White smokers (OR 0.84 (0.43-1.64).

Among a set of secondary data analyses conducted in 2010 that have not been peer-reviewed, Muscat analyzed data from a community cross-sectional study of 525 African American and White smokers. The analysis found a statistically significant lower risk of lung cancer among current menthol smokers 50 years old and over (OR 0.76, p-value=0.049). There was a trend toward an association between menthol smoking status and lower risk of lung cancer among all current smokers (OR 0.82, p-value=0.110).

In addition to peer-reviewed articles and secondary data analyses, FDA also evaluated the association between menthol smoking and disease risk using data from the 1987 National Health Interview Survey that was linked to the National Death Index for mortality follow-up. Mortality data were available for approximately 5,000 participants who were current menthol and nonmenthol smokers at the time of interview. FDA estimated mortality hazard ratios for menthol smokers compared to nonmenthol smokers, adjusting for demographic and smoking characteristics. The hazard ratio for lung cancer mortality for menthol smokers overall was 0.69 (95% CI: 0.45-1.06). The hazard ratio for lung cancer mortality for menthol smokers 50 years old and over was 0.59 (95% CI = 0.36-0.96). No differences existed in overall mortality from all causes of death, other than lung cancer, for menthol and nonmenthol smokers.

In an industry supported study, Lee (2011) conducted a systematic review and meta-analysis of eight epidemiological studies examining the relationship between lung cancer risk and menthol smoking. The meta-analysis included the seven articles previously discussed in this section as well as a conference abstract (Jockel, Pohlabeln, and Jahn, 2004) that was conducted in Germany and for which the results have only been reported in English in a journal abstract. The overall adjusted relative risk estimate for menthol smoking compared to nonmenthol smoking from the meta-analysis was 0.93 (95% CI 0.84-1.02, n=8). A statistically significant lower risk was observed in females (RR 0.80, 0.67-0.95, n=5 studies) and in studies published since 2001 (0.88, 0.77-0.99, n=5 studies). No difference in risk was observed in males (1.01, 0.84-1.22, n=5 studies) or in studies published between 1991 and 2000 (1.00, 0.86-1.15, n=3). Estimates of relative risk for menthol smokers compared to nonmenthol smokers trended toward being lower for whites (0.87, 0.75-1.03, n=4) and African Americans (0.90, 0.73-1.10, n=4 studies), but the differences failed to reach significance.

*Oropharyngeal cancer*

Kabat and Hebert (1994) conducted a hospital-based, case-control study of tobacco-related cancers among current smokers in eight hospitals in four U.S. cities. This was a moderately sized study, with 194 male and 82 female newly diagnosed oropharyngeal cancer cases, and 845 male and 411 female controls. After adjusting for demographic factors, as well as cpd, BMI, alcohol intake, filtered or unfiltered cigarette use, and duration of smoking, they found no association between menthol cigarette use and oropharyngeal cancer risk (OR (95% CI): 0.9 (0.5-1.6)) for male menthol smokers and 0.7 (0.5-1.7) for females menthol smokers compared to nonmenthol smokers. Although the authors stated that menthol cigarette use was positively associated with pharynx cancer in males 1.7 (0.8-3.4), the difference was not statistically significant. Menthol use was self-reported. The control cases were hospitalized with conditions thought not to be related to smoking, however it included cancers that could be smoking-related (e.g., breast cancer, colon cancer). The sample size in subgroups was small, with limited power. Generalizability may be limited since the sample was not nationally representative and limited to hospitalized patients.

*Esophageal cancer*

In a letter to the editor, Hebert and Kabat (1988) reported results of an analysis of case-control study data of esophageal cancer and found no effect of menthol smoking on esophageal cancer risk. The risks for esophageal cancer for men and women who smoked menthol cigarettes for 10 years or more versus nonmenthol smokers were not significantly different (men = OR (95% CI): 0.70 (0.29-1.73); women = OR (95% CI): 1.53 (0.61-3.86)). This is a relatively small study, with 96 female and 216 male cases and 157 female and 305 male controls. It is not clear from the letter if the authors controlled for factors such as alcohol consumption and socioeconomic status in the analysis.

In a follow-up to the 1988 letter to the editor, Hebert and Kabat (1989) again sought to investigate the relationship between menthol cigarette smoking and esophageal cancer. They analyzed a larger dataset from 20 hospitals in nine U.S. cities in the American Health Foundation Comprehensive Tobacco Questionnaire, a large, matched, case-control study. This time, investigators found a trend toward reduced risk (p=0.08) among male menthol smokers (<10 yrs) versus male never smokers (OR (95% CI): 0.50 (0.23-1.07)), but this trend failed to reach significance. There was no increased risk for those who had been menthol smokers for more than 10 years. Logistic analysis for females showed a non-statistically significant trend toward increased risk for those who had been menthol smokers for more than 10 years (OR (95% CI: 2.3 (0.93-5.720) (p=0.07)). In this investigation, researchers included major risk factors for esophageal cancer for analysis, such as lifetime exposure to tobacco (cpd, menthol vs. nonmenthol) and alcohol (duration, amount). Statistical analysis included adjustment for demographic factors.

*Multiple Cancers*

Freidman et al. (1998) conducted a cohort study among 5,770 men and 5,990 women 30-89 years old who were enrolled in Kaiser Permanente health insurance from 1979-1985 in Northern California, with follow-up through 1994. The subjects had each smoked for at least 20 years. The study examined relative risks for upper aerodigestive cancer, pancreatic cancer, renal adenocarcinoma, other urinary tract cancer, uterine cervical cancer, and all of these cancers combined among menthol smokers compared to nonmenthol smokers. Analyses were controlled for race and age. There were no significant differences, although the relative risks for menthol smoking for seven of the nine estimates (five cancer sites by sex) trended toward being reduced. The overall relative risk for all smoking-related cancers was not significantly different between male menthol and nonmenthol smokers (0.76 with 95% CI 0.52-1.11) or female menthol and nonmenthol smokers (0.79 with 95% CI 0.53-1.18). The overall relative risk for both sexes combined was not presented; it is not clear if this result would have shown a statistically significant lower risk of these cancers for menthol smokers compared to nonmenthol smokers.

Among a set of secondary data analyses conducted in 2010 that have not been peer-reviewed, Stellman and Neugut produced a follow-up to their 2003 study by analyzing data on cancer risk from the American Health Foundation hospital-based, multi-center, case-control study (3,728 cases and 4,888 controls). The researchers estimated the odds ratios for the association between menthol smoking and cancer risk of the oral cavity, larynx, lung, esophagus, and bladder and among the overall population and in subgroups stratified by sex, controlling for age, race, educational attainment, BMI, and pack-years of smoking. Nine of the 10 odds ratios for the cancers by sex were less than 1.0 and the tenth, lung cancer among males, was 1.0, although the differences were not statistically significant. The odds ratio for lung cancer for female menthol smokers versus female nonmenthol smokers was 0.8 (95% CI 0.6-1.0). Since the authors did not report odds ratios to the nearest hundredth, it is not possible to determine how close this result was to statistical significance. That is, if the 1.0 was a result of rounding up, the odds ratio would reach significance, indicating reduced lung cancer risk for female menthol smokers, but if it was a result of rounding down, it would indicate overlapping data and therefore no significant differences.

*Multiple non-cancer diseases*

Pletcher et al. (2006) evaluated the associations between menthol cigarette use, coronary calcification and changes in pulmonary function test among 1,544 current smokers who were participants in CARDIA. CARDIA is a population-based longitudinal cohort study of risk factors for coronary artery diseases among healthy African Americans and Whites 18-30 years old. The subjects were followed for 15 years. The study found no difference in the association between menthol or nonmenthol exposure (in pack-years) and the prevalence of coronary calcification and 10-year decline in lung function. This is one of only two studies in this section that assessed menthol use on multiple occasions, finding that menthol status was relatively stable, suggesting little misclassification. Although the sample was diverse, it was not nationally representative, which may limit generalizability. While this is a large study, sample sizes in certain groups were small (e.g., African American nonmenthol smokers).

Murray et al. (2007) examined the associations between menthol cigarette use and health risks among 5,887 Lung Health Study participants with early signs of obstructive lung impairment. They conducted analyses of mortality from selected causes and concluded menthol cigarette use was not significantly associated with mortality caused by coronary heart disease, cardiovascular disease, and any causes during 14 years of follow-up. Estimates were adjusted for age, sex, race, educational attainment, cpd, predicted respiratory volume, and randomization group assignment. This is a fairly large study with long-term follow up, and researchers assessed menthol use at multiple time points. Generalizability may be limited, as the sample is not nationally representative and limited to people with mild or moderate airway obstruction who participated in a smoking cessation program.

Among a set of secondary data analyses conducted in 2010 that have not been peer-reviewed, Hyland and Kasza analyzed data from the International Tobacco Control Four Country Survey, with data from the United States, United Kingdom, Canada and Australia. Data were collected from 7,532 individuals between 2002 and 2008. This study had a large and nationally representative sample population. Hyland and Kasza used case-control data collected between 2005 and 2010 by Roswell Park Cancer Institute and interview data collected between 1957 and 1965 by Roswell Park Memorial Institute to analyze the association between menthol smoking and risks of lung cancer and COPD. Adjusted relative risks for lung cancer or COPD trended toward being lower for female menthol smokers (OR 0.48, 0.23-1.02) and smokers overall (0.68, 0.38-1.22) compared to nonmenthol smokers, however the differences were not statistically significant. No difference was observed between male menthol and male nonmenthol smokers (1.16, 0.43-3.10). Analysis of data collected during the 1957-1965 time period indicated no menthol:nonmenthol differences for smokers overall (1.15, 0.73-1.81) or by sex. Relative risks were adjusted for age, race, and pack-years of smoking.

*Other health characteristics*

Mendiondo et al. (2010) examined the health characteristics between menthol and nonmenthol smokers using data from the 2005 NHIS-CCS, a large, nationally representative, cross-sectional survey. The study demonstrated that former menthol smokers had slightly higher BMI (OR (95% CI): 1.01(1.00-1.02)) and were more likely to have visited the emergency room due to asthma (OR 2.30: 1.04, 5.09).

*Conclusion*

Although menthol or nonmenthol classification and cigarette use data were self-reported and could be associated with misclassification, self-report of this kind of data are the standard of this research field and not considered detrimental to the study results. Furthermore, the data do not support the claim that a substantial number of adult respondents intentionally under-report tobacco use (Everhart et al, 2009; Yeager & Krosnick, 2010). Furthermore, as noted by Caraballo et al. (2011), although there is evidence that there is some self-report bias in reporting menthol:nonmenthol cigarette use, especially among adolescents, this is not necessarily problematic since it is likely that this type of bias is fairly constant over time.

Eleven studies (Brooks et al., 2003; Carpenter et al., 1999; Etzel et al., 2008; Freidman et al., 1998; Hebert and Kabat, 1988; Hebert and Kabat, 1989; Kabat and Hebert, 1991; Kabat and Hebert, 1994; Murray et al., 2007; Pletcher et al., 2006; Stellman et al., 2003) failed to find any significant differences in disease risk between menthol and nonmenthol smokers. One study found a greater disease risk in some groups (Sidney et al., 1995). Two studies (Blot et al., 2011; Lee, 2011) suggest that, in some groups, menthol smoking may be associated with lower cancer risk as compared to nonmenthol smoking. It is possible, but not clear at this time, that this association might be related to historical differences in cigarette design features (such as tip ventilation between menthol and nonmenthol cigarettes) or other demographic factors. No physiological cause for an association between cancer risk and menthol in cigarettes has been established.  From the available studies, the weight of evidence supports the conclusion that menthol in cigarettes is not associated with an increase in disease risk to the user.

Disease Risk: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Blot WJ, Cohen SS, Aldrich M, McLaughlin JK, Hargreaves MK, Signorello LB. | Lung cancer risk among smokers of menthol cigarettes. | 2011 | The National Cancer Institute | Prospective | 12,373 smokers who participated in a follow up of the Southern Community Cohort Study | 440 incident lung cancer case patients and 2213 matched control subjects | A lower lung cancer incidence was noted in menthol vs nonmenthol smokers (for smokers of <10, 10–19, and ≥20 cigarettes per day, compared with never smokers, OR = 5.0 vs 10.3, 8.7 vs 12.9, and 12.2 vs 21.1, respectively). These trends were mirrored for lung cancer mortality. |
| Brooks DR, Palmer JR, Strom BL, Rosenberg L. | Menthol cigarettes and risk of lung cancer. | 2003 | The National Institutes of Health and the US Food and Drug Administration | Case-control | 40-74 years of age who had no history of cancer, had smoked cigarettes for at least 20 years, and had been interviewed during the period 1981-2000 fpr the Slone Epidemiology Center Case Control Surveillance Study | N=643ses N=4110 controls | The lung cancer risk for long-term smokers of menthol cigarettes was similar to that for smokers of nonmenthol cigarettes(odds ratio= 0.97,95% confidence interval: 0.70, 1.34). Odds ratios were also close to 1. 0 in separate analyses of male, female, Black, and White subjects. The results of this study do not support the hypothesis that smoking menthol cigarettes increases the risk of lung cancer relative to smoking nonmenthol cigarettes. |
| Carpenter CL, Jarvik ME, Morgenstern H, McCarthy WJ, London SJ. | Mentholated cigarette smoking and lung-cancer risk. | 1999 | The State of California Tobacco-Related Disease Research Program and the National Institutes of Health; the California Public Health Foundation which is supported by the California Department of Health Services | Case-control | Incident cases of lung cancer were identified between 1991 and 1994 from 35 hospitals in Los Angeles County, CA; African Americans and Caucasians ages 40-84 yrs, with no prior cancer other than melanoma of skin | Number of incident cases= 337 and Population control=478 | Our results suggest that lung cancer risk for smoking mentholated cigarettes resembles risk of smoking non-mentholated cigarettes. |
| Etzel CJ, Kachroo S, Liu M, D'Amelio A, Dong Q, Cote ML, Wenzlaff AS, Hong WK, | Development and validation of a lung cancer risk prediction model for African-Americans. | 2008 | National Cancer Institute grant K07CA093592; National Cancer Institute grants CA55769, CA123208, CA60691, and CA87895; National Cancer | Case-control | African-American, Men and Women, from The University of Texas M. D. Anderson Cancer Center and the Midrael E. DeBakey VA Medical | Cases N=491 Controls N=497 | In our analysis, we observed no significant risks of lung cancer among former or current smokers who reported smoking mentholated cigarettes (OR range 0.69 -.0.99) |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

# Disease Risk: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Greisinger AJ, Schwartz AG, Spitz MR. | | | Institute contract N01-PC35745; Flight Attendant Medical Research Institute | | Center, both in Houston, from 1995 to 2005. All cases with newly diagnosed, histopathologically confirmed, and untreated lung cancer were eligible for the study. Case exclusion criteria for the study included prior hemotherapy or radiotherapy or recent blood transfusion. We recruited our control population from Houston area community centers and the Kelsey-Seybold Clinic, Houston's largest multispecialty physicians group practice. | | |
| Everhart J, Ferketich AK, Browning K et al. | Acculturation and misclassification of tobacco use status among Hispanic men and women in the United States. | 2009 | Summer Research Opportunities Program at the Ohio State University | Cross-sectional survey | Data from self-reported "Mexican American" or "other Hispanic" participants of the 1999-2002 National Health and Nutrition Examination Surveys who were at least 20 years old. | N=3982 for the 1999-2000 wave<br><br>N=3293 for the 2001-2001 wave | Among males ( n = 1,175), the prevalence estimates of misclassification were 4.8%, 1.8%, and 2.2% for low, medium, and highly acculturated males, respectively ( p < .02). Among females (n = 1,345), the prevalence estimates of misclassification were 0.8%, 2.0%, and 4.9% for low, medium, and highly acculturated females, respectively ( p < .03).<br><br>[not menthol specific] |
| Friedman GD, Sadler M, Tekawa IS, | Mentholated cigarettes and non-lung smoking | 1998 | National Cancer Institute grant R35 CA 49761 | Retrospective Survey | In 1979-1985, 79,946 subscribers of the Kaiser Permanente | N=5770 men and N=5990 women, | Risk was not increased among persons who currently smoked mentholated compared with plain cigarettes for all of the non-lung smoking |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Disease Risk: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| Sidney S. | related cancers in California, USA. | | | | Medical Care Program in northern CA, age 30-89 years, completed a detailed questionnaire about smoking habits and were followed up through 1994. | currently smoking cigarettes and for at least 20 years, no smoking related cancer at entry, recorded whether their current cigarette was mentholated. . | related cancers combined or for most sites studied |
| Hebert JR, Kabat GC. | Menthol cigarettes and esophageal cancer. | 1988 | No funding source(s) provided. Authors affiliated with the American Health Foundation | Case-control | Male and female menthol smokers | Cases: N=96 female, N=216 male; Control: N=157 female, N=305 male | We analyzed existing data from a case-control study ofesophageal cancer and found no menthol effect. |
| Hebert JR, Kabat GC. | Menthol cigarette smoking and oesophageal cancer. | 1989 | National Cancer Institute and American Cancer Society | Hospital-based, case-control | Patients were interviewed in 20 hospitals in 9 US cities from 1969 to 1984; Smokers were included in cases and control | N=172 cases<br><br>N=184 controls | Our results do not support the hypothesized relationship between menthol cigarette smoking and oesophageal cancer. |
| Jöckel K-H, Pohlabeln H, Jahn I. | Use of menthol cigarettes and risk of lung cancer. | 2004 | No funding source(s) provided. Author affiliated with the Institut fur Medizinishche Informatik | Hospital-based study | Not specified | 1004 incident lung cancer cases (839 males and 165 females) | The present study gives no indication for an additional risk of ever smoking menthol cigarettes if total amount of smoking is taken into account. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Disease Risk: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | | and the same number of population controls | |
| Kabat GC, Hebert JR. | Use of mentholated cigarettes and lung cancer risk. | 1991 | National Cancer Institute Program Project Grant CA32617 and Center Grant CAI7613 | Case-control | Current cigarette Smokers interviewed between 1985 and 1990. | N=588 male lung cancer cases and 914 male control patients; N=456 female lung cancer cases and 410 female controls | No significant association was observed between either short-term (1-14 years) or long- term (15+ years) menthol use and lung cancer in logistic regression analyses adjusting for covariates. For specific histological types of lung cancer there was no indication of an association with menthol usage. |
| Kabat GC, Hebert JR. | Use of mentholated cigarettes and oropharyngeal cancer. | 1994 | National Cancer Institute Program Project Grant CA32617 and Center Grant CAI7613 | Case-control | Current smokers | N=194 male and 82 female newly diagnosed, histologically confirmed cases of oropharyngeal cancer; 845 male and 411 female controls | Use of mentholated cigarettes is unlikely to be an important independent factor in oropharyngeal cancer. |
| Lee PN | Systematic review of the epidemiological evidence comparing lung cancer risk in | 2011 | Lorillard Tobacco Company | Meta-analysis | Eight epidemiological studies | Not Applicable | The data do not suggest any effect of mentholation on lung cancer risk. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

Disease Risk: Table of Referenced Sources

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | smokers of menthol and unmenthol cigarettes | | | | | | |
| Mendiondo MS, Alexander LA, Crawford T. | Health profile differences for menthol and nonmenthol smokers: findings from the National Health Interview Survey. | 2010 | No funding source(s) provided. Authors affiliated with University of Kentucky | Cross-sectional study (2005 National Health Interview Survey and its cancer control supplement) | Current and former smokers 18+ years old | N=12,004 | Overall, current menthol and non-menthol smokers have similar health profiles. |
| Murray RP, Connett JE, Skeans MA, Tashkin DP. | Menthol cigarettes and health risks in Lung Health Study data. | 2007 | Grant HR 46002 from the Division of Lung Disease; National Heart, Lung, and Blood Institute; National Institutes of Health | Randomized Controlled Trial | Adult smokers in a clinical trial of smoking cessation and ipratropium in the prevention of chronic obstructive pulmonary disease. | N=5,887 | We conclude that our data contain no evidence that mentholation of cigarettes increases the hazards of smoking. |
| Pletcher MJ, Hulley BJ, Houston T, Kiefe CI, Benowitz N, Sidney S. | Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. | 2006 | Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute | Multi-center U.S. cohort study (CARDIA) | African American and European American smokers aged 18 to 30 years and healthy at the time of enrollment in 1985 | 1544 (non-menthol smokers (n = 563) and menthol smokers (n = 972)) | Menthol and nonmenthol cigarettes seem to be equally harmful per cigarette smoked in terms of atherosclerosis and pulmonary function decline, but menthol cigarettes may be harder to quit smoking. |
| Sidney S, Tekawa IS, Friedman GD, Sadler MC, Tashkin DP. | Mentholated cigarette use and lung cancer. | 1995 | Grants R01 CA 36704 and R35 CA 49761 from the US National Cancer Institute | Cohort | Members of the Northern California Kaiser Permanente Medical Care Program, Oakland (5771 men and 3990 women), aged 30 | N=11,761 | This study suggests that there is an increased risk of lung cancer associated with mentholated cigarette use in male smokers but not in female smokers. |

* Note: these statements are taken directly from articles and may not include all relevant results/conclusions. [Bracketed notes added by FDA]

| Author Name(s) | Article Title | **Year Pub.** | Funded By | Type of Study | Subject Description (Including Special population(s)) | Sample Size (N) | Authors' Results/Conclusion(s) related to Menthol* (excerpted directly from article) |
|---|---|---|---|---|---|---|---|
| | | | | | to 89 years, who underwent a multiphasic health checkup in 1979 through 1985 and reported that they were current cigarette smokers who had smoked for at least 20 years. | | |
| Stellman SD, Chen Y, Muscat JE, Djordjevic MV, Richie JP Jr, Lazarus P, Thompson S, Altorki N, Berwick M, Citron ML, Harlap S, Kaur TB, Neugut AI, Olson S, Travaline JM, Witorsch P, Zhang ZF. | Lung cancer risk in white and black Americans. | 2003 | US Public Health Service grants CA-68384, CA-91401, and CA-17613 | Comparative, case-control | white males, white females, black males, black females | N=1,710 white male and 1,321 white female cases of histologically confirmed lung cancer, 254 black male and 163 black female cases, and 8,151 controls. | Lung cancer risks were similar for whites and blacks with similar smoking habits, except possibly for blacks who were very heavy smokers; this sub-group is unusual in the general population of African American smokers. Explanations of racial disparities in lung cancer risk may need to account for modifying factors including type of cigarette (yield, mentholation), diet, occupation, and host factors such as ability to metabolize mainstream smoke carcinogens. |
| Yeager DS & Krosnick JA. | The validity of self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. | 2010 | No funding source(s) provided. Authors affiliated with Stanford University | Area-probability sample survey | NHANES respondents 20+ years old who participated in 2001–2002, 2003–2004, 2005– 2006, and 2007–2008 surveys | N=4000+ respondents for each wave | These data do not support the claim that a substantial number of adult respondents intentionally under- report nicotine consumption in face-to-face interviews.<br><br>[not menthol specific] |

*Note: these statements are taken directly from articles and may not include all relevant results/conclusions.

References


1. Blot WJ, Cohen SS, Aldrich M, McLaughlin JK, Hargreaves MK, Signorello LB (2011) Lung cancer risk among smokers of menthol cigarettes. Journal of the National Cancer Institute 103:810-6. [Funded by National Cancer Institute]
2. Brooks DR, Palmer JR, Strom BL, Rosenberg L (2003) Menthol cigarettes and risk of lung cancer. American Journal of Epidemiology 158:609-16. [Funded by by National Institutes of Health and by the US Food and Drug Administration]
3. Carpenter CL, Jarvik ME, Morgenstern H, McCarthy WJ, London SJ (1999) Menthol cigarette smoking and lung-cancer risk. Annals of Epidemiology 9:114-20. [Funded by the State of California Tobacco-Related Disease Research Program and the National Institutes of Health; the California Public Health Foundation which is supported by the California Department of Health Services]
4. Etzel CJ, Kachroo S, Liu M, D'Amelio A, Dong Q, Cote ML, Wenzlaff AS, Hong WK, Greisinger AJ, Schwartz AG, Spitz MR (2008) Development and validation of a lung cancer risk prediction model for African-Americans. Cancer Prevention Research (Philadelphia) 1:255-65. [Funded by National Cancer Institute grant K07CA093592; National Cancer Institute grants CA55769, CA123208, CA60691, and CA87895; National Cancer Institute contract N01-PC35745; Flight Attendant Medical Research Institute]
5. Everhart J, Ferketich AK, Browning K et al (2009) Acculturation and misclassification of tobacco use status among Hispanic men and women in the United States. Nicotine and Tobacco Research 11(3): 240-247. [Funding provided by the Sumemr Research Opportunities Program at the Ohio State University].
6. Friedman GD, Sadler M, Tekawa IS, Sidney S (1998) Menthol cigarettes and non-lung smoking related cancers in California, USA. Journal of Epidemiology and Community Health 52:202. [Funded by National Cancer Institute grant R35 CA 49761]
7. Hebert JR, Kabat GC (1988) Menthol cigarettes and esophageal cancer. American Journal of Public Health 78:986-7. [No funding source(s) provided. Authors affiliated with the American Health Foundation]
8. Hebert JR, Kabat GC (1989) Menthol cigarette smoking and oesophageal cancer. International Journal of Epidemiology 18:37-44. [Funded by National Cancer Institute and American Cancer Society]
9. Jöckel K-H, Pohlabeln H, Jahn I (2004) Use of menthol cigarettes and risk of lung cancer. Biometrical Journal 46:33. [No funding source(s) provided. Author affiliated with the Institut fur Medizinishche Informatik]
10. Kabat GC, Hebert JR (1991) Use of menthol cigarettes and lung cancer risk. Cancer Research 51:6510-3. [Funded by National Cancer Institute Program Project Grant CA32617 and Center Grant CAI7613]
11. Kabat GC, Hebert JR (1994) Use of menthol cigarettes and oropharyngeal cancer. Epidemiology 5:183-8. [Funded by National Cancer Institute Program Project Grant CA32617 and Center Grant CAI7613]
12. Lee PN (2011) Systematic review of the epidemiological evidence comparing lung cancer risk in smokers of menthol and unmenthol cigarettes. BMC Pulmonary Medicine 11:18. [Funded by the Lorillard Tobacco Company]

13. Mendiondo MS, Alexander LA, Crawford T (2010) Health profile differences for menthol and nonmenthol smokers: findings from the National Health Interview Survey. Addiction 105(suppl 1):124-40. [No funding source(s) provided. Authors affiliated with University of Kentucky]
14. Murray RP, Connett JE, Skeans MA, Tashkin DP (2007) Menthol cigarettes and health risks in Lung Health Study data. Nicotine & Tobacco Research 9:101-7. [Funding provide by Grant HR 46002 from the Division of Lung Disease; National Heart, Lung, and Blood Institute; National Institutes of Health]
15. Pletcher MJ, Hulley BJ, Houston T, Kiefe CI, Benowitz N, Sidney S (2006) Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Archives of Internal Medicine 166:1915-22. [Funded by Contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095 from the National Heart, Lung, and Blood Institute]
16. Sidney S, Tekawa IS, Friedman GD, Sadler MC, Tashkin DP (1995) Menthol cigarette use and lung cancer. Archives of Internal Medicine 155:727-32. [Funded by Grants R01 CA 36704 and R35 CA 49761 from the US National Cancer Institute]
17. Stellman SD, Chen Y, Muscat JE, Djordjevic MV, Richie JP, Lazarus P, Thompson S, Altorki N, Berwick M, Citron ML, Harlap S, Kaur TB, Neugut AI, Olson S, Travaline JM, Witorsch P, Zhang ZF (2003) Lung cancer risk in white and black Americans. Annals of Epidemiology 13:294-302. [Funded by US Public Health Service grants CA-68384, CA-91401, and CA-17613]
18. Yeager DS & Krosnick JA (2010) The validity of self-reported nicotine product use in the 2001-2008 National Health and Nutrition Examination Survey. Medical Care 48(12): 1128-1132. [No funding source(s) provided. Authors affiliated with Stanford University]

# Communication from Public

**Name:** Campaign for Tobacco -Free Kids
**Date Submitted:** 07/11/2019 11:06 AM
**Council File No:** 18-1104
**Comments for Public Posting:**

# Letters

RESEARCH LETTER

## Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014

Most tobacco use begins during youth and young adulthood.[1] Recent declines in prevalence of cigarette smoking among youth have coincided with increased use of e-cigarettes and hookahs.[2] Although flavors other than menthol are prohibited in cigarettes in the United States,[3] flavored noncigarette tobacco products are widely available and may appeal to youth. We examined flavored tobacco use among a nationally representative sample of US youth.

Supplemental content at jama.com

**Methods |** The Population Assessment of Tobacco and Health (PATH) Study is a household-based, nationally representative, longitudinal cohort study of 45 971 adults and youth (12-17 years) in the United States. We analyzed youth data from wave 1, collected September 2013 through December 2014 (the survey is available in the eAppendix in the Supplement). Among youth within participating households (weighted household screener rate, 54%), 78.4% participated in an audio computer-assisted interview. Nonresponse analysis showed few differences with referent national surveys.[4] Survey weights were adjusted for nonresponse.

Parents and emancipated youth provided written informed consent, whereas youth assented to participate. Further details regarding the study methods are available.[4] The study was conducted by Westat and approved by the Westat institutional review board.

Youth responded to questions about ever and past 30-day use of tobacco products including cigarettes, e-cigarettes, hookahs, cigars (traditional cigars, cigarillos, filtered cigars),

Table 1. Prevalence of Ever and Past 30-Day Use of Tobacco Products, Proportion of Ever Users Reporting That the First Product Used Was Flavored, and Proportion of Past 30-Day Users Reporting Use of a Flavored Product, by Product—Population Assessment of Tobacco and Health Study Youth Respondents Aged 12-17 Years, 2013-2014

| | Ever Product Use | | | | Past 30-d Tobacco Product Use | | | |
|---|---|---|---|---|---|---|---|---|
| | Prevalence of Ever Product Use[a,b] | | Proportion of Ever Users Reporting First Product Used Was Flavored[a,c] | | Prevalence of Past 30-d Product Use[a,d] | | Proportion of Flavored Use Among Past 30-d Youth Tobacco Users[a,e] | |
| Tobacco Product | Unweighted, No. | Weighted, % (95% CI) | Unweighted, No. | Weighted, % (95% CI) | Unweighted, No. | Weighted, % (95% CI) | Unweighted, No. | Weighted, % (95% CI) |
| Any tobacco[f] | 2900 | 21.4 (20.4-22.4) | 2256 | 80.8 (79.1-82.5) | 1152 | 8.5 (7.9-9.1) | 919 | 79.8 (77.3-82.3) |
| Cigarettes | 1838 | 13.4 (12.6-14.2) | 902 | 50.1 (47.1-53.1) | 634 | 4.6 (4.2-5.0) | 383 | 59.5 (55.1-64.0) |
| e-Cigarettes | 1452 | 10.7 (10.0-11.3) | 1154 | 81.0 (78.5-83.5) | 418 | 3.1 (2.7-3.5) | 354 | 85.3 (81.2-89.5) |
| Any cigars[g] | 1048 | 7.6 (7.1-8.2) | 652 | 65.4 (62.4-68.3) | 340 | 2.5 (2.2-2.7) | 245 | 71.7 (65.9-77.4) |
| Hookahs | 1006 | 7.4 (6.8-8.1) | 877 | 88.7 (86.6-90.7) | 226 | 1.7 (1.3-2.0) | 198 | 89.0 (84.8-93.1) |
| Smokeless tobacco (excluding snus) | 574 | 4.4 (3.9-4.8) | 391 | 68.9 (64.7-73.1) | 180 | 1.4 (1.2-1.7) | 146 | 81.0 (75.7-86.2) |
| Snus pouches | 227 | 1.7 (1.4-2.0) | 184 | 81.2 (75.9-86.4) | 64 | 0.5 (0.4-0.6) | 54 | 80.4 (70.5-90.4) |
| Pipes | 259 | 1.9 (1.6-2.1) | 77 | 29.4 (23.2-35.6) | 41 | 0.3 (0.2-0.4)[h] | 14 | NA[h] |

Abbreviation: NA, not available (suppressed).

[a] Individuals whose response was missing or who responded "don't know" were excluded from the denominator.

[b] Defined as ever having used the product, even 1 to 2 puffs or times. Excluded from denominator: n = 141 for any tobacco, n = 20 for cigarettes; n = 21 for e-cigarettes, n = 5 for any cigars, n = 9 for hookahs, n = 120 for smokeless tobacco, n = 120 for snus pouches, and n = 6 for pipes.

[c] Excluded from denominator: n = 107 ever any tobacco users, n = 53 ever cigarette smokers, n = 22 ever e-cigarette users, n = 54 ever any cigar users, n = 14 ever hookah users, n = 9 ever smokeless tobacco users, n = 2 ever snus pouch users, and n = 7 ever pipe tobacco smokers.

[d] Excluded from denominator: n = 74 for any tobacco, n = 18 for cigarettes, n = 30 for e-cigarettes, n = 9 for cigars, n = 7 for hookahs, n = 13 for smokeless tobacco products, n = 2 for snus pouches, and n = 10 for pipes.

[e] Excluded from denominator: n = 1 for cigarettes and n = 1 for cigars.

[f] Represents combination of cigarette, e-cigarette, any cigar, hookah, smokeless tobacco, snus pouch, pipe, bidi, kretek, and dissolvable tobacco product use. Estimates of ever and current use of bidis, kreteks, and dissolvable tobacco products are not presented owing to small sample sizes of product users.

[g] Respondents who indicated ever having used a cigar were asked about use of traditional cigars, cigarillos, and filtered cigars separately. Respondents indicating use of 2 or more types of cigars (traditional, cigarillo, filtered cigars) were asked about the flavor status of each type of cigar separately. Any respondent who reported ever using 2 or more types of cigars had their responses aggregated, so that if any of the first traditional, cigarillo, or filtered cigars they used were flavored, they were included in the estimate of ever cigar users reporting that their first cigar was flavored. Likewise, respondents who reported using 2 or more types of cigars in the past 30 days and reported past 30-day flavored use of any cigar were included in the estimate of flavored cigar use among past 30-day cigar users.

[h] Past 30-day use estimates for pipes are flagged because of unstable estimates (relative standard error >30%); proportion of flavored product use among past 30-day pipe users are suppressed because of small denominators (<50).

Table 2. Leading Reasons for Noncigarette Tobacco Product Use Among Past 30-Day Tobacco Users, by Product—Population Assessment of Tobacco and Health Study Youth Respondents Aged 12-17 Years, 2013-2014[a,b]

| | % (95% CI) | | | | |
|---|---|---|---|---|---|
| Reasons for Use | e-Cigarettes (n = 418)[c] | Any Cigars (n = 340)[c,d] | Hookahs (n = 226)[c] | Smokeless Tobacco (n = 180)[c] | Snus Pouches (n = 64)[c] |
| I use [product] because they come in flavors I like | 81.5 (77.9-85.0) | 73.8 (68.2-79.4) | 78.9 (73.4-84.3) | 69.3 (62.6-76.0) | 67.2 (55.7-78.6) |
| I use [product] because they are affordable | 47.8 (42.9-52.6) | 58.2 (52.7-63.6) | 43.7 (36.5-51.0) | 60.6 (52.6-68.6) | 45.5 (32.1-58.8) |
| I use [product] because I can smoke/use them at times when or in places where smoking cigarettes isn't allowed | 58.9 (54.1-63.7) | 10.9 (7.1-14.8) | 30.8 (24.1-37.5) | 69.7 (63.3-76.0) | 70.7 (58.7-82.7) |
| I use [product] because I like socializing while using them | 40.3 (34.9-45.8) | 57.0 (51.7-62.4) | 79.6 (74.6-84.5) | NA | NA |
| I use [product] because it doesn't bother non-tobacco users | 53.9 (48.1-59.8) | NA | NA | 47.7 (40.4-55.0) | 50.4 (39.7-61.2) |
| I use [product] because they might be less harmful to me than cigarettes | 79.1 (75.2-83.0) | 29.9 (25.3-34.5) | 60.6 (53.9-67.3) | 51.4 (44.3-58.4) | 36.9 (24.3-49.6) |
| I use [product] because they might be less harmful to people around me than cigarettes | 78.1 (74.3-81.8) | NA | NA | 68.3 (62.1-74.6) | 51.4 (38.7-64.2) |
| I use [product] because they don't smell | 58.7 (54.2-63.2) | NA | NA | 33.3 (27.4-39.1) | 34.2 (22.1-46.4) |
| I use [product] because they help people to quit smoking cigarettes | 59.5 (54.6-64.5) | 9.9 (6.6-13.2) | 24.2 (18.1-30.2) | 26.8 (21.2-32.5) | 25.1 (15.1-35.1) |
| I use [product] because people who are important to me use them | 34.9 (30.6-39.2) | 28.4 (23.5-33.2) | 35.9 (30.3-41.6) | 40.7 (32.9-48.6) | 28.8 (17.8-39.7) |
| I use [product] because people in the media or other public figures use them | 36.1 (31.5-40.7) | 30.7 (26.1-35.4) | 28.8 (22.7-35.0) | 27.4 (20.8-34.1) | 23.8 (13.2-34.5) |

Abbreviation: NA, not asked.

[a] Past 30-day noncigarette tobacco users were asked to indicate (yes/no) whether particular reasons applied to their use of each specific product. A set of 14 items were asked of e-cigarette, smokeless tobacco, snus pouch, and dissolvable tobacco users; 10 were asked of cigar and hookah smokers; and a set of 9 were asked of pipe smokers and users of bidis and kreteks. Items can be accessed on the PATH Youth Baseline Questionnaire available in the eAppendix in the Supplement.

[b] Individuals whose response was missing or responded "don't know" to whether they used products in the past 30 days were excluded from the denominator, including n = 30 for e-cigarettes, n = 9 for cigars, n = 7 for hookahs, n = 13 for smokeless tobacco, and n = 2 for snus pouches. Estimates for pipe, dissolvable tobacco, bidi, and kretek users are not presented owing to small denominators of past 30-day users (n <50). Cited sample sizes reflect unweighted Ns.

[c] Past 30-day users whose response was missing or who responded "don't know" to any item regarding reasons for use were excluded from the denominator (range of missing for each item, by product: n = 0-5 for cigars, n = 0-4 for e-cigarettes and hookahs, n = 0-3 for smokeless tobacco, and n = 0-1 for snus pouches).

[d] Questions regarding reasons for use were asked separately for past 30-day use of traditional cigar, cigarillo, and filtered cigar. Any respondents reporting past 30-day use of 2 or more types of cigars were asked to report on reasons for use for each type of cigar separately. Responses were aggregated so that if the reason was endorsed for any of the types of cigars, it was counted overall as a positive response.

pipe tobacco, all types of smokeless tobacco, dissolvable tobacco, bidis, and kreteks. For each product ever used, youth endorsed whether the first product they used was flavored (eg, "Was the first e-cigarette you used flavored to taste like menthol, mint, clove, spice, candy, fruit, chocolate, alcohol [such as wine or cognac], or other sweets?"). Users of noncigarette products reported any past 30-day use of a flavored product. Past 30-day noncigarette tobacco users also reported reasons for product use, including "(It) comes in flavors I like," for each product. Past 30-day cigarette smokers reported smoking cigarettes flavored to taste like menthol or mint.

We used SAS version 9.3 (SAS Institute Inc) survey procedures to account for weighting and calculated proportions with 95% confidence intervals for all measures. Estimates from denominators of fewer than 50 users are suppressed; estimates with relative standard errors greater than 30% are flagged.

**Results** | Of the 13 651 youth enrolled and included in this analysis, 51.3% were male, 54.5% non-Hispanic white, 13.7% non-Hispanic black, and 22.5% Hispanic. Mean respondent age was 14.5 (SD, 0.02) years. **Table 1** summarizes ever and past 30-day use of flavored tobacco products. The majority of youth ever-users reported that the first product they had used was flavored, including 88.7% of ever hookah users, 81.0% of ever e-cigarette users, 65.4% of ever users of any cigar type, and 50.1% of ever cigarette smokers. For past 30-day youth tobacco use, the overall proportion of flavored product use was 79.8% (95% CI, 77.3%-82.3%) among users of any product and 89.0% among hookah users, 85.3% among e-cigarette users, 71.7% among users of any cigar type, and 59.5% among cigarette smokers.

**Table 2** presents leading reasons for use among past 30-day noncigarette tobacco users. Youth consistently reported product flavoring as a reason for use across all product types, including e-cigarettes (81.5%), hookahs (78.9%), cigars (73.8%), smokeless tobacco (69.3%), and snus pouches (67.2%).

**Discussion** | Among a survey of youth aged 12 to 17 years, the majority who self-reported ever experimenting with tobacco started with a flavored product, and most current youth tobacco users reported use of flavored products. This study extends a recent national report[5] on youth use of flavored tobacco products by examining first use of flavored product among ever users by products and flavorings as a reason for noncigarette tobacco use. Consistent with national school-based estimates,[5] this study confirms widespread appeal of flavored products among youth tobacco users. In addition to continued proven tobacco control and prevention strategies, efforts to decrease use of flavored tobacco products among youth should be considered.[1]

Study limitations include potential difficulty with recall because youth often experiment with many products. This cross-sectional analysis does not allow direct estimation of flavoring's role in initiation of tobacco use among youth. In addition, there are mode differences in household- vs school-based youth tobacco surveys.[6] Data from future PATH Study waves can provide information on tobacco use trajectories following experimentation with flavored compared with nonflavored products.

**Bridget K. Ambrose, PhD, MPH**
**Hannah R. Day, PhD**
**Brian Rostron, PhD**
**Kevin P. Conway, PhD**
**Nicolette Borek, PhD**
**Andrew Hyland, PhD**
**Andrea C. Villanti, PhD, MPH**

**Author Affiliations:** Center for Tobacco Products, US Food and Drug Administration, Silver Spring, Maryland (Ambrose, Day, Rostron, Borek); Division of Epidemiology, Services, and Prevention Research, National Institute on Drug Abuse, Bethesda, Maryland (Conway); Department of Health Behavior, Roswell Park Cancer Institute, Buffalo, New York (Hyland); Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, DC (Villanti).

**Corresponding Author:** Bridget K. Ambrose, PhD, MPH, Office of Science, Center for Tobacco Products, US Food and Drug Administration, 10903 New Hampshire Ave, Bldg 75, Room 4432, Silver Spring, MD, 20993 (bridget.ambrose@fda.hhs.gov).

**Published Online:** October 26, 2015. doi:10.1001/jama.2015.13802.

**Author Contributions:** Drs Ambrose and Day had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
*Study concept and design:* Ambrose, Conway, Borek, Hyland, Villanti.
*Acquisition, analysis, or interpretation of data:* All authors.
*Drafting of the manuscript:* Ambrose.
*Critical revision of the manuscript for important intellectual content:* All authors.
*Statistical analysis:* Day, Rostron.
*Administrative, technical or material support:* Ambrose, Borek, Villanti.
*Study supervision:* Conway, Borek, Hyland.

**Conflict of Interest Disclosures:** The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

**Funding/Support:** Funded by the National Institute on Drug Abuse (NIDA), National Institutes of Health, and the US Food and Drug Administration (FDA), Department of Health and Human Services, under contract HHSN271201100027C.

**Role of the Funders/Sponsors:** Staff from the NIDA and the FDA contributed to the design and conduct of the study; management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and the decision to submit the manuscript for publication. The NIDA and the FDA were not directly involved in the collection of study data.

**Disclaimer:** The views and opinions expressed in this article are those of the authors and do not necessarily represent the views, official policy, or position of the US Department of Health and Human Services or any of its affiliated institutions or agencies.

**Additional Contributions:** We thank David Maklan, PhD, and Charles Carusi, PhD, from Westat Inc for contributions to study design and supervision, as well as data acquisition. We also thank Kristie Taylor, PhD, from Westat Inc for contributions to the study design and analytic support. Drs Maklan, Carusi, and Taylor received compensation for their contributions to the PATH Study.

**1**. US Department of Health and Human Services. *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General.* Atlanta, GA: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2012.

**2**. Arrazola RA, Singh T, Corey CG, et al; Centers for Disease Control and Prevention (CDC). Tobacco use among middle and high school students—United States, 2011-2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(14):381-385.

**3**. Family Smoking Prevention and Tobacco Control Act, Pub L No. 111-31, 123 Stat 1776 (2009).

**4**. US Office of Management and Budget. PATH Study Interim Report. http://www.reginfo.gov/public/do/PRAViewDocument?ref_nbr=201506-0925-002. Accessed October 7, 2015.

**5**. Corey CG, Ambrose BK, Apelberg BJ, King BA. Flavored tobacco product use among middle and high school students—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(38):1066-1070.

**6**. Biglan M, Gilpin EA, Rohrbach LA, Pierce JP. Is there a simple correction factor for comparing adolescent tobacco-use estimates from school- and home-based surveys? *Nicotine Tob Res*. 2004;6(3):427-437.

# Communication from Public

**Name:** Campaign for Tobacco-Free Kids
**Date Submitted:** 07/11/2019 11:07 AM
**Council File No:** 18-1104
**Comments for Public Posting:**

TC Online First, published on October 20, 2016 as 10.1136/tobaccocontrol-2016-053329


# Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014

Andrea C Villanti,[1,2] Paul D Mowery,[3] Cristine D Delnevo,[4,5] Raymond S Niaura,[1,2,6] David B Abrams,[1,2,6] Gary A Giovino[7]

▸ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/tobaccocontrol-2016-053329).

[1]The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, DC, USA
[2]Department of Health, Behavior and Society, The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
[3]Biostatistics, Inc, Atlanta, Georgia, USA
[4]Center for Tobacco Studies, School of Public Health, Rutgers, the State University, New Brunswick, New Jersey, USA
[5]Cancer Institute of New Jersey, Rutgers, the State University, New Brunswick, New Jersey, USA
[6]Department of Oncology, Georgetown University Medical Center, Lombardi Comprehensive Cancer Center, Washington, DC, USA
[7]Department of Community Health and Health Behavior, School of Public Health and Health Professions, University at Buffalo, The State University of New York, Buffalo, New York, USA

**Correspondence to**
Dr Andrea C Villanti, Schroeder Institute for Tobacco Research and Policy at Truth Initiative, 900 G Street NW, Fourth Floor, Washington DC 20001, USA; avillanti@truthinitiative.org

Received 20 July 2016
Accepted 9 September 2016

**To cite:** Villanti AC, Mowery PD, Delnevo CD, *et al*. *Tob Control* Published Online First: [*please include* Day Month Year] doi:10.1136/tobaccocontrol-2016-053329

## ABSTRACT

**Introduction** National data from 2004 to 2010 showed that despite decreases in non-menthol cigarette use prevalence, menthol cigarette use prevalence remained constant in adolescents and adults and increased in young adults. The purpose of the current study was to extend these analyses through 2014.
**Methods** We estimated the prevalence of menthol cigarette smoking in the USA during 2004–2014 using annual cross-sectional data on persons aged ≥12 years from the National Survey on Drug Use and Health. Self-reported menthol status for selected brands that were either exclusively menthol or non-menthol were adjusted based on retail sales data. Data were weighted to provide national estimates.
**Results** Although overall smoking prevalence has decreased, the proportion of past 30-day cigarette smokers using menthol cigarettes was higher (39%) in 2012–2014 compared to 2008–2010 (35%). Youth smokers remain the most likely group to use menthol cigarettes compared to all other age groups. Menthol cigarette prevalence has increased in white, Asian and Hispanic smokers since 2010. Menthol cigarette prevalence exceeded non-menthol cigarette prevalence in youth and young adult smokers in 2014. Among smokers, menthol cigarette use was positively correlated with co-use of cigars. Menthol cigarette and smokeless tobacco co-use also increased from 2004 to 2014.
**Conclusions** The youngest smokers are most likely to use menthol cigarettes. Among smokers, increases in overall menthol cigarette use and menthol cigarette use in whites, Asians and Hispanics since 2010 are of concern. There is tremendous urgency to limit the impact of menthol cigarettes on public health, particularly the health of youth and young adults.

## INTRODUCTION

National data from 2004 to 2010 showed that despite decreases in non-menthol cigarette use prevalence, menthol cigarette use prevalence remained constant in adolescents and adults and increased in young adults.[1] This was consistent with trends in non-menthol and menthol cigarettes in the USA over this time period.[2] While population data have shown significant declines in cigarette use among youth[3] and adults[4] in recent years, findings from the 2013–2014 wave of the Population Assessment of Tobacco and Health (PATH) Study indicate that 59.5% of youth smokers report using menthol cigarettes in the past 30 days.[5]

Evidence syntheses highlight greater experimentation with cigarettes and nicotine dependence among youth menthol cigarette smokers compared to non-menthol cigarette smokers.[6–8] Studies documenting the differential impact of menthol cigarettes (vs non-menthol cigarettes) on subsequent smoking outcomes among youth and young adults highlight the role of menthol cigarettes in facilitating increased smoking and progression to regular smoking in youth and young adults.[9 10] Recent studies have also documented the high proportion of polytobacco use in youth[11] and young adults,[12 13] though few studies have examined the relationship between menthol cigarette use and other tobacco use.

The 2009 Family Smoking Prevention and Tobacco Control Act required the US Food and Drug Administration (FDA) to ban fruit, candy and clove characterising flavours in cigarettes in September 2009 but did not extend that ban to menthol characterising flavours in cigarettes. FDA's recently issued deeming regulations also failed to propose a ban on menthol in cigarettes or other tobacco products. Since then, several countries have passed bans on menthol cigarettes, including the European Union, and many have implementation dates in 2020.[14] Local action has occurred more quickly with implementation of menthol cigarette sales bans in several Canadian provinces in 2015 and 2016[14] and the city of Chicago's 2014 ban on the sale of flavoured products (including menthol cigarettes) within 500 feet of schools.[15] The tobacco marketplace continues to evolve and the largest US cigarette manufacturers have renewed efforts to increase menthol's market share in their portfolios.[16 17] The purpose of this study was to extend our trend analyses through 2014, determine whether there were differences in the distribution of menthol cigarette users from 2008–2010 to 2012–2014 and examine correlations between menthol cigarette use and other tobacco product use over time.

## METHODS

### National Survey on Drug Use and Health

The National Survey on Drug Use and Health (NSDUH) is a nationally representative survey that assesses tobacco, alcohol and drug use behaviours in the US civilian, non-institutionalised population. Respondents are aged 12 years and older. NSDUH respondents were selected using a multistage probability sample. Respondents include persons living in households in addition to residents of non-institutional group quarters, such as college students living in dormitories, civilians residing on military bases and persons living in group homes, shelters and rooming houses. The sample excludes members of the active-duty military and individuals in institutional group quarters. Racial/ethnic minorities and persons aged 12–25 years were oversampled.

Cross-sectional surveys were administered annually from 2004 to 2014. Most interviews were conducted in the respondents' homes by trained interviewers. To increase measurement accuracy, drug use questions—including tobacco questions—were administered by audio computer-assisted self-interviews (A-CASI). The overall response rate from 2004 to 2014 ranged from 58.3% to 70.0%.

## Measures

Current cigarette smoking in the NSDUH was assessed by asking respondents who had ever smoked whether they had smoked part or all of a cigarette in the previous 30 days. Those who responded affirmatively were subsequently asked to report the brand of cigarettes they smoked most often. They were able to select and verify their usual brand from 2 lists with a total of 57 (60 in 2004) brand names that were presented on-screen. Once respondents selected and verified one of the brands on the screen, they were subsequently asked, "Were the <CIGFILL> cigarettes you smoked during the past 30 days menthol?" (note: '<CIGFILL>' was replaced by the computer programme with the name of the brand the respondent had previously reported and verified as having smoked most often). In 2014, ~94% of smokers selected a brand from the lists offered. The remaining 6% were asked, "Were the cigarettes you smoked during the past 30 days menthol?"

Owing to concerns about misclassification, especially among adolescents, we examined Nielsen market scanner data to classify major brands for which at least 99% of sales were menthol or non-menthol. Incorporating a method of Hersey *et al*,[18] if a respondent reported usually smoking Kool and also reported on the menthol question that the usual brand was non-menthol, the respondent's response to the menthol variable question was recoded as menthol. A similar adjustment was made for exclusively non-menthol brands.

Analyses used imputed values for age, gender, race and income available in the data sets. To aid comparison with our previous analyses,[1] age was categorised as 12–15, 16–17, 18–21, 22–25, 26–34 and 35 years and older. For estimating trends in menthol prevalence over time, age categories were collapsed into three groups: 12–17, 18–25 and 26 years and older. Race/ethnicity was grouped into Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, non-Hispanic more than one race and non-Hispanic other. Total family income was separated into three groups: <US$10 000–US $29 999, US$30 000—$74 999 and US$75 000 or more. Number of days smoked per month among past 30-day smokers was categorised as 1–5, 6–29 and 30 days. Past 30-day cigar use was ascertained by the question: "During the past 30 days, that is, since [DATEFILL], on how many days did you smoke part or all of a cigar?" Past 30-day use of snuff was measured by the item: "During the past 30 days, that is, since [DATEFILL], on how many days did you use snuff?" Similar item wording was used to measure past 30-day use of chewing tobacco: "During the past 30 days, that is, since [DATEFILL], on how many days did you use chewing tobacco?" We combined use of snuff and/or chewing tobacco into one variable measuring past 30-day use of smokeless tobacco. Data were missing for fewer than 2% on tobacco use items across all NSDUH waves.

## Statistical analyses

Three types of analyses were carried out. For assessing changes in use of menthol cigarettes between 2008–2010 and 2012–2014, we duplicated table 1 in Giovino *et al*.[1] For this phase of the analysis, NSDUH cross-sectional surveys administered annually from 2008 to 2010 were combined for analysis, as were annual surveys conducted from 2012 to 2014. Brand choices for 2008–2010 respondents were adjusted for 100% menthol based on 2012–2014 sales data. This provided comparisons

**Table 1** Prevalence (%) of menthol cigarette use among past 30-day smokers, by age and gender, race/ethnicity, household income and the number of days smoked/month in the USA, 2008-2010 and 2012–2014

| | 2008–2010 | | | | | | 2012–2014 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All Ages | 12–17 | 18–25 | 26–34 | 35–49 | 50+ | All Ages | 12–17 | 18–25 | 26–34 | 35–49 | 50+ |
| Overall | 34.7 | 52.5 | 43.6 | 34.6 | 30.3 | 30.6 | **38.8** | 53.9 | **50.0** | **43.9** | **32.3** | 32.9 |
| Gender | | | | | | | | | | | | |
| Male | 30.9 | 49.8 | 40.6 | 32.5 | 24.9 | 25.6 | **34.8** | 50.8 | **45.9** | **39.8** | **29.2** | 26.7 |
| Female | 39.1 | 55.5 | 47.4 | 37.3 | 36.3 | 35.7 | **43.5** | 57.6 | **55.9** | **49.3** | 35.9 | 39.1 |
| Race/Ethnicity | | | | | | | | | | | | |
| Non-Hispanic white | 25.6 | 49.5 | 36.1 | 23.6 | 20.0 | 22.5 | **28.9** | 51.6 | **41.7** | **33.4** | 20.9 | 24.0 |
| Non-Hispanic black | 86.0 | 74.2 | 85.7 | 91.3 | 89.0 | 80.4 | 84.6 | 71.3 | 84.3 | 90.5 | 87.2 | 79.8 |
| Non-Hispanic other | 45.1 | 56.0 | 56.1 | 38.7 | 48.5 | 31.6 | 46.7 | 52.6 | 54.4 | 51.6 | 41.9 | 41.8 |
| Non-Hispanic Asian | 30.3 | 58.5 | 48.1 | 27.0 | 24.9 | 17.0 | **38.0** | **39.5** | 54.3 | **42.5** | 25.2 | **27.4** |
| Non-Hispanic more than one race | 41.1 | 54.8 | 50.2 | 30.4 | 47.5 | 33.7 | 38.1 | 57.4 | 57.5 | **52.5** | **30.0** | 23.7 |
| Hispanic | 37.1 | 53.3 | 45.4 | 40.0 | 31.2 | 26.8 | **46.9** | 56.7 | **57.5** | **51.2** | **41.7** | 33.0 |
| Household income | | | | | | | | | | | | |
| <US$10 000 (including loss)–US$29 999 | 38.6 | 53.1 | 43.8 | 42.4 | 36.7 | 32.1 | **43.7** | 54.3 | **50.8** | **51.0** | 39.2 | **37.0** |
| US$30 000–US$74 999 | 33.2 | 53.3 | 43.4 | 32.8 | 27.9 | 30.2 | **37.2** | 57.0 | **49.9** | **42.1** | 30.7 | 30.7 |
| US$75 000 or more | 30.5 | 50.9 | 43.3 | 24.8 | 25.8 | 28.4 | 32.1 | 48.7 | **48.2** | **33.8** | 24.9 | 28.3 |
| Number of days smoked per month (days) | | | | | | | | | | | | |
| 1–5 | 37.7 | 51.2 | 40.8 | 32.4 | 33.4 | 39.1 | **41.4** | 55.3 | **50.0** | **42.3** | 34.3 | 32.3 |
| 6–29 | 40.5 | 55.5 | 45.2 | 37.7 | 36.8 | 38.6 | **45.7** | 55.7 | **52.4** | **49.0** | 41.1 | 39.2 |
| 30 | 31.8 | 50.5 | 44.0 | 34.1 | 27.7 | 27.7 | **35.4** | 48.5 | **48.3** | **42.2** | 29.3 | **31.2** |

Source: National Survey on Drug Use and Health. Self-reported menthol status was adjusted if necessary using retail checkout scanner data. Sample size=35 320.
Bolded percentages indicate statistically significant change from 2008–2010 to 2012–2014 (p<0.05).

between time periods in the prevalence of use of menthol cigarettes. Multivariable logistic models were used to estimate odds ratios (ORs) of menthol cigarette use among past 30-day cigarette smokers, adjusted for age, gender, race/ethnicity, income and number of days smoked; listwise deletion was used to handle respondents with item-level missing data.

Next, we estimated time trends in the use prevalence of menthol and non-menthol cigarettes. Annual prevalence estimates for the use of each type of cigarette were calculated for 2004 to 2014. Regression lines were fitted to the prevalence estimates using piecewise linear regression[19] in which the dependent variable was the annual prevalence estimates. Differences in the variances of the annual prevalence estimates were accounted for using weighted regression. Separate lines were fitted for menthol and non-menthol prevalence by age (12–17, 18–25 and 26 years and older). An inflexion point was included that allowed the slopes of the lines to change at year 2010 based on visual examination of the raw data, the last year of our previous analyses and the first full year in which other flavoured cigarettes were no longer on the market. Statistical tests were carried out to assess differences in the slopes of menthol and non-menthol regression lines and, within each type of cigarette, differences in slopes between two time periods: 2004–2010 and 2010–2014.

The third analysis investigated the use of cigars and smokeless tobacco among past 30-day cigarette smokers. Prevalence estimates for past 30-day cigar and smokeless tobacco use were compared for past 30-day menthol and non-menthol cigarette smokers by gender and age. Multivariable logistic models were used to estimate ORs for cigar and smokeless tobacco use between menthol and non-menthol cigarette smokers, adjusted for gender and age. For this analysis, NSDUH annual surveys were combined into three time periods: 2004–2007, 2008–2011 and 2012–2014. Changes over time in the odds of smoking cigars or using smokeless tobacco for menthol cigarette smokers compared with non-menthol cigarette smokers were also assessed. The top brands of cigars and smokeless used by menthol and non-menthol cigarette smokers were identified.

SAS V.9.4 was used for all analyses. The SAS survey procedures took into account NSDUH's complex survey design. Survey weights were used to adjust for different probabilities of selection and for non-response, producing estimates representative of the US population.

## RESULTS

### Change in prevalence of use of menthol cigarettes between 2008–2010 and 2012–2014

Table 1 compares the prevalence of use of menthol cigarettes among past 30-day smokers between two time periods: 2008–2010 and 2012–2014. Overall, the percentage of menthol cigarette smokers increased 4.1 percentage points between 2008–2010 and 2012–2014. Menthol prevalence increased for all age groups. The largest increase (9.3 percentage points) occurred among smokers aged 26–34 years. Youth smokers aged 12–17 years were more likely to use menthol cigarettes than smokers in any other age group in both time periods. This was true for male and female smokers.

By race, black smokers continued to smoke menthol cigarettes at higher rates than smokers of any other race. However, from 2008–2010 to 2012–2014, the prevalence of menthol cigarette use in black smokers declined 1.4 percentage points. This decline in menthol use occurred among black smokers of all ages, ranging from 0.6 percentage points among those ages 50 years and older to 2.9 percentage points among those who were 12–17 years old. In comparison to black smokers, white, Hispanic, Asian and non-Hispanic other races increased use of menthol cigarettes. The largest increase was found among Hispanic smokers. Overall, between 2008–2010 and 2012–2014 the percentage of Hispanic smokers using menthol cigarettes rose 9.8 percentage points. The next largest increase was found for Asian smokers for which the menthol prevalence increased 7.7 percentage points. White smokers also increased the use of menthol cigarettes by 3.4 percentage points between 2008–2010 and 2012–2014. The largest increase was found among white smokers aged 26–34 years where the menthol percentage increased 9.8 percentage points.

### Multivariable analyses

Online supplementary table S1 presents the adjusted odds of menthol cigarette use among past 30-day smokers. Consistent with our earlier analyses, the odds of menthol cigarette use are at least three times higher among the youngest smokers (ages 12–15 and 16–17) compared to smokers aged 35 and above. Female and black smokers remained significantly more likely to smoke menthol cigarettes than male and white smokers, respectively. Higher use of menthol cigarette use in women held for blacks and whites when examined separately, with the female/male difference in menthol prevalence being more pronounced for whites (OR=1.8; $p<0.01$) than for blacks (OR=1.4; $p<0.05$; see online supplementary table S2). There were no differences in the odds of menthol cigarette use among smokers by income, but menthol cigarette smokers were significantly less likely to smoke infrequently (1–5 days per month) than non-menthol cigarette smokers (OR=0.90; $p<0.05$).

### Trends in the prevalence of use of menthol compared with non-menthol cigarette use 2004–2014

Figure 1A–C and tables 2 and 3 show estimated time trends in the prevalence of using menthol and non-menthol cigarettes in the full sample from 2004 to 2014 using piecewise linear regression. Two straight lines with intersection at year 2010 were fitted to each time series for menthol and non-menthol cigarette prevalence. Separate lines were estimated for each age group. Note that the denominator here is all individuals in the relevant age groups, not just cigarette smokers. The fit of the piecewise linear regression models was adequate for menthol and non-menthol trends in all three age groups. Non-menthol prevalence decreased over time for all three age groups and both time periods. The non-menthol prevalence slope decreased most quickly among 18–25 year-olds in the 2004–2010 time period. Menthol prevalence increased among 18–25 year-olds in the first time period (0.5 percentage points per year; $p<0.01$) and among persons aged 26 years and older in the second time period (0.1 percentage points per year; $p<0.05$).

In 2004, 4.9% of youth smoked menthol cigarettes and this prevalence declined to 2.5% in 2014 (figure 1A). The rate of decline was significantly greater after 2010 ($p<0.01$; table 2). Similarly, non-menthol smoking declined among youth, from 6.3% in 2004 to 2.2% in 2014. The slopes of the non-menthol lines were not significantly different between 2004–2010 and 2010–2014. The slopes of the non-menthol and menthol lines were significantly different during 2004–2010 (table 3; $p<0.01$). After 2010, the menthol and non-menthol prevalence lines declined at about the same rates ($p=0.08$). By 2014, smoking rates among youth were low and about the same for menthol and non-menthol cigarette smoking.

Among young adults aged 18–25 years, non-menthol smoking prevalence declined over the study period, from 26.9% in 2004

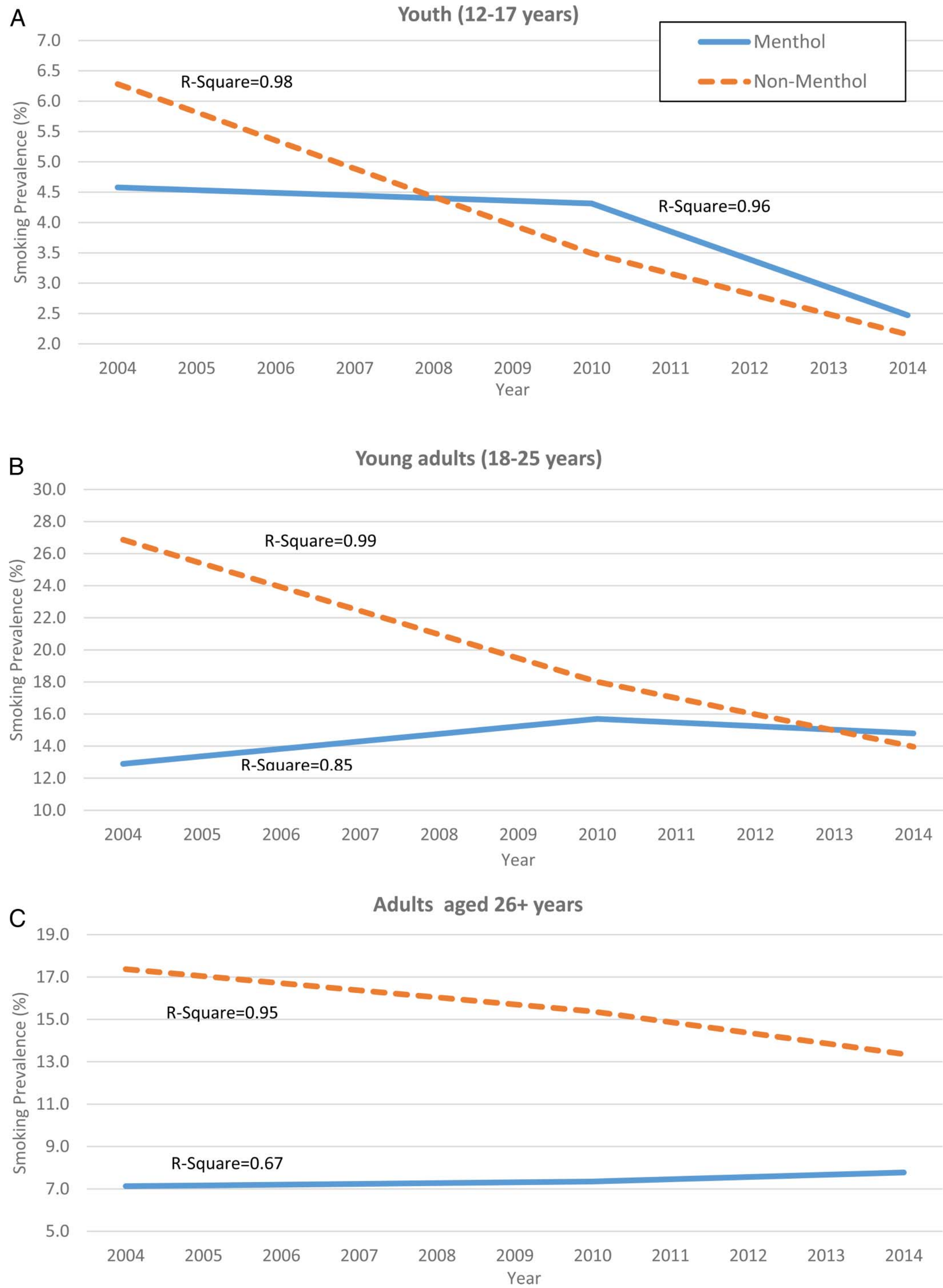



**Figure 1** Trends in the prevalence of menthol and non-menthol cigarette smoking (%) by age in the US population, National Survey on Drug Use and Health, 2004–2014.

to 14.0% in 2014 (figure 1B). From 2004 to 2010, the rate of decline was about 1.5 percentage points per year. After 2010, the decline lessened to about 1 percentage point per year. The rates of decline were statistically significant for both time periods ($p<0.01$), and the change in slopes at 2010 was statistically significant (table 2; $p<0.05$). Menthol smoking prevalence among persons aged 18–25 years increased at a rate of about 0.5 percentage points per year during 2004–2010. After 2010, menthol prevalence declined at about 0.2 percentage points per year. The change in slopes across the two time points was statistically significant ($p<0.01$). The slopes of the non-menthol and menthol lines were significantly different during 2004–2010 (Table 3; $p<0.01$), and they were significantly different after 2010 ($p<0.01$). Although menthol prevalence at the beginning of the time series was lower than non-menthol prevalence, by 2014, menthol prevalence was higher.

Among adults aged 26 and older, menthol prevalence was constant during 2004–2010 and increased slowly (slope=0.1 percentage points per year; $p<0.05$) after 2010 (figure 1C). Non-menthol prevalence decreased over the entire study period though the non-menthol slopes were not significantly different between time periods (table 2). The slopes of the non-menthol

**Table 2** Estimated trends* in the prevalence of cigarette smoking by type of cigarette and age, 2004–2014

| | Prevalence (%)† | | | Estimated slopes‡ 2004–2010 | | 2010–2014 | | Test for difference in slopes 2004–2010 vs 2010–2014 |
|---|---|---|---|---|---|---|---|---|
| | 2004 | 2010 | 2014 | Slope | p Value | Slope | p Value | p Value |
| 12–17 years | | | | | | | | |
| Menthol | 4.6 | 4.3 | 2.5 | −0.04 | 0.28 | **−0.46** | <0.01 | **<0.01** |
| Non-menthol | 6.3 | 3.5 | 2.2 | **−0.46** | <0.01 | **−0.33** | <0.01 | 0.13 |
| 18–25 years | | | | | | | | |
| Menthol | 12.9 | 15.7 | 14.8 | **0.47** | <0.01 | −0.23 | 0.13 | **<0.01** |
| Non-menthol | 26.9 | 18.0 | 14.0 | **−1.48** | <0.01 | **−1.01** | <0.01 | **<0.05** |
| 26+ years | | | | | | | | |
| Menthol | 7.1 | 7.3 | 7.8 | 0.04 | 0.28 | **0.11** | <0.05 | 0.34 |
| Non-menthol | 17.4 | 15.4 | 13.4 | **−0.33** | <0.01 | **−0.50** | <0.01 | 0.26 |

*Time trends estimated using piecewise linear regression with one inflexion point at year 2010.
†Prevalence estimates are predicted from model.
‡Slopes measure the percentage point change in prevalence per year. Bolded slopes indicate statistically significant change between 2004 and 2010 and 2010–2014 (p<0.05).

and menthol lines were significantly different during 2004–2010 and after 2010 (table 3; both p<0.01).

### Past 30-day use of cigars and smokeless tobacco among smokers of menthol cigarettes

Past 30-day use of cigars varied by menthol cigarette use status (table 4). Cigars included big cigars, cigarillos and little cigars, flavoured and non-flavoured. In order to assess changes over time, the total time series was separated into three periods: 2004–2007, 2008–2011 and 2012–2014. Over all three time periods, the prevalence of cigar use among menthol cigarette users remained approximately the same. However, menthol cigarette smokers were more likely to use cigars than non-menthol cigarette smokers. In 2012–2014, ~12.9% of menthol cigarette smokers used cigars compared with 10.6% of non-menthol cigarette smokers. This difference was statistically significant for all three time periods. Higher cigar prevalence was seen for male and female menthol cigarette smokers compared to non-menthol cigarette smokers. Online supplementary table S3 shows the cigar brand smoked most often by past 30-day cigar users, by cigarette menthol smoking. Black & Mild cigars were the most highly used among co-users of cigars and cigarettes, with higher prevalence of use among menthol cigarette smokers than non-menthol cigarette smokers across all time periods. In 2012–2014, 43.6% of menthol cigarette smokers who also used cigars preferred Black & Mild compared to 30.4% of non-menthol cigarette smokers.

Over all three time periods, use of smokeless tobacco increased from 3.3% to 5.0% in past 30-day menthol cigarette smokers and from 6.0% to 6.5% in past 30-day non-menthol cigarettes smokers (table 4). While the odds of using smokeless tobacco remained lower among menthol compared to non-menthol cigarette smokers over time, the prevalence of smokeless use among menthol cigarette smokers approached that seen in non-menthol cigarette smokers in the 2012–2014 period (OR=0.8) compared to the earlier time points (OR=0.5 in 2004–2007 and OR=0.6 in 2008–2011). The higher smokeless tobacco prevalence among non-menthol cigarette smokers was observed for most age groups. Men who smoked non-menthol cigarettes used smokeless tobacco at higher rates than male menthol cigarette smokers. Approximately 6.2% of male menthol cigarette smokers used smokeless tobacco between 2004 and 2007. This prevalence increased to 9.4% in 2012–2014 and was statistically significant (p<0.01). Among male non-menthol cigarette smokers, there was no statistically significant increase in smokeless use between 2004–2007 and 2012–2014. Unlike cigars, there was not a consistent pattern of brand preference for smokeless products (see online supplementary table S4). In 2004–2007, Skoal was the top smokeless brand identified by cigarette smokers and menthol cigarette smokers reported a higher prevalence of Skoal use than non-menthol cigarette smokers. In the latter two time periods, Grizzly became the top brand, with relatively equal proportions of menthol and non-menthol cigarette smokers using this brand.

## DISCUSSION

Findings from this study highlight five key points: first, although overall smoking prevalence has decreased, the prevalence of menthol cigarette use among past 30-day cigarette smokers

**Table 3** Change in slopes of linear regression lines comparing rates of change in menthol and non-menthol smoking prevalence, by time period*

| Age | | Slopes Menthol | Non-menthol | Difference in slopes (Non-menthol—menthol) | p Value for different slopes |
|---|---|---|---|---|---|
| 12–17 | 2004–2010 | −0.04 | −0.46 | −0.42 | **<0.01** |
| 12–17 | 2010–2014 | −0.46 | −0.33 | 0.13 | 0.08 |
| 18–25 | 2004–2010 | 0.47 | −1.48 | −1.94 | **<0.01** |
| 18–25 | 2010–2014 | −0.23 | −1.01 | −0.79 | **<0.01** |
| 26+ | 2004–2010 | 0.04 | −0.33 | −0.37 | **<0.01** |
| 26+ | 2010–2014 | 0.11 | −0.50 | −0.61 | **<0.01** |

*Slopes measure the percentage point change in prevalence per year. Bolded p values indicate statistically significant difference between menthol and non-menthol cigarette smoking during the time period noted (p<0.05).

**Table 4** Past 30-day use (%) of cigars* and smokeless† and non-menthol cigarette smokers, by gender and age, USA, 2004–2014

**Cigars***

| | 2004–2007 (N=57 451) | | | | 2008–2011 (N=53 961) | | | | 2012–2014 (N=35 296) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Menthol smoker | Non-menthol smoker | OR (menthol vs non-menthol‡) | p Value | Menthol smoker | Non-menthol smoker | OR (menthol vs non-menthol‡) | p Value | Menthol smoker | Non-menthol smoker | OR (menthol vs non-menthol‡) | p Value |
| Overall | 13.5 | 11.5 | **1.2** | <0.01 | 13.9 | 10.7 | **1.4** | <0.01 | 12.9 | 10.6 | **1.3** | <0.01 |
| Gender | | | | | | | | | | | | |
| Male | 20.6 | 16.7 | **1.3** | <0.01 | 20.6 | 15.1 | **1.5** | <0.01 | 19.5 | 14.7 | **1.4** | <0.01 |
| Female | 7.0 | 4.8 | **1.5** | <0.01 | 7.9 | 4.9 | **1.7** | <0.01 | 6.8 | 5.0 | **1.4** | <0.01 |
| Age | | | | | | | | | | | | |
| 12–17 | 25.1 | 27.8 | **0.9** | <0.05 | 26.7 | 26.8 | 1.0 | 0.96 | 22.3 | 25.0 | 0.9 | 0.19 |
| 18–25 | 23.3 | 20.6 | **1.2** | <0.01 | 22.1 | 19.7 | **1.2** | <0.01 | 20.1 | 20.1 | 1.0 | 0.99 |
| 26–34 | 15.1 | 12.0 | **1.3** | <0.01 | 15.3 | 10.8 | **1.5** | <0.01 | 14.2 | 12.2 | 1.2 | 0.16 |
| 35–49 | 8.7 | 8.6 | 1.0 | 0.88 | 9.7 | 8.6 | 1.1 | 0.19 | 11.1 | 7.8 | **1.5** | <0.05 |
| 50+ | 5.7 | 5.8 | 1.0 | 0.88 | 6.0 | 6.1 | 1.0 | 0.92 | 5.4 | 7.0 | 0.8 | 0.09 |

**Smokeless tobacco†**

| | 2004–2007 (N=57 514) | | | | 2008–2011 (N=54 016) | | | | 2012–2014 (N=35 320) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Menthol Smoker | Non-menthol smoker | OR (menthol vs non-menthol§) | p Value | Menthol smoker | Non-menthol smoker | OR (menthol vs non-menthol§) | p Value | Menthol smoker | Non-menthol smoker | OR (menthol vs non-menthol§) | p Value |
| Overall | 3.3 | 6.0 | **0.5** | 0.01 | 4.4 | 6.7 | **0.6** | <0.01 | 5.0 | 6.5 | **0.8** | <0.01 |
| Gender | | | | | | | | | | | | |
| Male | 6.2 | 10.0 | **0.6** | 0.01 | 8.2 | 11.3 | **0.7** | <0.01 | 9.4 | 10.8 | **0.9** | <0.05 |
| Female | 0.6 | 0.6 | 0.9 | 0.74 | 0.9 | 0.6 | 1.4 | 0.06 | 0.9 | 0.7 | 1.2 | 0.28 |
| Age | | | | | | | | | | | | |
| 12–17 | 8.2 | 13.8 | **0.6** | <0.01 | 12.1 | 15.0 | **0.8** | <0.01 | 15.7 | 18.7 | 0.8 | 0.13 |
| 18–25 | 5.9 | 10.6 | **0.5** | <0.01 | 8.1 | 12.4 | **0.6** | <0.01 | 8.6 | 13.2 | **0.6** | <0.01 |
| 26–34 | 3.8 | 7.4 | **0.5** | <0.01 | 4.2 | 9.2 | **0.4** | <0.01 | 5.4 | 10.2 | **0.5** | <0.01 |
| 35–49 | 1.7 | 4.5 | **0.4** | <0.01 | 2.5 | 5.5 | **0.4** | <0.01 | 3.7 | 5.1 | **0.7** | <0.05 |
| 50+ | 0.9 | 1.9 | 0.5 | 0.07 | 0.9 | 2.1 | **0.4** | <0.05 | 1.2 | 1.9 | 0.6 | 0.18 |

*Includes big cigars, cigarillos and little cigars.
†Includes chewing tobacco or snuff or both.
‡Estimated OR comparing past 30-day cigar prevalence among menthol cigarette smokers with past 30-day cigar prevalence among non-menthol cigarette smokers. Bolded ORs indicate statistically significant differences between menthol and non-menthol cigarette smokers.
§Estimated OR comparing past 30-day smokeless prevalence among menthol cigarette smokers with past 30-day smokeless prevalence among non-menthol cigarette smokers. Bolded ORs indicate statistically significant differences between menthol and non-menthol cigarette smokers.

increased significantly from 35% in 2008–2010 to 39% in 2012–2014. Second, youth smokers remain the most likely group to use menthol cigarettes compared to all other age groups and there were significant increases in menthol cigarette use among adults ages 18–25, 26–34 and 35–49 between the two time periods. Third, while menthol cigarette prevalence has remained constant among black smokers, it has increased in white, Asian and Hispanic smokers. Fourth, dramatic reductions in youth and adult cigarette smoking in recent years have resulted in decreases in menthol cigarette prevalence in youth and young adults, but those declines have not occurred as rapidly as in non-menthol cigarettes. Menthol cigarette prevalence now exceeds non-menthol cigarette prevalence in youth and young adult smokers. Finally, among past 30-day smokers, menthol cigarette use is positively correlated with co-use of cigars, another harmful combustible product. There has also been an increase in co-use of menthol cigarettes and smokeless tobacco over time. Both are possibly due to the pervasiveness of characterising flavours, including menthol, in these products.[20 21]

Tobacco companies have noted that the menthol segment of the market continues to grow.[16] The 2015 merger of Lorillard and Reynolds American tobacco companies[22] has resulted in a strategic push to accelerate the retail impact of the Newport brand,[17] the top menthol brand in the USA, which has resulted in strong growth of the Newport market share in 2016. Philip Morris USA also continues to expand their menthol distribution, including new brands such as Marlboro Midnight menthol which were rolled out nationally in November 2015.[16]

This study is limited in several ways. First, the definition of menthol use is based on brand preference. We did not estimate the number of menthol and non-menthol cigarettes smoked during a period of time by each smoker. Rather, we estimate the menthol status of the brand smoked most often. Second, we measured prevalence of use and not incidence of initiation. However, prevalence in young people is largely driven by initiation rather than migration, cessation or death. Third, we did not assess sales data prior to 2008. Nevertheless, brands such as Kool, Newport and Salem have long been classified as menthol brands.[23] In the latter years, we were unable to recode Newport as menthol due to the increasing prevalence of Newport non-menthol cigarettes in the market. Finally, our data (table 1) indicate that the use of menthol cigarettes among older smokers was less common than among adolescent and young adult smokers. It is impossible to discern with serial cross-sectional data from 2004 to 2014 whether smokers switched away from menthol cigarettes as they aged. The findings might simply indicate higher rates of menthol use among more recent birth cohorts. Cohort surveys with appropriate age groups like the PATH Study will facilitate the study of switching behaviours.

As in our earlier analyses,[1] younger age, female gender and black race were significant correlates of menthol cigarette use among past 30-day smokers even after controlling for potential confounders. The age gradient in menthol use persists, such that the youngest smokers are the most likely to use menthol. Increases in overall menthol cigarette use and among white, Asian and Hispanic smokers over a 5 year period are of concern. Similarly, dramatic reductions in cigarette smoking at the population level have been reflected in continued declines in non-menthol cigarette use, but mixed changes in menthol cigarette use in the full sample. The data presented in this study highlight that menthol cigarette prevalence has increased among smokers in recent years and that menthol cigarette use now exceeds non-menthol cigarette use in youth and young adults. Given that cigarettes are the dominant product used in the USA and the most harmful, there is tremendous urgency to enact large-scale efforts at FDA and in state and local policy to limit the impact of menthol cigarettes on public health, particularly the health of youth and young adults.

### What this paper adds

The data presented in this study highlight that among smokers, menthol cigarette prevalence has increased overall since 2010, that age remains inversely associated with menthol cigarette use and that there is co-use of menthol cigarettes with other tobacco products likely to be flavoured (ie, cigars and smokeless tobacco). In 2014, past 30-day menthol cigarette use exceeded non-menthol cigarette use in youth and young adults.

**Twitter** Follow Cristine Delnevo at @lozzola

**Contributors** All authors conceived of the study. ACV and PDM wrote the initial draft of the manuscript. PDM conducted the data analysis. ACV, PDM, CDD, RSN, DBA and GAG contributed to the analysis, interpretation of the data and to the review, revision and approval of the final article.

**Funding** This study was funded by Truth Initiative.

**Competing interests** The authors have read and understood Tobacco Control's policy on declaration of interests and declare that they have no competing interests.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES


1. Giovino GA, Villanti AC, Mowery PD, *et al*. Differential trends in cigarette smoking in the USA: is menthol slowing progress? *Tob Control* 2015;24:28–37.
2. Delnevo CD, Villanti AC, Giovino GA. Trends in menthol and non-menthol cigarette consumption in the USA: 2000–2011. *Tob Control* 2014;23(e2):e154–5.
3. Singh T, Arrazola RA, Corey CG, *et al*. Tobacco use among middle and high school students—United States, 2011–2015. *MMWR Morb Mortal Wkly Rep* 2016;65:361–7.
4. Ward BW, Clarke TC, Nugent CN, *et al*. *Early release of selected estimates based on data from the 2015 National Health Interview Survey*. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2016 [updated May 24]. http://www.cdc.gov/nchs/data/nhis/earlyrelease/earlyrelease201605.pdf
5. Ambrose BK, Day HR, Rostron B, *et al*. Flavoured tobacco product use among US youth aged 12–17 years, 2013–2014. *JAMA* 2015;314:1871–3.
6. Tobacco Products Scientific Advisory Committee. *Menthol cigarettes and public health: review of the scientific evidence and recommendations*. Rockville (MD): Center for Tobacco Products, Food and Drug Administration, 2011.
7. US Food and Drug Administration. *Preliminary scientific evaluation of the possible public health effects of menthol versus nonmenthol cigarettes*. Silver Spring (MD): Center for Tobacco Products, Food and Drug Administration, 2013.
8. US Food and Drug Administration. *Reference addendum: preliminary scientific evaluation of the possible public health effects of menthol versus nonmenthol cigarettes*. Silver Spring (MD): Center for Tobacco Products, Food and Drug Administration, 2013.
9. Delnevo CD, Villanti AC, Wackowski OA, *et al*. The influence of menthol, e-cigarettes and other tobacco products on young adults' self-reported changes in past year smoking. *Tob Control* 2016;25:571–4.
10. Nonnemaker J, Hersey J, Homsi G, *et al*. Initiation with menthol cigarettes and youth smoking uptake. *Addiction* 2013;108:171–8.
11. Arrazola RA, Neff LJ, Kennedy SM, *et al*. Tobacco use among middle and high school students—United States, 2013. *MMWR Morb Mortal Wkly Rep* 2014;63:1021–6.
12. Lee YO, Hebert CJ, Nonnemaker JM, *et al*. Multiple tobacco product use among adults in the United States: cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Prev Med* 2014;62C:14–19.
13. Fix BV, O'Connor RJ, Vogl L, *et al*. Patterns and correlates of polytobacco use in the United States over a decade: NSDUH 2002–2011. *Addict Behav* 2014;39:768–81.
14. Tobacco Control Legal Consortium. How other countries regulate flavoured tobacco products 2015. http://publichealthlawcenter.org/sites/default/files/resources/tclc-fs-global-flavoured-regs-2015.pdf
15. City of Chicago. City of Chicago Rules: tobacco—flavoured products 2015 [updated December 15]. http://www.cityofchicago.org/content/dam/city/depts/bacp/tobacco/flavouredtobaccorulesfinal121115.pdf
16. Altria Group's (MO) CEO Marty Barrington on Q4 2015 results—earnings call transcript: seeking alpha; 2016 [updated January 28]. http://seekingalpha.com/article/3843306-altria-groups-mo-ceo-marty-barrington-q4–2015-results-earnings-call-transcript
17. Reynolds American. *RAI investor day: business update*. London, UK: Reynolds American, 2016 [updated May 16]. http://s2.q4cdn.com/129460998/files/doc_presentations/2016/RAI-LONDON-2016-FINAL.pdf.
18. Hersey JC, Nonnemaker JM, Homsi G. Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. *Nicotine Tob Res*. 2010;12:S136–46.
19. Draper NR, Smith H. *Applied regression analysis*. New York: John Wiley and Sons, 1998.
20. Delnevo CD, Giovenco DP, Ambrose BK, *et al*. Preference for flavoured cigar brands among youth, young adults and adults in the USA. *Tob Control* 2015;24:389–94.
21. Delnevo CD, Wackowski OA, Giovenco DP, *et al*. Examining market trends in the United States smokeless tobacco use: 2005–2011. *Tob Control* 2014;23:107–12.
22. Press release: Reynolds American completes acquisition of Lorillard and related divestitures: Reynolds American; 2015 [updated June 15]. http://www.reynoldsamerican.com/About-Us/Press-Releases/Press-Release-Details-/2015/Reynolds-American-completes-acquisition-of-Lorillard-and-related-divestitures/default.aspx
23. Nielsen AC. Sales data from the 2006 and 2009 Food/Drug/Mass cigarette data base and the 2009 C-Store data. Accessed September 2010.

# Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014

Andrea C Villanti, Paul D Mowery, Cristine D Delnevo, Raymond S Niaura, David B Abrams and Gary A Giovino

*Tob Control* published online October 11, 2016

# Communication from Public

**Name:** Campaign for Tobacco-Free Kids
**Date Submitted:** 07/11/2019 11:08 AM
**Council File No:** 18-1104
**Comments for Public Posting:**

# Nicotine arms race: JUUL and the high-nicotine product market

Robert K Jackler, Divya Ramamurthi

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/tobaccocontrol-2018-054796).

Stanford Research into the Impact of Tobacco Advertising, Stanford University, Stanford, California, USA

**Correspondence to**
Professor Robert K Jackler, Department of Otolaryngology, Stanford University, Stanford, CA, 94305, USA; jackler@stanford.edu

Received 15 October 2018
Revised 4 January 2019
Accepted 8 January 2019

Check for updates



**To cite:** Jackler RK, Ramamurthi D. *Tob Control* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/tobaccocontrol-2018-054796

## ABSTRACT

**Objective** Until recently, purveyors of vaping products marketed e-liquids in the 1%–3% range of nicotine concentration with those at 3% described as 'super high' intended for two packs/day smokers. The goal of this study is to evaluate the degree to which JUUL, with its 5% nicotine and 75% US market share, has spurred other e-liquid vendors to raise the nicotine levels of their products.

**Methods** Online search to identify brands offering e-liquid in exceptionally high nicotine concentration (≥5%) and to catalogue the appearance of devices which emulate JUUL.

**Results** JUUL compatible pods (14) and JUUL knock off devices (39) were identified which offer equal or higher nicotine than JUUL. More than 70 e-liquid brands sell high-nicotine products (≥5%) in bulk (≥30 mL) equivalent to >40 cigarette packs. All of these products come in multiple youth appealing sweet and fruity flavours. It was noted that nicotine percentage is inconsistently reported (eg, JUUL is 5% by weight vs 5.9% by volume).

**Conclusions** JUUL has triggered a widespread rush among aerosol purveyors to market e-liquid in unprecedentedly high nicotine concentrations. The rapidly rising popularity of high-nicotine e-liquids threatens to addict a generation of youth. When sold in large quantity bottles (eg, 30 mL) they represent a childhood poisoning risk. Labelling of nicotine concentration in e-liquids needs to be standardised to avoid consumer confusion. The addictiveness and toxicity of these products makes it imperative that regulators act swiftly to enact protective measures.

## INTRODUCTION

Representing a new generation of e-cigarettes, JUUL was introduced in June 2015 with a novel chemistry (nicotine salts) enabling higher concentrations in a limited aerosol plume.

As addiction is central to their business model, the tobacco industry has long sought to enhance the bioavailability of nicotine in their cigarette products.[1] Nicotine comes in different pH-dependent forms. The more alkaline variant, possibly boosted during manufacture of traditional cigarettes, is unprotonated and exists as a free base. Raising pH has been shown to enhance the absorption of aerosolised nicotine by the respiratory system.[2] While free base nicotine is rapidly absorbed in the lungs, it is relatively bitter and has greater harshness sometimes described by smokers as 'throat hit'. In its protonated form, nicotine exists at a lower pH as a salt with a weak acid.

Among numerous possible acids, benzoic has become most popular as a nicotine salt e-liquid. JUUL's original patent stated: '*It has been unexpectedly discovered herein that certain nicotine salt formulations provide satisfaction in an individual superior to that of free base nicotine, and more comparable to the satisfaction in an individual smoking a traditional cigarette. The satisfaction effect is consistent with an efficient transfer of nicotine to the lungs of an individual and a rapid rise of nicotine absorption in the plasma.*'[3] Nicotine salts are not only less harsh, but they are also less bitter, making e-liquids more palatable despite higher nicotine levels. Shortly before the product was introduced to the marketplace, JUUL design engineer Steve Christensen explained the nicotine chemical innovation: '*You won't find raw nicotine in nature. It's mixed in with organic acids and other substances. It's this cocktail that makes nicotine palatable. We figured out how to incorporate some of these organic acids into the juice . . . so we were able to get a very cigarette-like experience.*'[4]

The tobacco in a traditional combustible cigarette has a nicotine concentration of approximately 1.5%–2% (1.5–2 mg/mL).[5] The definition of 'high' and 'super high' nicotine in e-liquid has evolved over recent years. Before 2015, most e-liquids were in the 1%–2% nicotine range and 3% was usually the highest offering described by e-liquid purveyors as intended for two packs a day smokers.[6–8] JUUL introduced 5% nicotine salt solution consisting of 59 mg/mL in 0.7 mL pods. Each pod delivers around 200 puffs and the company claims it releases a similar amount of nicotine to a pack of 20 cigarettes. Study of nicotine absorption biomarkers show JUUL and other high-nicotine pod devices deliver nicotine at substantially higher levels than earlier e-cigarette devices.[9] The high rate of adoption of JUUL by American youth has been described as an epidemic by public health leaders including US Food and Drug Administration (FDA) Commissioner Scott Gottlieb.[10–12] An online survey of JUUL users between the ages of 15 and 24 show that 63% were unaware that the product contained nicotine.[13]

In focusing on JUUL, many critics in the public health community have missed a key issue of major concern. Following JUUL's lead, many purveyors of nicotine salt-based e-liquids offer nicotine concentrations at the 5%, 6% and even 7% level. The goal of this paper is to describe the proliferation of high-concentration salt-based nicotine products, spurred by the financial success of JUUL, and to analyse the potential consequences of the rapidly emerging shift in the aerosol market.

## METHODS

A systematic online search was undertaken, between August and September 2018, to identify devices which emulate JUUL in their design (JUUL-a-likes) and offer high nicotine (≥5%) salt e-liquid. Google search terms included: nicotine salts, high nicotine, nicotine e-liquid, nicotine e-juice, nicotine pod and JUUL compatible pods. A large number of online US vape stores and brand websites were reviewed. A JUUL-a-like was defined as a small pod-based system of similar size to JUUL. Because newly introduced vaping products vigorously strive to get a foothold in the marketplace by promoting their wares online, we believe that the spectrum of products identified comprehensively reflects the market during the study period.

A second category of interest was JUUL compatible pods offered by competitors seeking to carve out a share of the robust demand for JUUL consumables. Also compiled were vendors offering high-nicotine e-liquid in bulk quantity, typically in 30 mL bottles. Data for each brand of pod and bulk e-liquid were compiled for nicotine concentration, volume and flavour offerings. The master data base is available as a supplemental digital file (online supplementary file 1).

In describing e-liquid flavours, two descriptive categories were used. Tobacco flavours included e-liquids named tobacco, original, cigar, Cubano, Carolina bold, golden leaf and classic tobacco. Not included in the tobacco category were sweetened or mint flavoured tobacco descriptors such as candied tobacco, sweet tobacco, ice tobacco, creamy tobacco, tobacco chill, etc. The category of youth-oriented flavours included three groups: (1) desserts such as gummies, cookie, custard, pie, cake, peanut butter, butterscotch, sorbet, taffy, sugar, marshmallow, caramel, mint, Danish, donut, creamsicle, mocha and so on; (2) fruity flavours such as mango, strawberry, raspberry, melon, apple, watermelon, kiwi, peach, grape, pineapple, banana, lime, cherry, blueberry, grapefruit, passion fruit, lemon, tangerine, guava and so on; and (3) conceptual flavour names included whimsical descriptions such as unicorn, God's gift, illuminati, very cool, mtn doo, cryptic blast, antidote, pinkie, dragon and so on.

## RESULTS

### JUUL pods and pods marketed as JUUL compatible

We identified 14 brands marketing 15 JUUL compatible pods, some with higher nicotine concentrations than JUUL (up to 6.5%) (table 1). Most devices were introduced by established e-cigarette companies or startups with a few offerings by major tobacco companies. Most of these pod systems have a capacity between 0.7 mL and 2 mL of e-liquid. Pods fall into two categories: those prefilled with nicotine and flavour and those which can be filled with e-liquid by the consumer. Twelve of these offer closed pods prefilled with e-liquids and three were refillable. Ten of the 12 undersell JUUL's pod price of $4 by as much as $1.50. Most also offer higher capacity pods than JUUL (1 mL vs 0.7 mL). Among the 12 prefilled pods, all offered sweet and fruity flavours but only half carried an unsweetened tobacco variety. JUUL's most popular flavour is mango.[14] Seeking to emulate JUUL's success, all but one vendor of JUUL compatible pods offer mango flavour.

### Small, pod-based vaping devices which emulate JUUL

Thirty-nine small, elongated, pod-based devices were identified: 19 non-refillable, 17 refillable and 3 disposables (table 2, online supplementary table 2). Some resembled JUUL (JUUL-a-likes) while others had a distinctive design. None of these were present on the market prior to the introduction of JUUL. All of their

**Table 1** Nicotine concentration and flavour types among JUUL pods and pods marketed as JUUL compatible (September 2018)

| | Highest nicotine (%) | Tobacco flavours | Youth-oriented flavours | Pod price | Pod volume (mL) |
|---|---|---|---|---|---|
| JUUL pods | | | | | |
| | 5.9 | 2 | 6 | $4.00 | 0.7 |
| JUUL-compatible pods (prefilled, not refillable) | | | | | |
| 4X | 6.5 | 0 | 6 | $3.75 | 1 |
| Eon Smoke | 6 | 1 | 9 | $3.75 | 1 |
| Edge | 6 | 0 | 5 | $4.25 | 0.7 |
| Fuma | 5.5 | 1 | 3 | $4.00 | 1 |
| Viv | 5 | 0 | 6 | $3.75 | 1 |
| ZIIP | 5 | 1 | 5 | $2.75 | 1 |
| Airbender | 5 | 0 | 10 | $3.50 | 1 |
| 3X | 5 | 0 | 4 | $3.00 | 1 |
| Loon | 5 | 1 | 8 | $2.60 | 0.7 |
| Magic Mist | 5 | 1 | 1 | $2.50 | – |
| VQ | 5 | 0 | 4 | $3.50 | 1 |
| Zalt | 5 | 1 | 7 | $3.25 | 1.1 |
| JUUL-compatible pods (fillable) | | | | | |
| J Pod | – | – | – | $3.25 | 1 |
| Blankz! | – | – | – | $3.25 | 1 |
| 4X fillable | – | – | – | $3.00 | 0.7 |

pods exceed JUUL's 0.7mL capacity, with most between 1 mL and 2 mL. All but three of the prefilled varieties carry unsweetened tobacco flavours, but all offer a variety of sweet and fruity flavours. The refillable pod systems allow consumers to choose among the innumerable e-liquid brands (online supplementary file 2). The three disposable JUUL-a-like devices were relatively inexpensive and offer nicotine strengths equivalent or higher than JUUL.

### High-volume, high-nicotine e-liquid products

We identified 71 American e-liquid brands that were found to sell high-nicotine salt e-liquids (≥5%) products in bulk (≥30 mL) (table 3, figure 1). These were characteristically packaged in brightly coloured plastic bottles and came in a wide variety of sweet and fruity flavours (online supplementary table 1).

### Measurement of nicotine concentration

JUUL, unlike most e-liquid brands, measures its nicotine content by weight rather than by volume (eg, JUUL is 5% by weight vs 5.9% by volume). JUUL's method takes into account the higher specific gravities of propylene glycol and glycerin, thus reducing the calculated percent nicotine when compared with many other e-liquid providers. Most e-liquids labelled as 5% nicotine contain 50 mg/mL. This inconsistency in labelling of nicotine concentration is likely to cause confusion among consumers.

## DISCUSSION

Since its introduction in June 2015, JUUL has disrupted the e-cigarette market in several important ways. Among other attributes, JUUL is easily concealable and has a novel nicotine formulation. Our study documents that JUUL's success in the e-cigarette marketplace has spurred a variety of new pod-based products with exceptionally high nicotine. Despite the cleverness of its design features, a historian 20 years from now may

**Table 2** Nicotine concentration and flavour types of small pod devices which emulate JUUL ('JUUL-a-likes') (September 2018)

| | Highest nicotine | Tobacco flavours | Youth-oriented flavours | Pod price | Pod volume (mL) |
|---|---|---|---|---|---|
| Pod devices | | | | | |
| Stig | 6% | 1 | 3 | $6.66 | 1.2 |
| Space Jam The Byrd | 6% | 1 | 3 | $5.00 | 0.85 |
| Bo | 5.5% | 1 | 7 | $6.66 | 1.5 |
| Sol | 5% | 1 | 3 | $5.00 | 2 |
| Phix | 5% | 1 | 7 | $5.00 | 1.5 |
| XFIRE | 5% | 1 | 3 | $4.00 | 0.75 |
| Kwit stick | 5% | 0 | 4 | $5.00 | 1 |
| Stix | 5% | 2 | 3 | $4.50 | 1.7 |
| Zoor | 5% | 0 | 4 | $7.24 | 2 |
| Myle | 5% | 1 | 4 | $4.50 | 0.9 |
| Vaptio C-Flat | 5% | 0 | 6 | $4.00 | 1 |
| Jak Epic | 5% | 1 | 3 | $2.50 | 0.75 |
| Hangsen IQ | 5% | 1 | 2 | $3.66 | 0.90 |
| Baton Vapour | 5% | 1 | 4 | $6.00 | 1 |
| NicoPod | 5% | 1 | 3 | $5.00 | 1.1 |
| Kilo | 4.5% | 1 | 9 | $5.00 | 1.5 |
| Pod Devices of Major Tobacco Company | | | | | |
| Vuse Alto (RJ Reynolds) | 5% | 2 | 2 | $6.75 | 1.8 |
| MyBlu Intense (Imperial) | 4% | 3 | 13 | $5.00 | 1.5 |
| MarkTen Elite (Altria) | 1.8% | 1 | 4 | $4.49 | 1 |
| Disposable JUUL-a-Likes | | | | | |
| Eon Smoke | 7% | 1 | 6 | $20 | 1.3 |
| Teemo | 6% | 1 | 4 | $11.50 | 1.3 |
| Fogg | 5% | 2 | 3 | $18 | – |

**Table 3** Large volume (≥30 mL), high-nicotine (≥5%) salt e-liquid brands sold in bottles in multiple sweet and fruity flavours (September 2018)

| | | |
|---|---|---|
| 13th Floor Elevapors | iQuit Salt | Slush salts |
| Air Factory | Juice Head | Solace |
| Airbender Saltz | Juice Roll UPZ | SUA vapours |
| Alternative Salts | Khali Vapors | Sugoi Vapor |
| Aqua salts | Lix Nic Salts | Superb Salt Nic |
| Back2Back Salts | Lung Hit Salts | SVLT |
| Beard Salts | Might Salts | The Finest Salt Nic |
| BLVk unicorn | Mighty Vapors | Time Bomb Salts |
| Boho Vape | Milk Pop | Vapetasia |
| Bomb Bombz | Minute Man Vape | Vapetasia Salts |
| Brella Salts | Nic Salt | VGOD salt nic |
| Candy King on Salt | Nkd 100 | Xen Smart Vape |
| Clancys | Nujuice | Yami salts |
| Cloud Nurdz Salts | Okami salt | Yogi Salts |
| Dinner Lady salt | Pod Juice | Zoor |
| Foodfighter Salts | Pop Clouds the salt | |
| Fresh Pressed Salts | Premier Nic Salts | |
| Frisco Vapor | Prophet Premium | |
| Fruit freeze salts | Propoganda Salts | |
| Glas Basix | Ripe Vines | |
| Gorilla Warfare Salt | Ruthless Nic Salt | |
| Halo Evo | Salt Factory | |
| Halo Tribeca | Saltbae | |
| Humble salts | Salty Krew | |
| I Love Salts | Salty Man | |
| Infamous salt collection | Salty Podz | |
| INFZN Salts | Saucy Salts | |
| iONIC Nic Salts | Shijin | |

conclude that JUUL's most consequential impact was that it introduced markedly higher nicotine concentrations to the e-cigarette market.

As of September 2018, there were at least 39 JUUL knock off devices on the market. The vast majority of these emulate, and sometimes exceed, JUUL's exceptionally high nicotine levels. Like JUUL, they are also inconspicuous, small enough to easily fit in a pocket or purse, and their purpose as a nicotine delivery system may not be obvious to many casual observers, including parents and teachers.[15] The proliferation of newly introduced JUUL-a-like devices in 2018 would seem to contravene the requirement spelled out in the FDA deeming regulation which requires premarket approval of all newly introduced vaping devices proposed for entry to the market after August 2016.[16 17] In October, 2018 the FDA announced notice of possible enforcement actions against these recently launched devices.[18]

JUUL has been active in opposing the new entries to the market its success inspired. In August 2018, JUUL filed trademark filing against 30 alleged '*counterfeiters*' in the US District Court of Eastern Virginia.[19] In both October and November 2018, JUUL filed complaints to the US International Trade Commission seeking to block the importation of nearly 40 devices which it described as a: '*cascade of copy-cats entering the market*'.[20 21] The company's alleges that the motivation of the newly introduced devices was to exploit JUUL's success: '*Seeing an opportunity to capture some of JLI's (JUUL Labs, Inc.) success with minimal investment, Respondents blatantly emulated the distinctive design of the JUUL system.*' The complaint goes on to allege: '*Respondents market these JLI look-alike devices—often at a fraction of the price of the JUUL system—without the same attention to quality control that JLI employs.*'[20] JUUL is not intended as a means of weaning off of nicotine addiction, but rather has a business model based on ongoing sales of consumables (JUUL pods). In 2015, Ari Atkins, a JUUL engineer, commented: '*We don't think a lot about addiction here because we're not trying to design a cessation product at all.*'[22] This helps to explain the vigour of JUUL's action against counterfeit and copycat pods which enable users to purchase discounted JUUL devices and then refill them with non-JUUL products.

While first-generation cig-a-like devices did not deliver comparable nicotine levels to a cigarette, advanced personal vaporisers, with their larger aerosol volumes, may achieve similar absorption curves to combustible cigarettes.[23–25] The average traditional cigarette contains 8–9 mg of nicotine and delivers approximately 1–1.5 mg of nicotine to the bloodstream.[5] The amount absorbed varies according to how the cigarette is smoked. JUUL states that its pods are equivalent in nicotine delivery to a pack of 20 traditional cigarettes which contains some 160–180 mg of nicotine of which some 20–30 mg are absorbed by the smoker. The absorption of nicotine in JUUL can be compared with cigarettes using the company's data. A JUUL pod contains only a quarter of the nicotine of a cigarette pack (0.7 mL x 59 mg/mL=41.3 mg per pod) implying that its pulmonary absorption of nicotine is some four times that of a combustible cigarette. The difference may be accounted for by nicotine lost in combustible products by side stream smoke, the fraction of nicotine lost into the air from


**Figure 1** Examples of large volume (30 mL), highly concentrated (5%, 5.5%, 5.9%), salt nicotine e-liquids on the market in youth-oriented flavours.

the smouldering tip, as well as nicotine remaining in the butt. In addition, unlike the aerosolised nicotine from e-cigarettes, a portion of the nicotine in tobacco smoke is bound to particulate matter and only the fraction which adheres to the alveoli may be absorbed.[26] The threshold for addiction of a young person has been estimated at 5 mg/day, or about 4–5 traditional cigarettes.[5] A youth would reach the addictive threshold by inhaling the aerosol generated by merely ¼ of a JUUL pod per day.

This study identified over 70 brands offering highly concentrated nicotine e-liquids (≥5%) in quantities 43 times greater (30 mL) than in JUUL (0.7 mL). Actual levels of nicotine in refill bottles may diverge, either higher or lower, from what is listed on the label.[27]

Most bottles were brightly coloured and depicted sweet or fruity flavours (eg, mango, gummy bear). Bulk nicotine may be used either in refilling low volume pods which deliver modest aerosol plumes or in high powered open tank advanced personal vaporisers which expel much larger clouds of aerosol. Some bulk nicotine vendors include a caution against the latter. Although traditionally it has been said that 60 mg of nicotine is sufficient to kill an adult, more contemporary analysis shows that the lethal dose is closer to 500 mg (7 mg/kg).[28] The lethal amount for a 70 kg adult (490 mg) is clearly many times that of a 10 kg 2-year-old (70 mg). A JUUL pod contains 41 mg of nicotine (59 mg/mL x 0.7 mL). This is vastly less than a similarly concentrated 30 mL bottle of nicotine salt e-liquid (1770 mg) which is theoretically potent enough to kill 25 toddlers. While a toddler is unlikely to ingest the e-liquid in a closed pod, small bottles with colourful labels showing sweet or fruity flavours are likely very tempting to children. Deaths have been reported in children following ingestion of earlier generation, much lower nicotine e-liquids.[29] Calls to poison control centres due to childhood nicotine exposure have proliferated since the introduction of e-cigarettes.[30] As nicotine will absorb through intact skin, even contact of a concentrated e-liquid with a child's skin could lead to toxicity.

Another theoretical danger of flavoured bulk nicotine in high concentration is excessive dosing using a high powered tank system. Because of the large volume of aerosol produced, even low levels of nicotine in the e-liquid have been shown to achieve cigarette-like levels of nicotine absorption.[24] JUUL has demonstrated that its low power, low volume, 59 mg/mL nicotine achieved levels similar to a cigarette.[3] Using a similarly concentrated nicotine in a high power, large volume device, which delivers many times the volume of aerosol as JUUL, can theoretically result in deleteriously high levels of nicotine exposure.

High concentration nicotine aerosol may also exacerbate secondhand effects. Czogala and co-workers tested 3 brands of early generations of e-cigarettes with nicotine concentrations of 11, 18 and 19 mg/mL which showed potential exposures on approximately 10% that of combustible cigarettes.[31] While JUUL and its emulators are 3–6 times more concentrated than those tested in this study, their exhaled volume is small. However, when concentrated nicotine e-liquids are used in high powered tank devices, the giant plume of exhaled aerosol could well lead to involuntary exposure to nicotine greater than that emanated by traditional cigarettes.

The proliferation of highly concentrated nicotine e-liquid has lowered the price of addiction. Pricing is a crucial factor in youth adoption as adolescents are notably price sensitive due to their limited discretionary income. The price of a pack of cigarettes is between $6 and $8 in most states and higher in some populous states such as New York ($14). A JUUL pod, which delivers nicotine similar to a pack of cigarettes, has a retail price of $4 and JUUL compatible pods are as low as $2.50. Bulk e-liquid in 30 mL (5% nicotine) bottles average $16–$17. For example, Pod Juice sells "Loops" (picturing fruit loops cereal) with 5.5% salt nicotine in 30 mL bottles for $13.99.[32] Used in a refillable pod device of 0.7 mL (as with JUUL), this is the nicotine equivalent of 40 packs to cigarettes or about 35¢ per cigarette pack's worth of nicotine.

JUUL has portrayed their company as wholly focused on rescuing adult smokers. '*What started as a design challenge has become a mission to impact the lives of adult smokers*' (JUUL Tweet July 12, 2017). The company's 2018 mission statement specifies its goal is to: '*Improve the lives of the world's one billion adult smokers*' (initial appearance on JUUL Twitter feed on April 2, 2018).[33] It is important to acknowledge that pod-based high-nicotine e-cigarettes may well be more effective means of transitioning nicotine addicted smokers from combustible products, a change likely beneficial to their health. Whether ≥5% nicotine devices are more effective in transitioning cigarette smokers than other cessation aids has yet to be established by independent research. The body of data regarding lower nicotine devices suggests low grade evidence that e-cigarettes assist with smoking cessation better than placebo.[34] Others reviewing data for e-cigarettes on the market in 2015 have concluded that e-cigarettes are associated with significantly less quitting among smokers.[35] Compared with high powered tank systems, whose high temperature coils produce potential carcinogens such as formaldehyde, JUUL uses a low power aerosolisation system which may generate fewer deleterious chemicals.[24 36]

In June 2018, JUUL made the bold, and likely unsupported pronouncement on its website that: '*The company's research shows more than one million smokers have already switched to JUUL, and we are working to enable millions more to switch in the coming years through technological innovations.*'[37] In October 2015, JUUL co-founder James Monsees has said; "*We need to be the most educated company, the most diligent, the most well-researched company in vaporization more broadly—not just for the tobacco industry.*"[38] The company has not released data on underage use of JUUL.

## Policy Implications

Discussions among the public health community concerning high concentration nicotine aerosol products focus on the need to develop effective reduced risk tobacco products for adult smokers while simultaneously protecting adolescents from using them as a gateway to nicotine addiction. It is a challenge to formulate an optimal regulatory formula which would simultaneously protect youth from nicotine addiction while encouraging the transition of smokers to safer nicotine delivery systems or, even better, to break their addiction altogether.

Various measures could be considered to achieve both protection of adolescents while maintaining high nicotine for heavy smokers. In 2009, the US Congress banned characterising flavours from traditional cigarettes except for tobacco and menthol.[39] In 2015, the Center for Disease control reported that 7 or 10 students who use tobacco use a flavoured product.[40] Many public health experts advocate regulation banning youth appealing flavours from all nicotine containing e-liquids and allowing only unsweetened tobacco flavour to accompany nicotine. Opponents, primarily from the vaping industry, point to industry sponsored studies which suggest that flavours are important to adult transition from smoke to aerosol.[41 42]

Another regulatory option would be to cap the amount of nicotine permissible in e-cigarettes. JUUL, as it is sold in the USA (59 mg/mL nicotine), would not be permitted in Europe or the UK which have adopted limits of 20 mg/mL nicotine.[43] If the USA adopted this standard, it would almost certainly reduce the tendency of e-cigarettes to act as a gateway to youth nicotine addiction. However, it may also reduce their efficacy in cigarette smoking cessation. As high-nicotine versions may well prove more efficacious in transitioning cigarette smokers to aerosol, one option would be to allow sale of high-nicotine e-liquids only by doctor's prescription.

Another measure to reduce youth nicotine exposure would be to require purveyors of high-nicotine e-liquids to carry zero nicotine versions of their flavours along with the high-nicotine versions. A sizeable price differential, with the zero nicotine version priced less, would enhance appeal to youth who have limited discretionary income. The goals of non-nicotine versions would be subverted if the products were not made equally available in all vending channels (eg, online, retail outlets) and if they did not carry the same age restrictions as the nicotine version. Disadvantages of this approach includes the fact that chronic inhalation of aerosols containing propylene glycol and glycerin together with flavourant chemicals may have adverse health effects.[44] In addition, such an approach would have the potential to encourage youth to initiate smoking behaviour and then potentially transition to nicotine containing products. In addition, zero nicotine products in sweet flavours may encourage wider youth use and thus contribute to the renormalisation of smoking behaviour. However, countering this argument is the reality that JUUL has made vaping pervasive among American youth and that renormalisation among the school age demographic has already occurred.

A limitation of this study is that our online searches, while comprehensive, captured only products promoted online and likely only a fraction of these. Many local vape shops prepare their own high-nicotine formulations, a segment of the market which would have escaped our detection. In addition, the high-nicotine marketplace is expanding at impressive speed and by the time this paper is published many other new products will have entered this nascent market.

There is a clear need to regulate the sale of higher concentration nicotine solutions in larger volumes. Colourful bottles depicting sweet dessert labels with 5, 10, 20 or even 30 mL of highly concentrated nicotine carry an excessive risk of lethal child poisoning. Child-resistant packaging resistant packaging for e-liquids is being enacted by an increasing number of American states, but with inconsistent standards and weak enforcement.[45] While small quantities (eg, ≤1 mL) of concentrated nicotine solutions may be of lower risk when sold in hermetically closed pods, regulators should consider whether or not larger volumes of flavoured high-nicotine liquids should remain allowed on the marketplace unfettered by regulation.

**Contributors** RKJ conceived the project. RKJ and DR collected and analysed the data and prepared the manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

## What this paper adds

- Until recently, most e-cigarette liquids carried 1%–2% nicotine with a few at 3% labelled as 'super high' intended for the 'two packs a day smoker.'
- In 2015, JUUL introduced a 5% (59 mg/mL) pod vaping device with a novel nicotine chemistry (nicotine salts) which improved palatability enabling higher concentrations without undue bitterness.
- Following JUUL's phenomenal success in the marketplace, numerous knock-off devices were introduced which emulated, or even exceeded, JUUL's very high nicotine level.
- All purveyors of high-nicotine e-liquids offer them in sweet and fruity flavours.
- Bulk high-nicotine e-liquids, typically sold in 30 mL bottles, represent a poisoning risk for children.
- Nicotine percentage is inconsistently portrayed on labels.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES

1 Ferris Wayne G, Connolly GN, Henningfield JE. Brand differences of free-base nicotine delivery in cigarette smoke: the view of the tobacco industry documents. *Tob Control* 2006;15:189–98.
2 Burch SG, Gann LP, Olsen KM, *et al*. Effect of pH on nicotine absorption and side effects of aerosolized nicotine. *J Aerosol medicine* 1993;6:45–52.
3 JUUL patent. JUUL patent: Nicotine salt formulations for aerosol devices and methods thereof. 2013 https://patents.google.com/patent/CA2909967A1/en (Accessed 4 Jan 2019).
4 Pierce D. This might just be the first great e-cig Wired magazine. 2015 https://www.wired.com/2015/04/pax-juul-ecig/ (Accessed 4 Jan 2019).
5 Benowitz NL, Henningfield JE. Establishing a nicotine threshold for addiction. The implications for tobacco regulation. *N Engl J Med* 1994;331:123–5.
6 Goniewicz ML, Kuma T, Gawron M, *et al*. Nicotine levels in electronic cigarettes. *Nicotine Tob Res* 2013;15:158–66.
7 Goniewicz ML, Gupta R, Lee YH, *et al*. Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the U.S., Korea, and Poland. *Int J Drug Policy* 2015;26:583–8.
8 High nicotine flavors. Stanford Research into the Impact of Tobacco Advertising. http://tobacco.stanford.edu/highnicotineflavors (Accessed 4 Jan 2019).
9 Goniewicz ML, Boykan R, Messina CR, *et al*. High exposure to nicotine among adolescents who use Juul and other vape pod systems ('pods'). *Tob Control* 2018:tobaccocontrol-2018-054565.
10 U.S. Food and Drug Administration. Statement from FDA commissioner scott Gottlieb, M.D., on new steps to address epidemic of youth e-cigarette use. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620185.htm (Accessed 14 Jan 2019).
11 Rosenbaum E. FDA's nicotine stain: Juul isn't only culprit in teen e-cigarette smoking epidemic. 2018 https://www.cnbc.com/2018/09/22/the-other-key-culprit-in-juuls-teen-e-cig-smoking-epidemic-the-fda.html (Accessed 4 Jan 2019).
12 Tobin B. Back-to-school smoking: Juul Labs e-cigarette sales growth vexes teachers USA Today. 2018 https://www.usatoday.com/story/money/2018/08/16/juul-labs-back-school-teachers-e-cigarettes/917531002/ (Accessed 4 Jan 2019).
13 Willett JG, Bennett M, Hair EC, *et al*. Recognition, use and perceptions of juul among youth and young adults. *Tob Control* 2019;28:tobaccocontrol-2018-054273.
14 Mann J. What JUUL pod is the most popular flavor? Vaping 360. *Published* 2018 http://vaping360.com/juul/juul-pods/ (Accessed 4 Jan 2019).
15 Ramamurthi D, Chau C, Jackler RK. JUUL and other stealth vaporisers: hiding the habit from parents and teachers. *Tob Control* 2018:tobaccocontrol-2018-054455.
16 US Food and Drug Administration. Premarket tobacco product applications for electronic nicotine delivery systems (ENDS). 2016 https://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm499351.htm (Accessed 4 Jan 2019).
17 Food and Drug Administration, HHS. Deeming tobacco products to be subject to the federal food, drug, and cosmetic act, as amended by the family smoking prevention and tobacco control act; restrictions on the sale and distribution of tobacco products and required warning statements for tobacco products. final rule. *Fed Regist* 2016;81:28973–9106.
18 FDA News release. FDA advances investigation into whether more than 40 e-cigarette products are being illegally marketed and outside agency's compliance policy. 2018 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm623256.htm (Accessed 4 Jan 2019).
19 JUUL vs Counterfeiters. Case 1:18-cv-01063-TSE IDD. Filed 08/24/18. 2018 https://www.scribd.com/document/388333709/Juul-vs-Counterfeits#from_embed (Accessed 4 Jan 2019).
20 JUUL Complaint to the US. International trade commission - certain electronic nicotine delivery systems and components thereof. 2018 https://s3.amazonaws.com/juul-prod-us-east-1-juulio/juulio/pdf/2018-10-03-Juul-Labs-Inc-Complaint-337-3346.pdf (Accessed 4 Jan 2019).
21 JUUL Complaint to the US. International trade commission - certain cartridges for electronic nicotine delivery systems and components thereof. 2018 https://newsroom.juul.com/wp-content/uploads/2018/11/2018.11.20-Juul-Labs-Inc.-Complaint.pdf (Accessed 4 Jan 2019).
22 Tiku N. Startup behind the lambo of vaporizers just launched an intelligent e-cigarette the verge. 2015 https://www.theverge.com/2015/4/21/8458629/pax-labs-e-cigarette-juul (Accessed 4 Jan 2019).
23 Hajek P, Przulj D, Phillips A, *et al*. Nicotine delivery to users from cigarettes and from different types of e-cigarettes. *Psychopharmacology* 2017;234:773–9.
24 Wagener TL, Floyd EL, Stepanov I, *et al*. Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tob Control* 2017;26:e23–e28.
25 St Helen G, Havel C, Dempsey DA, *et al*. Nicotine delivery, retention and pharmacokinetics from various electronic cigarettes. *Addiction* 2016;111:535–44.
26 Pankow JF, Tavakoli AD, Luo W, *et al*. Percent free base nicotine in the tobacco smoke particulate matter of selected commercial and reference cigarettes. *Chem Res Toxicol* 2003;16:1014–8.
27 Etter JF, Bugey A. E-cigarette liquids: constancy of content across batches and accuracy of labeling. *Addict Behav* 2017;73:137–43.
28 Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Arch Toxicol* 2014;88:5–7.
29 Chen BC, Bright SB, Trivedi AR, *et al*. Death following intentional ingestion of e-liquid. *Clin Toxicol* 2015;53:914–6.
30 Govindarajan P, Spiller HA, Casavant MJ, *et al*. E-Cigarette and liquid nicotine exposures among young children. *Pediatrics* 2018;141:141:e20173361.
31 Czogala J, Goniewicz ML, Fidelus B, *et al*. Secondhand exposure to vapors from electronic cigarettes. *Nicotine Tob Res* 2014;16:655–62.
32 Loops by Pod Juice. https://www.myvaporstore.com/Loops-by-Pod-Juice-p/pdj-loo.htm (Accessed 1 Feb 2019).
33 JUUL Mission-values. JUUL mission statement. https://www.juul.com/mission-values (Accessed 4 Jan 2019).
34 Hartmann-Boyce J, McRobbie H, Bullen C, *et al*. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2016;9:CD010216.
35 Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med* 2016;4:116–28.
36 Logue JM, Sleiman M, Montesinos VN, *et al*. Emissions from electronic cigarettes: assessing vapers' intake of toxic compounds, secondhand exposures, and the associated health impacts. *Environ Sci Technol* 2017;51:9271–9.
37 JUUL. Announcement on June 14, 2018. https://support.juul.com/learn/read/juul-labs-implements-new-social-media-policy (Accessed 4 Jan 2019).
38 Haar MV. PAX Stays Ahead of the Curve. CSP's exclusive interview with PAX Lab's CEO CSP. 2015 https://www.cspdailynews.com/category-news/tobacco/articles/pax-stays-ahead-curve (Accessed 4 January 2019).
39 H.R.1256. Family smoking prevention and tobacco control act. 2009 https://www.congress.gov/bill/111th-congress/house-bill/1256 (Accessed 4 Jan 2019).
40 Centers for Disease Control and Prevention. 7 in 10 students who currently use tobacco used a flavored product. 2015 http://www.cdc.gov/media/releases/2015/p0930-flavored-tobacco.html (Accessed 4 Jan 2019).
41 Shiffman S, Sembower MA, Pillitteri JL, *et al*. The impact of flavor descriptors on nonsmoking teens' and adult smokers' interest in electronic cigarettes. *Nicotine Tob Res* 2015;17:1255–62.
42 Russell C, McKeganey N, Dickson T, *et al*. Changing patterns of first e-cigarette flavor used and current flavors used by 20,836 adult frequent e-cigarette users in the USA. *Harm Reduct J* 2018;15:15–33.
43 European Union. European Union law on the manufacture, presentation and sale of tobacco and related products. 2014 https://ec.europa.eu/health/sites/health/files/tobacco/docs/dir_201440_en.pdf (Accessed 4 Jan 2019).
44 U.S. Department of Health and Human Services.. Health Effects of E-Cigarette Use Among U.S. Youth and Young Adults. E-cigarette use among youth and young adults. a report of the surgeon general, 2016. https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/pdfs/2016_sgr_entire_report_508.pdf. (Accessed 4 Jan 2019).
45 Frey LT, Tilburg WC. Child-Resistant Packaging for E-Liquid: a review of us state legislation. *Am J Public Health* 2016;106:266–8.

## Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:35 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

LAW ENFORCEMENT ACTION PARTNERSHIP
ADVANCING JUSTICE AND PUBLIC SAFETY SOLUTIONS

121 Mystic Avenue, Suite 9
Medford, Massachusetts 02155
T: (781) 393.6985



Date: March 27th, 2019

Re: Item No. 18-1104 - a proposed strategy to restrict the sale of flavored tobacco products to youth and young adults

Position: Oppose

To: Health, Education, Neighborhoods, Parks, Arts, and River Committee

As a retired veteran sergeant of the Los Angeles Police Department, having spent my entire 20 year career in patrol, I know firsthand police culture. My professional experiences form the basis form my opposition to criminalization of menthol tobacco. This ban would disproportionately affect black and brown folks who are the majority users of menthol tobacco.

A ban on menthol tobacco would create additional opportunities for [some] police officers to exacerbate an already contentious relationship between police and marginalized communities of color under the guise of pretextual stops.

The *LA Times* recently reported more than 90% of drivers pulled over for pretextual stops – which use a minor infraction such as a broken taillight (we can always find something) to pull someone over – by the LAPD's Metro Division have been black or Latino[1].

This abuse has prompted an audit request by Mayor Garcetti of the Inspector General of what has been referred to as "stop and frisk in a car."

Giving officers even more reason to detain and engage on the basis of a menthol tobacco ban would assuredly lead to encounters that are likely to escalate to the unnecessary use of force, arrests, and possibly deadly force.

As a police supervisor I see the potential for abuse and I oppose the ban.

Cheryl Dorsey
Retired Los Angeles Police Department Sergeant
Speaker, Law Enforcement Action Partnership
PO Box 1131, Corona, CA 92878
951.523.8190



[1] https://www.latimes.com/local/lanow/la-me-lapd-crime-trends-20190128-story.html

## Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:36 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

# Baptist Ministers Conference of Los Angeles and Southern California

4269 South Figueroa Street, Los Angeles California 90037

Office of the President


March 27th, 2019

Re: Item No. 18-1104/Proposed strategy to restrict the sale of flavored tobacco products to youth and young adults, including menthol

To: Health, Education, Neighborhoods, Parks, Arts, and River Committee

I am Reverend K. W, Tulloss, president of the Baptist Ministers Conference of Los Angeles and Southern California. I am also president of the Los Angeles Chapter of the National Action Network, created and founded by Reverend Al Sharpton, Since over 80 percent of African Americans who choose to smoke prefer menthol cigarettes, a possible ban on menthol cigarettes will clearly affect African American communities more than other segments of the population in Los Angeles City and County.

The National Action Network does not want people to smoke. We do not want youth to smoke and we want to help people who would like to stop smoking, to quit.

We appreciate the efforts of the Los Angeles County Board of Supervisors to protect the health and well-being of all Angelinos including African Americans. However, a ban on menthol cigarettes in our community would be a repeat of past poor policies. People who choose to consume these products will still do so, regardless of the legality. Youth use of menthol cigarettes is under two percent that is less than non-menthol cigarettes or any other tobacco product. The data from the California Department of Public Health shows that more teens are using non-menthol cigarettes than mentholated cigarettes.

Criminalizing the sale of products people wish to consume only encourages the establishment of an illicit trade to provide these products to consumers who want them. At a time in which we know that interactions between law enforcement and young men and women of color lead all-too-often to tragic results, we should be looking to lessen any negative encounters in our community with law enforcement.

We wholeheartedly support the proven methods of education and treatment to reduce smoking. We urge the Los Angeles City, County Staff and the Board of Supervisors to remove the consideration of a menthol ban from any further discussion about regulating tobacco products in Los Angeles.

Sincerely,

Rev. K. W. Tull

Rev. K.W. Tulloss
President, Baptist Ministers Conferences of Los Angeles & Southern California

# Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:37 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

LAW ENFORCEMENT ACTION PARTNERSHIP
ADVANCING JUSTICE AND PUBLIC SAFETY SOLUTIONS

121 Mystic Avenue, Suite 9
Medford, Massachusetts 02155
T: (781) 393.6985



Date: March 27th, 2019

Re: Item No. 18-1104 - a proposed strategy to restrict the sale of flavored tobacco products to youth and young adults

Position: Oppose

To: Health, Education, Neighborhoods, Parks, Arts, and River Committee

Distinguished members of the Committee,

Thank you for the opportunity to submit testimony. My name is Terry Blevins, and I was a police officer for twelve years and am a representative of the Law Enforcement Action Partnership (LEAP), a nonprofit of law enforcement officers working to improve the criminal justice system. I am also a resident and business owner in Los Angeles.

While I applaud the committee's intention of trying to improve the health of young people, my concern with this legislation is that it's not going to eliminate the market for menthol cigarettes and enforcing this law will waste precious police time and resources, impacting our ability to solve and prevent more serious crimes.

In addition, I fear this will only create more antagonism between police and the communities we're sworn to protect and serve. The more encounters we initiate, the more opportunity there is for hostility, and the less effective we are at our jobs. This is especially true because black people are more likely to smoke menthol cigarettes and we already have strained relations with many people of color. If they don't trust us, they don't work with us to solve crimes, and we can't do our jobs.

Thank you for your time.

Terry Blevins

## Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:38 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

LAW ENFORCEMENT ACTION PARTNERSHIP
ADVANCING JUSTICE AND PUBLIC SAFETY SOLUTIONS

121 Mystic Avenue, Suite 9
Medford, Massachusetts 02155
T: (781) 393.6985



Date: March 27th, 2019

Re: Item No. 18-1104 - a proposed strategy to restrict the sale of flavored tobacco products to youth and young adults

Position: Oppose

To: Health, Education, Neighborhoods, Parks, Arts, and River Committee

As a retired Assistant City Prosecutor and member of the Law Enforcement Action Partnership, I'm very concerned about the unintended consequences of arrests for possessing or selling menthol cigarettes by people of color if this measure were to pass. Increasing enforcement efforts for menthol cigarettes will lead to broader problems with long term negative effects while not stopping kids from smoking.

I support public health efforts, but over the years I've seen too many arrests and prosecutions for minor offenses. This leads to entry into the criminal justice system which opens the door to a discriminatory impact in communities of color. For example, conviction and arrest records can lead to not being able to get a job, student loans, housing, and public benefits.. All of these things can make it more likely that young people unable to support themselves will be forced into crime.

It's time to change aggressive enforcement efforts in the approach to curtail menthol use in teens and adults and instead invest in education and prevention.

Yvette McDowell
Retired Assistant City Prosecutor, City of Pasadena
Speaker, Law Enforcement Action Partnership
715 N Spruce Ave, Rialto, CA 92376
626-483-4151

## Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:39 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

CALIFORNIA STATE CONFERENCE OF THE NATIONAL ASSOCIATION FOR THE ADVANCEMENT OF COLORED PEOPLE

Esquire Plaza, 1215 K Street, 1609 • Sacramento, CA. 95814 • 916.498.1898 • FAX 916.498.1895



# FLOOR ALERT

| | |
|---|---|
| To: | Members of the California State Senate |
| From: | CA-HI State Conference of the NAACP |
| **Re:** | **SB 38 (Hill)** |
| **Position:** | **Oppose** |

On behalf of the California-Hawaii State Conference of the NAACP (CA- HI NAACP), representing 48 branches and 23 youth units statewide, we express our opposition to SB 38 (Hill), which would ban the sale of flavored tobacco products.

The CA – HI NAACP, advocates against punitive laws that disproportionately affect African Americans. SB 38, includes menthol cigarettes, which is the preferred choice of the over 80% of African Americans who choose to smoke cigarettes.

SB 38 would also authorize an enforcing agency to assess civil penalties to retailers for selling flavored tobacco products, but also has unintended consequences for Black communities. A ban on menthol cigarettes would give police another reason to interact negatively on the retail level or with individual citizens for a low-level, non-violent offense. At a time in which we know that interactions between law enforcement and young men and women of color lead to all-too-often tragic results, we should be looking at a way to lessen any negative encounters in our community with law enforcement.

All Californians under the age of 21 are already banned from purchasing any tobacco products. Prohibiting adults from being able to purchase menthol cigarettes, in an effort to address the sale of tobacco products to minors will principally affect African-American smokers. We believe SB 38 creates another racially discriminatory public policy and will lead to increased crime, targeted enforcement, unfair treatment and illegal street sales.

It is for these reasons the CA-HI State Conference of the NAACP opposes SB 38 (Hill), and urges you to vote "NO" on this measure.

# Communication from Public

**Name:**
**Date Submitted:** 07/18/2019 03:39 PM
**Council File No:** 18-1104
**Comments for Public Posting:**

March 28, 2019

To Whom It May Concern;

Criminal Justice reform is at the center of a national debate among policymakers and others interested in justice and fairness. Of particular note locally is a matter that could set back the fight for reform: the drive to ban menthol cigarettes with little regard for the unintended consequences associated in Los Angeles.

Local government is where the direct impact of public policy can be seen and felt by the individuals it is meant to benefit. Sound public policy requires that elected officials consider the unintended consequences of policy decisions before taking action. Unintended consequences of policy decisions have been seen at the federal level with mandatory minimum sentencing laws, at the state level with "stand your ground" laws, and in cities like San Francisco and others through housing policies that have forced certain populations from their homes.

Ordinances that regulate menthol cigarettes, which African Americans smokers overwhelmingly prefer, differently than non-menthol cigarettes, which White smokers overwhelmingly prefer, is another example of policy decisions that could lead to troubling problems in communities of color.

Some policymakers and advocates have convinced themselves that such restrictions on menthol can be implemented without the aid of law enforcement by simply punishing retailers who sell newly banned products. What those policymakers and advocates fail to understand or refuse to acknowledge is that by pushing menthol cigarettes out of the licensed and regulated retail chain, they are simply forcing tobacco products to underground markets with "entrepreneurs/opportunist" looking to sell their lucrative products to anyone willing to buy, regardless of age.

This newly unfunded mandate and overall bad policy would put law enforcement organizations on the front line of enforcing a public-health issues, diverting resources from higher priority crime problems. Officers would be ultimately responsible for enforcing the ban since menthol cigarettes will be sold illegally on the street. And this illegal activity could likely attract other crime.

Tobacco use is a public-health issue not law enforcement. Cessation will come through public education, including programs for youth and teens. In fact, smoking rates continue to decline and are at historic lows. We must sustain this progress, but it will not come from law enforcement officers forced to fight an underground market that was foreseen and created by bad policy.

Criminal justice reform remains attainable. However, there is real concern that the recent progress made during the Obama era will be rolled back. Small victories for communities' disproportionately impacted by the failed "War on Drugs" may be reversed by prosecutors instructed to seek the harshest possible penalty in all cases, no matter how minor.

In closing, we should not establish nor allow public policy that would move us backward, especially when the unintended consequences are preventable. While those who suggested the menthol ban may have had good intentions, our communities must pursue measures that advance criminal justice reforms and decriminalize our communities, not policies that will make them worse.

With Regards,

Thea Williams
President
Los Angeles Black Pride & Promote
CA State ID #**C3940167**
**Fiscal Sponsor – Minority AIDS Project 501c3 #95-41756**