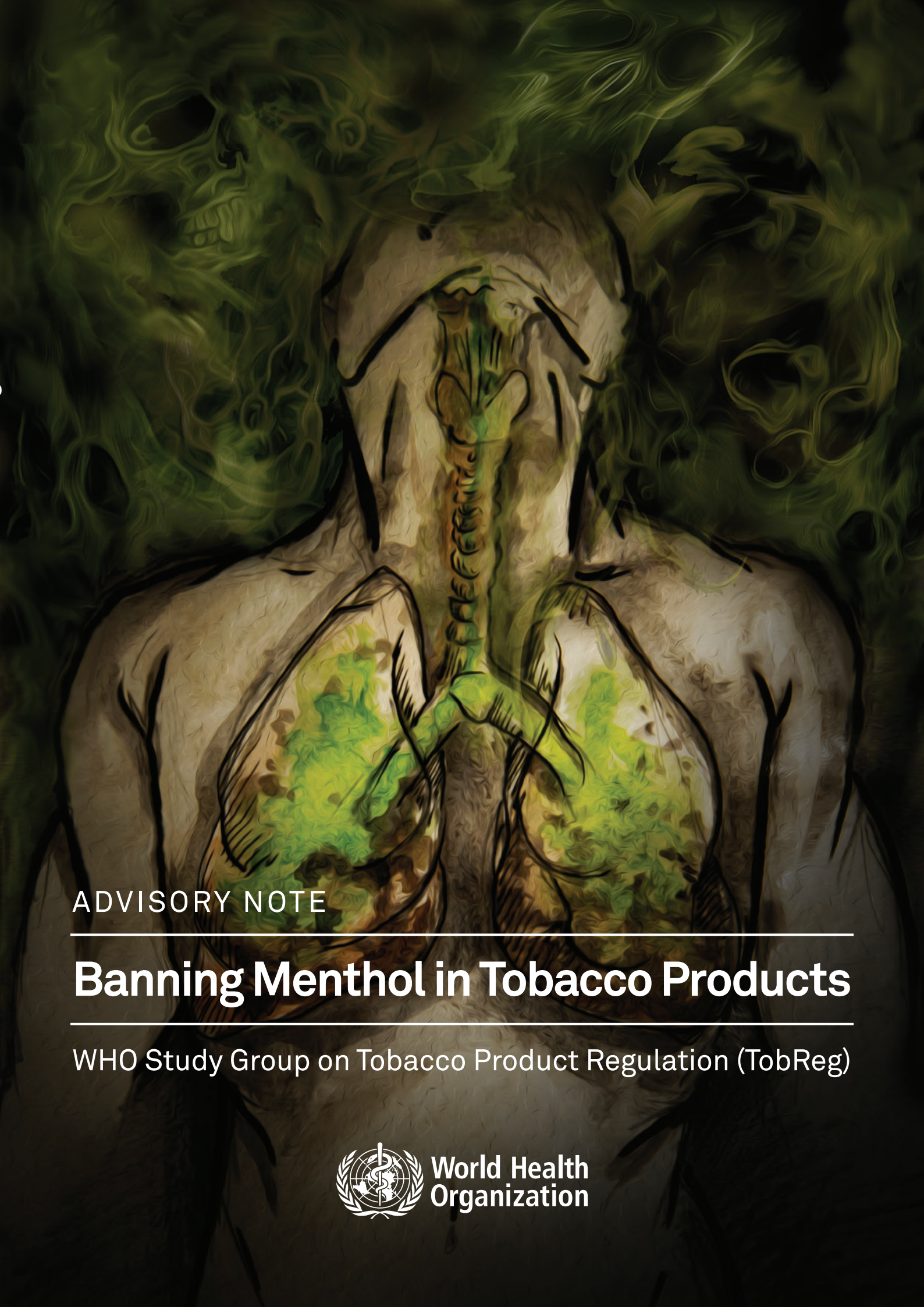

ADVISORY NOTE

Banning Menthol in Tobacco Products

WHO Study Group on Tobacco Product Regulation (TobReg)

World Health Organization

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1. Preface

Tobacco product regulation, which involves regulating the contents and emissions of tobacco products by testing, mandating the disclosure of the test results and regulating the packaging and labelling of tobacco products, is one of the pillars of any comprehensive tobacco control programme. The WHO Framework Convention on Tobacco Control (WHO FCTC), a binding international treaty, acknowledges the importance of tobacco product regulation in Articles 9, 10 and 11, and Parties to the Convention are bound by the provisions of those articles.

A WHO scientific advisory group on tobacco product regulation was established in 2000 to fill gaps in knowledge. The information provided by that group served as a basis for negotiation of the FCTC and the consensus reached on the wording of those three articles of the Convention.

In November 2003, in recognition of the critical importance of regulating tobacco products, the WHO Director-General formalized the ad hoc Scientific Advisory Committee on Tobacco Product Regulation by changing its status to that of a study group, which became the WHO Study Group on Tobacco Product Regulation (TobReg). The Group is composed of national and international scientific experts on product regulation, treatment of tobacco dependence and laboratory analysis of tobacco ingredients and emissions. Its work is based on the latest research on tobacco product issues. It makes recommendations and proposes testing for filling regulatory gaps in tobacco control. As a formalized entity of WHO, TobReg reports to the WHO Executive Board through the Director-General to draw Member States' attention to the Organization's work in tobacco product regulation.

At its Fifth Meeting in Durban, South Africa, in November 2008, TobReg discussed the use and effects of menthol cigarettes. At that time, however, TobReg

was unable to formulate conclusions or recommendations on menthol cigarettes because of insufficient scientific evidence. Since then, more evidence on menthol in tobacco products has emerged. The Food and Drug Administration (FDA) and the Tobacco Products Scientific Advisory Committee (TPSAC) in the USA and the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks have all issued reports on tobacco additives.

This document was prepared to synthesize the results of those reports, to provide evidence from 64 new peer-reviewed studies that were not included in those reports and to make generalizations and recommendations for policy-makers.

TobReg is pleased to present this first advisory note on menthol in tobacco products. It unequivocally recommends banning the use of menthol and its analogues, precursors or derivatives in cigarettes and possibly all tobacco products.

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WHO is grateful to Mr Geoffrey Ferris Wayne for drafting the background paper that served as the basis for this TobReg Advisory Note. Mr Wayne's work was guided by Dr Dorothy Hatsukami, who reviewed various drafts. We also thank the members of TobReg both for substantive input to the document and for support to WHO during the years of policy development in tobacco product regulation. It should be noted that TobReg members serve in their personal capacities, rather than as representatives of governments or other bodies, and without remuneration for their invaluable contributions to WHO.

Administrative support in the production of this paper was provided by Ms Miriamjoy Aryee-Quansah, Mr Gareth Burns, Mr Luis Madge, Ms Elisabeth Tecson, Ms Rosane Serrao, Ms Moira Sy and Ms Angeli Vigo.

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We received help from so many people that there are undoubtedly some who are not mentioned here. We apologize for any omission.

1. Introduction

Evidence on the use and effects of menthol in cigarettes was presented at the fifth meeting of the WHO Study Group on Tobacco Product Regulation (TobReg) in Durban, South Africa, in November 2008.[1] TobReg concluded that the scientific evidence at that time was not sufficient to warrant recommendations with respect to menthol. Since then, the research has advanced significantly. In 2009, the Family Smoking Prevention and Tobacco Control Act in the USA formed the Tobacco Products Scientific Advisory Committee (TPSAC) and mandated it to report on the public health impact of menthol in cigarettes. The Committee's report, issued in 2011, was based on evidence from both public health and industry sources (TPSAC, 2011). It concluded that removal of menthol cigarettes from the marketplace would benefit public health in the USA. The US Food and Drug Administration (FDA) independently reviewed the available peer-reviewed scientific literature, industry submissions and other material provided to TPSAC and performed or commissioned additional analyses to fill gaps in the literature. The report underwent peer review in August 2011 and was published in 2013 (FDA, 2013a). Because of the delay between peer review and publication of the FDA report, a literature review covering the period 1 July 2011–27 March 2013 was published separately (FDA, 2013b). The FDA concluded:

> "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.[2] Further, the data indicate that menthol in cigarettes is likely

[1] Clark PI, Babu S, Sharma E. Menthol cigarettes: What do we know? Background paper presented to WHO, November 2008.

[2] The studies used various definitions of "youth" and young adults. Generally, "youth" are people aged 11-17, while young adults are people aged 18-30 years.

> 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."

In the current document, a review was conducted to identify studies on menthol in tobacco products that had been conducted since TobReg last considered the issue, in 2009. Peer-reviewed articles were identified on the PubMed database with generalized search terms such as "menthol and cigarette", "menthol and tobacco" and "menthol and smoking". A total of 137 articles were considered to be directly relevant to this review. Of these, more than 64 were published after March 2013, indicating substantial new evidence on the effects of menthol in cigarettes since the TPSAC and FDA reviews. Relevant data on the use and effects of menthol in non-combusted[3] tobacco products were also identified.

The approach adopted for this review was to generalize the research and conclusions presented by Clark et al.,[4] the TPSAC review and the FDA reviews. Thus, only evidence from peer-reviewed studies not included in the previous reports (i.e. March 2013–October 2015) is presented. Conclusions are drawn from all the evidence but particularly the most recent publications. The stated goal of both the TPSAC and the FDA reviews was to inform policy in the USA. Important questions are the degree to which conclusions from those reviews may reasonably be applied in other countries and whether evidence from other countries supports US research findings. Although non-combusted tobacco products are commonly flavoured with methyl salicylate (i.e. "wintergreen"), menthol is also found in a number of such products, including *snus* and moist snuff. "Mint"-flavoured products are a rapidly growing non-combusted category. Available data on the use of menthol in non-combusted tobacco products and on individual or population health effects are also presented.

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[3] Throughout this document, the term "combusted" is used rather than "combustible" to describe certain types of tobacco products. "Combustible" means capable of being burnt, while "combusted" refers directly to how the products are used.

[4] Clark PI, Babu S, Sharma E. Menthol cigarettes: What do we know? Background paper presented to WHO, November 2008.

2. Use of menthol in tobacco products

Menthol is a widely used flavouring agent characterized by a minty flavour and by its well-known cooling effect. Natural menthol is isolated from flowering mint plants, *Mentha piperita* and *M. arvensis*; the compound is also produced synthetically. It is a monocyclic terpene alcohol, which occurs as four pairs of optical isomers: (+)- and (–)-menthol, (+)- and (–)-neomenthol, (+)- and (–)-isomenthol and (+)- and (–)-neoisomenthol (Eccles, 2000). (–)-Menthol is the isomer that occurs most frequently in nature (Kamatou et al., 2013). Menthol has a number of known biological effects: it is used as an antipruritic, an antiseptic and an analgesic in the symptomatic treatment of gastrointestinal disorders and to enhance the dermal penetration of pharmaceuticals (Ahijevych & Garrett, 2004; Kamatou et al., 2013). It is most commonly used in confectionery products, in oral care products such as toothpaste, in over-the-counter medicinal products and in tobacco.

2.1 Form and method of application in tobacco

Both natural and synthetic menthols are used in tobacco products; however, (–)-menthol is the only form that has been detected by chemical analysis of cigarettes and non-combusted products, and no evidence has been found of thermal racemization of menthol upon smoking (Chen et al., 2011). Because of its volatility, menthol may be added to products in a variety of ways, after which it migrates throughout the product until equilibrium is reached. For example, menthol may be added directly to tobacco or filters or transferred to the product from packaging foil or it may be dispersed in ethanol or another solvent. When used in filters, menthol is commonly added in crystal form (Ferris Wayne & Connolly, 2004; TPSAC, 2011).

A recent innovation for release of menthol is insertion of flavour capsules into the cigarette filter (Dolka et al., 2013; Thrasher et al., 2015). These capsules may contain any number of chemicals, including menthol, which are not released until the capsule has been manually crushed by the smoker. Commercial brands have been released in markets throughout the world, including Japan, Lithuania, the Republic of Korea, Switzerland and the USA (Dolka et al., 2013). A survey of smokers indicated high variation in both the frequency and timing of crushing the flavour capsules, with differences also among countries (Thrasher et al., 2015).

Chemical compounds have been synthesized to mimic the "cooling" effect of menthol, the best known being the WS compounds developed by Wilkinson Sword Ltd in the 1970s (Leffingwell, 2015). The current or potential use of these analogue compounds either to replace or combined with menthol in tobacco products is not known.

2.2 Menthol content of cigarettes

Menthol is found both at high doses in commercial cigarettes characterized as menthol and in low doses in regular or non-menthol cigarettes (Ferris Wayne & Connolly, 2004). In a study of menthol levels in 45 US cigarette brands assessed by gas chromatography–mass spectrometry, cigarettes labelled as "menthol" had levels of 2.9–19.6 mg/cigarette, and those not labelled as "menthol" contained 0.002–0.07 mg/cigarette; thus, products labelled as containing menthol have levels that are 50–5000 times higher (Ai et al., 2015). The study also showed wide variation in the level of menthol in products characterized as "menthol" cigarettes. In a previous analysis of menthol cigarettes, the concentration of menthol was only 2–5 mg/cigarette (Celebucki et al., 2005). No difference in menthol content was found with the type of packaging (hard or soft) (Ai et al., 2015); however, the menthol content is generally higher in lower-yield[5] cigarette brands than in regular-yield brands (Celebucki et al., 2005; Ferris Wayne & Connolly, 2004). Menthol delivery is probably increased to overcome air dilution of the smoke in more highly ventilated, lower-yield brands.

[5] "Lower-yield" products have more tip ventilation, to lower the machine-smoked yields of emissions. Smokers adjust their smoking behaviour with these products to take larger or more frequent puffs or partially or fully block the ventilation holes.

2.3 Menthol content of non-combusted tobacco

In a study of non-combusted tobacco products, the menthol content in South-East Asian products, including *zarda*, *kiwan*, *gutkha* and *khaini*, was 1.1–21.7 mg/g, and the mean in "mint"-flavoured US moist snuff products was 3.2 mg/g (Lisko et al., 2014). Menthol levels as high as 5.3 mg/g were found in US moist snuff brands in 2010), similar to those measured in mint-flavoured confectionery (Chen et al., 2010).

2.4 Summary

Menthol is added to cigarettes in a variety of ways, but equilibrium is reached in the final product regardless of the method, except from capsules and other novel techniques for controlling menthol delivery. The measured menthol content of menthol cigarettes varies widely in cigarettes characterized as "menthol" and even more widely in non-combusted tobacco products, particularly in South-East Asia.

3. Patterns of use of menthol

The availability and use of menthol cigarettes differ significantly by country and by demographic group among and within populations (Giovino et al., 2004; TPSAC, 2011).

3.1 Prevalence of menthol tobacco use

Giovino and colleagues (2004) reported the market share of menthol cigarettes in over 40 countries in 1999 or 2001. The prevalence among smokers of menthol cigarettes was highest in the Philippines (60%) and then Cameroon (35–40%), Hong Kong (China) (26%), the USA (26%) and Singapore (22%).[6] A report prepared by Oxford Economics Ltd (2012) was based on estimates of the market share of menthol cigarettes in 52 countries in 2010, from data provided by The Nielsen Company and by Philip Morris International. Menthol cigarettes represented 10% of the entire cigarette market in these countries. More than half the countries had a market share of < 5%, while 14 countries had a market share > 15% (Cameroon, El Salvador, Guatemala, India, Japan, Kenya, Malaysia, Nigeria, Panama, Peru, Philippines, Poland, Singapore and Thailand), and the market share in the Philippines and Singapore approached 50%.[7] In the USA, menthol smokers account for 28–35% of all cigarette smokers, depending on the data used (Lawrence et al., 2010; Substance Abuse and Mental Health Services Administration, 2011; Giovino et al., 2015).

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[6] The prevalence rates for the Philippines and Singapore are based on data for 1999–2000.

[7] The figures for the market share in the Philippines and Singapore are based on 2010 data.

3.2 Demographic patterns of menthol use

Menthol cigarettes are used disproportionately more frequently by specific populations of smokers, including youth and young adults, women and ethnic minorities (Giovino et al., 2004; Caraballo & Asman, 2011; Delnevo et al., 2011; TPSAC, 2011; FDA, 2013a; Kasza et al., 2014; Giovino et al., 2015).

3.2.1 Youth and young adults

In the USA, menthol cigarette use is significantly higher among younger than older smokers, and adolescents smoke menthol cigarettes more than any other age group (Giovino et al., 2004; Hersey et al., 2010; Lawrence et al., 2010; Rock et al., 2010; TPSAC, 2011; FDA 2013a). In the US cohort of the International Tobacco Control Four Country Survey (conducted between 2002 and 2011), the prevalence among 18–24-year-old smokers was 36%, while the overall use rate was 27% (Kasza et al., 2014). Giovino et al. (2015) used data from the National Survey on Drug Use and Health for 2004–2010, with adjustment for self-reported data on exclusively menthol brands; they found that 57% of 12–17-year-olds, 45% of 18–25-year-olds and 31–35% of older groups smoked menthol cigarettes. The rate of menthol cigarette use among US high-school-age smokers was 43–45% (Hersey et al., 2010; TPSAC, 2011).

Only a few studies were found in PubMed from elsewhere than the USA. King et al. (2012) reported that the rates of menthol cigarette use among adolescents in Australia peaked in 1987, with a high of 11% among girls, followed by a steep decline. The Global Youth Tobacco Surveys in Brazil in 2005–2009 indicated that more than one third of smokers aged 13–15 years used menthol cigarettes.[8] In a Canadian survey of young adults in 2010, use of menthol cigarettes as a proportion of all smoking ranged from a low of 26% in Quebec to 37% in both Alberta and the Atlantic provinces (PROPEL Centre for Population Health Impact, 2014). In New Zealand, 18% of 14- to 15-year-old smokers indicated a preference for menthol cigarettes (Li et al., 2012). A second analysis of the same population suggested an increase in the number of menthol cigarette smokers over

[8] Figueiredo VC. Flavored cigarettes: perceptions, use and regulatory responses in Brazil. Presentation at the 4th Latin American and Caribbean Conference on Tobacco or Health. Center for Studies on Tobacco and Health. National School of Public Health; 2014 (http://www.tobaccoorhealthlac.org/files/Cigarrillos_con_saborizantes-VALESKA_CARVALHO.pdf).

time with a concomitant decrease in non-menthol cigarette smokers (Marsh et al., 2012). In Poland, young smokers were more likely to smoke flavoured cigarettes, including menthol, than older smokers (Kaleta et al., 2015).

3.2.2 Women

Women are more likely than men to use menthol cigarettes (Lawrence et al., 2010; Rock et al., 2010; Caraballo & Asman, 2011; Faseru et al., 2011; Giovino et al., 2015). In a survey in 2004, female smokers were significantly more likely than males to use mentholated brands in Australia (5.4% vs 1.8%), Canada (4.7% vs 1.5%), the United Kingdom (3.7% vs 2.0%) and the USA (31.8% vs 22.1%) (Giovino et al., 2004). In New Zealand, the odds ratio for menthol cigarette preference among adolescent girls was more than twice that for boys (Li et al., 2012). In Australia, the rate of menthol cigarette smoking among women aged ≥ 30 was approximately 20% in 2008, which was four times that of men of a similar age, and the rate of menthol cigarette use by young women remained significantly higher than that of young men, despite the decline in menthol cigarette use (King et al., 2012). Female high-school students in Japan had significantly higher rates of menthol cigarette use than boys in both 1996 and 2000, and nearly half the girls used menthol cigarettes in 2000 (Connolly et al., 2011). In Poland, women were significantly more likely than men to smoke flavoured cigarettes, including menthol cigarettes (Kaleta et al., 2014).

3.2.3 Racial and ethnic minorities

Studies in the USA have consistently shown higher rates of menthol cigarette use among racial and ethnic minorities (TPSAC, 2011; FDA, 2013a; FDA, 2013b). Between 70% and 90% of Black smokers in the USA use menthol cigarettes (Giovino et al., 2004; Caraballo & Asman, 2011; Kazsa et al., 2014; Giovino et al., 2015), and they are at least 10 times more likely to smoke menthol cigarettes than white smokers (Lawrence et al., 2010; Rock et al., 2010). Other groups of non-white smokers (with the exception of American Indian, Aleut and Eskimo smokers) are also significantly more likely to smoke menthol cigarettes than white smokers (Lawrence et al., 2010; FDA, 2013b; Hickman, 2014). Black, Hispanic and Asian or Pacific Islander youth in the USA have higher rates of menthol use than their older age cohorts (Giovino et al., 2004; Lawrence et al., 2010; Giovino et al., 2015), and the rates among Hispanic youth have increased sharply from 34% in 2004 to 42% in 2008 (Rock et al., 2010).

The preference for menthol cigarettes of adult Black smokers surveyed in Canada and the United Kingdom was not as strong as that in the USA (Giovino et al., 2004); however, Minaker and colleagues (2014) found significantly higher rates of menthol cigarette use among high-school-aged Black and Hispanic smokers in Canada. In New Zealand, high-school aged Maori, Asian and Pacific Islander ethnic minorities were more likely to smoke menthol cigarettes (Li et al., 2012).

3.2.4. People with psychiatric disorders

The TPSAC (2011) observed that, while the prevalence of smoking is higher among people with mental illness, no peer-reviewed studies of use of menthol cigarettes by this population were found. Hickman et al. (2014) examined the association between mental illness and menthol cigarette use in a nationally representative sample in the USA. People who reported severe distress had greater odds for smoking menthol cigarettes than those who reported no or mild distress, after control for socio-demographic characteristics and number of cigarettes smoked per day. Moderate distress was not associated with a greater likelihood of smoking menthol cigarettes. Another study of smokers with mental illness in the USA found that most (57%) reported smoking menthol cigarettes. The factors associated with greater menthol cigarette use in this population included younger age, racial or ethnic minority status, fewer perceived interpersonal problems and more psychotic symptoms (Young-Wolff et al., 2015).

3.3 Trends in menthol cigarette use

The percentages of both adult and adolescent smokers of menthol cigarettes in the USA are rising. A study in 2014 showed that 89% of the decrease in cigarette consumption in the USA between 2000 and 2011 was attributable to non-menthol cigarettes, consumption falling from 323 billion to 203 billion cigarettes (37%), while menthol cigarette consumption decreased far more slowly, from 112 billion to 90 billion cigarettes (20%) (Delnevo et al., 2014). The percentage of adolescents aged 12–17 years who smoked non-menthol cigarettes decreased between 2004 and 2010, while the rate of menthol cigarette smoking remained constant. Among young adults (18–24 years), the percentage that smoked non-menthol cigarettes decreased, while the menthol cigarette smoking rate increased (Giovino et al., 2015). These findings confirm those of earlier studies (Kreslake et a., 2008a; Rock et al., 2010).

No reliable data were found on trends elsewhere than the USA. The proportion of menthol cigarette smokers among adolescents in New Zealand is increasing (Marsh et al., 2012), while King et al. (2012) found no significant change in menthol cigarette consumption among adults or adolescents in Australia between 2000 and 2008. The volume of sales of menthol cigarettes in Brazil doubled between 1997 and 2012, from approximately 4.5% to 10.5%.[9] A comparison of the estimates of the prevalence of adult use of menthol cigarettes in 1998 by Giovino et al. (2004) and those prepared for Philip Morris International (Oxford Economics Ltd, 2012) suggested markedly higher rates of menthol cigarette use in Guatemala (15% vs 40%), India (< 1% vs 22%), Japan (6–7% vs 24%), Nigeria (13% vs 34%), Singapore (22% vs 48%) and Thailand (18% vs 35%) and markedly lower rates in others, including Cameroon (35–40% vs 20%) and Romania (15% vs 3%). It is not clear whether these differences are artefacts or differences in data sources or methodology.

3.4 Summary

The prevalence of menthol cigarette use differs dramatically from country to country throughout the world. The rates among smokers approach 50% in some countries but are negligible in others. Few studies were found on trends outside the USA, where the share of the market is growing.

Evidence from a number of countries indicates that women more often smoke menthol cigarettes. The preference is generally in inverse relation to age. In New Zealand and the USA, a preference for menthol cigarettes is increasing among younger smokers, although the rate has fallen in Australia. Most adolescent smokers in the USA smoke menthol cigarettes. The rates of menthol cigarette smoking are frequently higher in racial and ethnic minorities, particularly in younger smokers, although data were found only for Canada, New Zealand, the United Kingdom and the USA. The rates of menthol cigarette use are particularly high among smokers with psychiatric disorders; a recent study in the USA showed that a majority of smokers in this population use menthol cigarettes.

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[9] Figueiredo VC. Flavored cigarettes: perceptions, use and regulatory responses in Brazil. Presentation at the 4th Latin American and Caribbean Conference on Tobacco or Health. Center for Studies on Tobacco and Health. National School of Public Health; 2014 (http://www.tobaccoorhealthlac.org/files/Cigarrillos_con_saborizantes-VALESKA_CARVALHO.pdf).

4. Marketing of menthol

There is an association between the marketing of menthol cigarettes and brand preference and use. In the USA, marketing strategies are aimed primarily at younger people and at African Americans (TPSAC, 2011; FDA, 2013a; FDA, 2013b). While evidence from industry reviews and empirical studies suggests that women have been targets of tailored marketing, TPSAC (2011) concluded that there was insufficient evidence to support the conclusion that menthol cigarette marketing is targeted disproportionally to women.

4.1 Pricing and retailing of menthol and non-menthol cigarettes

TPSAC (2011) reviewed studies on the role of price in the marketing of menthol cigarettes. The average price was slightly higher than that of non-menthol cigarettes. Price promotions (e.g. "buy one, get one free") were used more frequently than for non-menthol cigarettes, and more menthol cigarette smokers took advantage of price promotions. This was particularly true for African Americans. Menthol cigarette smokers showed a stronger cigarette preference than non-menthol cigarette smokers and were less sensitive to price fluctuations (Tauras et al., 2010; TPSAC, 2011). Menthol cigarette smokers were more likely to buy cigarettes by the pack, and the adjusted odds of smoking menthol cigarettes were significantly lower for smokers who reported buying cigarettes only by the carton (Fernander et al., 2010). These observations are consistent with the results of studies indicating that menthol cigarette smokers smoke fewer cigarettes (TPSAC, 2011; FDA, 2013a). Richardson et al. (2014) examined menthol cigarette advertising in the USA over 9 months in 2012–2013 and found that about 70% of expenditure was on direct postal advertisements, 87% of which contained coupons or other incentives known to appeal to price-sensitive customers. No comparable data were found for other markets.

4.2 Promotions, advertising and packaging

TPSAC (2011) reviewed marketing expenditure for menthol and non-menthol US cigarette brands and observed that the tobacco industry spent as much or more on magazine advertising for menthol as for non-menthol brands, even though the menthol brands represent a much smaller share of the market. Menthol cigarettes were marketed consistently more often in publications and at venues that attracted Blacks and African Americans (Rising & Alexander, 2011; FDA, 2013a). A study in 2013 also showed more cigarette advertising for menthol brands in the African American community (Dauphinee et al., 2013), and Lee et al. (2015) concluded that menthol cigarette marketing was more frequent in urban neighbourhoods and in neighbourhoods with more Black residents.

No direct comparisons were found of the packaging characteristics of menthol and non-menthol cigarettes. TPSAC (2011) noted that the results of research on packaging apply to both menthol and non-menthol cigarettes. For example, different shades of colour are commonly used to distinguish variants of the same brand family, lighter colours being used to signify "lower tar" cigarettes (DiFranza et al., 2002; Wakefield et al., 2002), and consumers interpret lighter shades on cigarette packaging to infer that the cigarettes are less harmful (Hammond & Parkinson, 2009).

4.3 Health reassurance messages

A link between menthol cigarette smoking and reduced health risk was introduced for the earliest menthol cigarettes, in the 1920s, which were promoted as an occasional remedy for the throat irritation and burning sensation caused by regular smoking[10] (Andersen, 2011; Rising & Alexander, 2011). Later, with growing concern about the health effects of smoking and the advent of "light" and "low-tar" cigarettes, the industry gradually repositioned menthol cigarettes as a healthier, less harsh alternative to regular use. The marketing included both explicit claims that smoking menthol cigarettes would improve smokers' health and sensory descriptors such as "refreshing", "clean", "cool" and "fresh" with related imagery to imply that menthol cigarettes are safer and easier to smoke than non-menthol cigarettes (Andersen, 2011; Lee & Glantz, 2011; TPSAC, 2011). Although most of the research on health messages and menthol cigarettes has been conducted in the USA, similar descriptors are used to promote menthol cigarette products in other parts of the world (Wilson et al., 2011; FDA, 2013b).

[10] Clark PI, Babu S, Sharma E. Menthol cigarettes: What do we know? Background paper presented to WHO. November 2008.

4.4 "Youthfulness", sociability and group belonging

Menthol cigarette marketing messages are designed to appeal to various group identities and to convey varied images of menthol cigarette smokers, rather than a single or unified image (Anderson, 2011; TPSAC, 2011). A major theme of menthol cigarette advertising is sociability and fun. Klausner (2011) reviewed menthol cigarette marketing strategies from internal industry documents and concluded that the marketing strategy of the leading US menthol cigarette brand (Newport) was based on the assumption that peer influence is critical to smoking uptake, and the advertising imagery sought to recreate and reinforce that influence. TPSAC (2011) reported that empirical studies showed that the message that Newport is a brand for younger consumers was apparent to both adults and adolescents.

A second marketing theme identified by TPSAC (2011) was a sense of belonging. A number of published studies have addressed the role of menthol cigarette marketing in establishing a connection with racial or ethnic identity in the USA, especially African-American identity but also others, including Hispanic and Latino (Rising & Alexander, 2011; TPSAC, 2011). The strategies identified included use of darker-skinned models, slang, clothing, music and other elements of popular culture (TPSAC, 2011). Specific brands were linked to more masculine or feminine imagery (Andersen, 2011). The development of identity is central to adolescence, particularly among racial and ethnic minorities (Castro, 2004).

4.5 Target groups (youth, women, specific racial or ethnic groups)

Reviews of internal tobacco industry documents provide strong evidence that the tobacco industry has tailored brands and marketing strategies to promote menthol cigarettes in specific communities (Andersen, 2011; Klausner, 2011; TPSAC, 2011). This conclusion is supported by the empirical studies described above, which demonstrate a preponderance of marketing and promotion to these communities.

In the USA, the groups most consistently identified as targets for menthol cigarettes are youth and racial and ethnic minorities. The FDA (2013a, 2013b) concluded that advertising is a strong driver of brand preference among US adolescents, and TPSAC (2011) concluded that industry marketing had positioned menthol cigarettes as an attractive starter product for new smokers including youth and young adults. Empirical studies demonstrate that youth pay attention to and are

attracted to menthol cigarette advertising (TPSAC, 2011). The high prevalence of menthol cigarette use among African-American smokers is clearly linked to industry marketing practices (TPSAC, 2011; FDA, 2013a). This population is surrounded by integrated marketing designed to promote growth in the brand share of menthol cigarettes among new and current African-American smokers, particularly in poor and urban areas (Cruz et al., 2010; TPSAC, 2011). Marketing directed to youthfulness and racial identity are often mutually reinforcing. Dauphinee et al. (2013) found that African-American youth were twice as likely as other youth to recognize the advertising for the leading menthol cigarette brand (Newport), and recognition of Newport cigarette advertising predicted smoking initiation, regardless of race. In an analysis of advertising placement, it was found that Newport advertisements with themes of sociability and sexuality were placed in magazines targeting African Americans and younger consumers (Richardson et al., 2014).

Although internal tobacco industry documents indicated marketing of menthol cigarettes to women, both Rising & Alexander (2011) and TPSAC (2011) concluded that, in the USA, the evidence was strongest for a link with youth and young adults in general and with racial and ethnic subgroups of women. This conclusion may be less applicable in other regions. For example, King et al. (2012) observed that the menthol cigarette market in Australia was strongly directed towards women before its decline, menthol cigarette brands being much more popular among female than male smokers in all age groups. Advertising and imagery for the most popular menthol cigarette brand was highly feminized. Likewise, Connolly et al. (2011) observed that the introduction of menthol cigarette brands into Japan was tailored to appeal to the nascent female market, which was concerned with social image and related issues.

4.6 Product differences

There are more than 350 varieties of menthol cigarettes in the USA, although five brand families account for the largest market share (TPSAC, 2011). Brands have physical characteristics and delivery that may be related to differences in how the products are marketed or targeted to specific populations. Lower concentrations of menthol are known to appeal to younger smokers and women (Kreslake et al., 2008b; Lee & Glantz, 2011), while more established menthol cigarette smokers appear to be tolerant of and even seek stronger sensory attributes, including

higher menthol levels. Smokers of these "stronger" menthol cigarettes are disproportionately Black and male (Kreslake et al., 2008b). A survey of products purchased and tested in 2003 showed lower concentrations of menthol in the filler of cigarettes labelled "light" or "ultralight" (Celebucki et al., 2005). Menthol cigarette brands with a low level of menthol were significantly more popular among younger people, and the introduction of low-menthol cigarette brands onto the US cigarette market corresponded to the rise in popularity of menthol cigarettes among youth (Kreslake et al., 2008a).

Flavour capsules with added menthol are an innovative means for achieving greater direct control over menthol delivery (Thrasher et al., 2015). Use of flavour capsules is growing rapidly in many parts of the world, including Asia, eastern Europe and Mexico (Dolka et al., 2013; Thrasher et al., 2015). A preference for flavour capsules is associated with younger age in a number of countries (Australia, Mexico and the USA), consistent with research on the importance of novelty for young people. Flavour capsule brands are preferred by more women than men in Mexico and the USA, and by smokers who are less dependent ("heaviness of smoking" index) in Australia (Thrasher et al., 2015). Use of flavour capsules may alter perceptions of a product; for example, Mexican smokers who preferred discount flavour capsule brands were more likely than smokers of regular premium brands to view their brand as smoother, lighter and less harmful (Thrasher et al., 2015).

4.7 Summary

Menthol cigarette branding elements that connote health benefits and marketing messages that feature socially and culturally relevant messages about group identity appeal to different market segments. In the USA, these messages have a particular reinforcing effect among adolescent and young adult smokers and racial and ethnic minorities. Little information was found for other countries, although themes designed to appeal to girls and women may be more prominent. The high rates of menthol cigarette use among youth and Blacks in the USA are associated with widespread advertising directed to these populations, use of promotions, tailored marketing messages and brand imagery and development of products that appeal specifically to them.

5. Consumer perceptions of menthol

Menthol cigarettes contain menthol at levels sufficient to alter the characterizing flavour and sensory properties of the product, and they are commonly marketed as a distinct flavour category. Thus, menthol plays a more significant, overt role in product differentiation than other common tobacco flavours, such as cocoa and sugars. Whereas switching among cigarette brands is common, there is relatively little switching between menthol and non-menthol products (Kreslake et al., 2008b; TPSAC, 2011; FDA, 2013a; Kasza et al., 2014).

5.1 Taste perception and sensory evaluation

Menthol products are commonly viewed as milder and having a less obvious tobacco flavour than non-menthol cigarettes; they are also considered distinct from "light" or "low-yield" brands (Kreslake et al., 2008b). The perceived product attributes of menthol and non-menthol cigarettes differ. For example, menthol smokers define cigarette "strength" according to menthol intensity, minty flavour and tobacco flavour, whereas non-menthol cigarette smokers define "strength" on the basis of throat impact and throat scratch (Ferris Wayne & Connolly, 2004; Kreslake et al., 2008b).

Product preferences differ among menthol cigarette smokers. Kreslake et al. (2008b) identified two types of menthol cigarette smokers: those who cannot tolerate the harshness and irritation of smoking non-menthol cigarettes and those who seek the specific menthol flavour and the associated physical sensation. The first group, which may include occasional smokers and young people, finds that menthol reduces the negative sensory characteristics of smoking and masks

the undesirable tobacco flavour. In contrast, some established menthol cigarette smokers appear to seek stronger sensory attributes, including more menthol. Some beginning or occasional smokers may adopt menthol cigarettes for their mild properties and to cover the taste of tobacco and then develop a stronger desire for the menthol taste (Kreslake et al., 2008b).

5.2 Perceptions of harm

In a national sample in New Zealand, misperceptions about the relative harm of menthol cigarettes were reported particularly by older, Maori, Pacific Islander and Asian smokers and people in financial difficulties or greater individual deprivation. Most smokers (56%), and most menthol cigarette smokers (73%), believed that menthol cigarettes are "smoother on your throat and chest" (Wilson et al., 2011). In a survey in Asia, 16% of Malaysian respondents and 35% of Thai respondents agreed with the statement that menthol cigarettes are less harmful on the basis of the perception of "smoother" smoke (King et al., 2010). In the International Tobacco Control Policy Evaluation Project in Brazil, nearly half (45%) of menthol cigarette smokers described these cigarettes as "smoother to the throat", and nearly twice as many menthol (22%) as non-menthol cigarette smokers (13%) described menthol cigarettes as "healthier".[11]

In the USA, TPSAC (2011) reviewed studies of internal tobacco documents (Kreslake et al., 2008b; Anderson 2011; Klausner, 2011) and empirical studies (Allen et al., 2010; Unger et al., 2010) and concluded that consumers perceive menthol cigarettes as offering some implicit health protection or medicinal benefit that non-menthol cigarettes do not provide. Menthol cigarette smokers were unlikely to express this perception explicitly and were more likely to identify it by using terms that suggest greater safety or health benefits, such as "light", "mild", "cooling" or "soothing". Few smokers endorsed an explicit statement that menthol cigarettes are safer or less harmful than non-menthol cigarettes (Davis et al., 2010; Wackowski et al., 2010). African Americans were more likely to believe that menthol cigarettes had health benefits, but there were no differences by age

[11] Figueiredo VC. Flavored cigarettes: perceptions, use and regulatory responses in Brazil. Presentation at the 4th Latin American and Caribbean Conference on Tobacco or Health. Center for Studies on Tobacco and Health. National School of Public Health; 2014 (http://www.tobaccoorhealthlac.org/files/Cigarrillos_con_saborizantes-VALESKA_CARVALHO.pdf).

group (Davis et al., 2010). Menthol cigarette smokers are more likely to perceive medicinal effects (such as "better for a sore throat" or "help to loosen a stuffed-up nose") of cigarette smoking than non-menthol cigarette smokers, particularly among males aged ≥ 40 years (Allen et al., 2010; Unger et al., 2010).

About 14% of smokers in an online survey perceived menthol tobacco products to be less harmful, with similar results for menthol and non-menthol cigarette smokers (Brennan et al., 2015). Wackowski and Delnevo (2015) found that only 2.5% of 18–34-year-olds rated menthol cigarettes as less risky, while 10 times as many respondents believed that menthol cigarettes presented a greater health risk than non-menthol cigarettes.

5.3 Roles of branding and labelling in taste perception and sensory evaluation

Expectancy can change both the subjective evaluation of a product and the neural response to it (Cardello & Wise, 2008; TPSAC, 2011). No peer-reviewed experimental studies on the effects of menthol cigarette branding on consumer taste and sensory evaluation were identified; however, reports of consumer testing conducted by tobacco companies indicate that manipulation of elements of menthol cigarette packaging influences consumer sensory experiences of perceived coolness, the amount of menthol, mildness and overall preference. Thus, menthol cigarette packaging reflects the tobacco industry's knowledge about how colour, labelling and other elements of branding improve a consumer's experience of the product's characterizing flavour (TPSAC, 2011). Further research in this area is needed.

5.4 Favourable views of menthol and tobacco use

The concepts of taste, sensory experience and harm are closely related in the minds of consumers (Hammond & Parkinson, 2009). In the case of menthol cigarettes, the notable sensory attributes of the product affect all other aspects of how it is perceived. In a survey conducted in 2015, adolescents who found menthol cigarettes more "refreshing" were significantly more likely to intend to use tobacco and more than twice as likely to intend to smoke menthol cigarettes (Brennan et al., 2015). Young adult respondents reacted similarly. Smokers who perceive menthol

cigarettes as "smoother" or "milder" may be more likely to initiate tobacco use (Kreslake et al., 2008a; Kreslake et al., 2008b; TPSAC, 2011).

Menthol cigarette branding and messaging influence the perceived sensory experience, contributing to the consumer's overall subjective evaluation and liking of the product (TPSAC, 2011). There is significant overlap between menthol cigarette advertising campaigns and the perceptions of these products held by consumers (Rising & Alexander, 2011). Brennan and colleagues (2015) found that a small but significant number of younger respondents (7–23%) believed that menthol cigarette smokers were more popular and/or more attractive than non-menthol cigarette smokers. Reflecting on the declining popularity of menthol cigarettes among younger smokers in Australia, King et al. (2012) inferred that targeted marketing plays a critical role in supporting menthol cigarette brand use. In Australia, "light" or "mild" brands may have taken over the role of the "easier-to-smoke" cigarettes that attract experimenting smokers.

5.5 Summary

Sensory and taste perceptions and marketing messages support consumer beliefs about menthol cigarettes. Consistent with marketing themes, consumers believe that the perceived "smoothness" or "mildness" of menthol cigarettes has medicinal and other implicit health benefits; in the USA, this is especially true among African Americans. With widespread public education about the harmfulness of tobacco use, explicit belief that menthol cigarettes are safer or less harmful than non-menthol cigarettes has become uncommon. The most recent evidence from the USA suggests that beliefs about the relative health risks of menthol cigarettes are increasing, including among younger populations. Limited data from other countries indicate more frequent misperceptions about the health effects of menthol cigarettes, particularly among menthol cigarette smokers, usually related to differences in sensory perceptions.

6. Physiological effects of menthol

Menthol is not only a flavouring agent but also has drug-like characteristics that modulate the effects of nicotine and tobacco smoke. Menthol is associated with a perception of increased nasal airflow and selectively stimulates cold receptors to produce a cooling effect. The FDA (2013a, 2013b) considered evidence from both in vitro and in vivo studies in human and animal models and concluded that menthol in cigarettes is associated with altered physiological responses to tobacco smoke. A similar conclusion was reached by TPSAC (2011). A recent review (Wickham, 2015) cited four biological mechanisms by which menthol cigarettes can support smoking: (i) it reduces the initially aversive experience of tobacco smoking; (ii) it serves as a reinforcing sensory cue when associated with nicotine; (iii) its action on nicotinic acetylcholine receptors changes the reinforcing effect of nicotine; and (iv) it alters nicotine metabolism to increase its bioavailability.

6.1 Reduced harshness or irritation

Internal tobacco industry studies indicate how menthol reduces the harshness of tobacco and alleviates the irritant effects of nicotine (Ferris Wayne & Connolly, 2004; Kreslake & Yerger, 2010; Yerger, 2011). Nicotine induces irritation by acting on both nicotinic cholinergic receptors and TRPA1 and TRPV1 receptors (Lee et al., 2009; Talavera et al., 2009), whereas menthol desensitizes these receptors (Karashima et al., 2007; Bessac & Jordt, 2008; Talavera et al., 2009; TPSAC, 2011), thus modulating sensitivity to chemical irritation (Wise et al., 2011; Wise et al., 2012; Plevkova et al., 2013).

The cold-sensitive cation channel TRPM8 is another target for menthol and other agonists, such as eucalyptol, which counter the irritant effects of many tobacco smoke constituents by activating this channel. Menthol applied to mice at concentrations lower than that found in cigarette smoke attenuated the response to both acrolein, an agonist of TRPA1, and cyclohexanone, an agonist of TRPV1 (Willis et al., 2011). Menthol also reduces the intensity of irritation of the nasal mucosa by capsaicin, thus increasing tolerance to this compound (Buday et al., 2012). Ha and colleagues (2015) examined the effects of menthol on the sensory irritation response in mice exposed for the first time to cigarette smoke and to the smoke irritants acrolein and cyclohexane. Menthol suppressed the response, even at high smoke concentrations. The counter-irritation effects were eliminated by treatment with a TRPM8 inhibitor.

Both the FDA (2013a, 2013b) and TPSAC (2011) concluded that menthol has cooling and anaesthetic effects that reduce the harshness of cigarette smoke, and recent studies support these conclusions. Adding menthol to cigarettes can increase the tolerability of tobacco smoke, reduce the sensitivity of the airway defence mechanism and conceal the irritation that naturally accompanies inhalation of tobacco smoke (Wise et al., 2012; Millqvist et al., 2013).

6.2 Sensory stimulation

The TRPM8 receptor is activated by both cold and menthol (Bautista et al., 2007; TPSAC, 2011; FDA, 2013a), which explains why menthol elicits a sensation of cooling. Menthol produces cooling and analgesia at low doses but can cause irritation and pain at higher doses by effects on the same receptors. The stimulation produced by menthol at higher doses is similar to but distinct from that of nicotine, potentially contributing to the perception of the "strength" of a cigarette. After prolonged stimulation, menthol desensitizes TRPM8 receptors (Kuhn et al., 2009).

The sensory stimulation induced by menthol could reinforce smoking. Although menthol in cigarettes has no direct cardiovascular effects (Pritchard et al., 1999), internal tobacco industry documents indicate that it can affect the electroencephalographic response, with strong correlations to measures of subjective response, including impact and liking (Ferris Wayne& Connolly, 2004). Further, industry studies suggest that menthol can play an important supplementary role in stimulating trigeminal response at very low delivery levels

(Kreslake & Yerger, 2010; Yerger, 2011). TPSAC (2011) concluded that menthol makes low-tar, low-nicotine cigarettes more acceptable to smokers by reducing the irritant effects of smoke.

6.3 Respiratory effects

Clark et al.[12] speculated that the respiratory effects of menthol (increased breath-hold time and cough suppression) could promote deeper inhalation or longer retention of smoke in the lungs of people smoking menthol cigarettes. In experimental animals, menthol appears to promote bronchodilation and clearance of mucus from the lungs. In humans, menthol allows easier breathing, even though upper airway resistance is not significantly affected (Ferris Wayne & Connolly, 2004; FDA, 2013a; Pereira et al., 2013).

Evidence from studies of smokers is mixed. In a cross-over study by Brinkman et al. (2012), nine participants smoked either menthol (Benson & Hedges Menthol Light 100s) or non-menthol (Kent 100s) cigarettes that had been matched to the menthol cigarettes for a number of machine-measured smoke toxicants, for 1 week. Participants who smoked the menthol test cigarettes inhaled a greater volume of smoke, took longer puffs and took more time to smoke. This suggests that they had greater exposure to smoke. No difference was found in inter-puff interval or in inspiration time. In a randomized laboratory study, a large increase in total puff volume was found for smokers of non-menthol cigarettes, with a smaller increase for smokers of menthol cigarettes (Strasser et al., 2013). The difference in the results of the two studies may have been due to the brand used (e.g. Camel Crush in the latter study). In a study by British-American Tobacco, subjective responses to low-yield cigarettes with different menthol contents were compared in a cross-over design in regular and occasional users of menthol cigarettes recruited in Japan and Poland. Subjective differences related to higher menthol loading included perceived menthol taste and "cooling", but there was no difference in perceived irritation and no increase in mouth-level exposure to smoke (Ashley et al., 2012). In the study in mice described above, however, Ha et al. (2015) found that inclusion of menthol in cigarette smoke resulted in a 1.5-times increase in plasma cotinine levels over those in mice exposed to smoke without added menthol.

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[12] Clark PI, Babu S, Sharma E. Menthol cigarettes: What do we kno w? Background paper presented to WHO. November 2008.

In guinea-pigs, menthol suppressed an induced cough only when administered as a vapour to the upper airway, indicating that it suppresses cough through a reflex initiated from the nose rather than deeper in the airway (Plevkova et al., 2013). This finding may have implications for evaluating the role of menthol in non-combusted tobacco use.

6.4 Conditioned reinforcement

Preliminary studies indicate that the sensory stimulation associated with menthol results in greater conditioned reinforcement of the effects of nicotine. Adolescent rats self-administered significantly more intravenous nicotine when it was accompanied by oral menthol than rats receiving nicotine with a vehicle cue (0.01% Tween 80), a mixture of saccharin (0.125%) and glucose (3%) or a flavour cue of unsweetened grape-flavoured Kool-Aid® (0.1%) (Wang et al., 2014). The odourless TRPM8 agonist WS-23 increased the rate of nicotine self-administration similarly to menthol, suggesting that the cooling sensation that accompanies menthol administration, rather than its flavour, is primarily responsible for its effectiveness as a conditioned reinforcer for nicotine.

6.5 Nicotinic acetylcholine receptors

The possibility that menthol interacts directly with nicotinic acetylcholine receptors has been considered only recently (Kabbani, 2013; Wickham, 2015). In vitro, menthol inhibits acetylcholine and nicotine-stimulated currents in the $\alpha4\beta2$ (Hans et al., 2012) and $\alpha7$ (Ashoor et al., 2013) nicotinic acetylcholine receptors, which are expressed predominantly in the brain. Brody et al. (2013) used positron emission tomography (PET) scans to compare the relative densities of $\alpha2\beta4$ acetylcholine receptors in menthol and non-menthol smokers. Menthol smokers had measurably higher receptor densities than non-menthol smokers in the brainstem, cerebellum and corpus callosum, showing that they have greater up-regulation of these receptors than non-menthol cigarette smokers. They may therefore have greater exposure to nicotine, although other mechanisms are possible. Co-administration of menthol and nicotine promoted significantly more $\beta2$ and $\alpha4$ nicotinic acetylcholine receptor subunit expression in various brain regions of mice than co-administration of nicotine and a vehicle control.

The increases were accompanied by signs of greater withdrawal intensity and a significant increase in nicotine plasma levels (Alsharari et al., 2015).

Ton et al. (2015) examined the effects of menthol on recombinant human α3β4 nicotinic acetylcholine receptors, the major subtype expressed in sensory nerves, and on native receptors in mouse sensory neurons. Menthol augmented desensitization of a neuronal receptor without activating or even binding to the receptor's ortho steric site. Menthol alone had no effect on receptor desensitization; however, application with either acetylcholine or nicotine markedly increased the rate and degree of desensitization induced by the agonist alone, without appreciably affecting peak response. The inhibitory effects of menthol increased with higher concentrations of the agonist, suggesting that it acts preferentially on the desensitized state of the receptor channel. Further, application of menthol prevented the recovery of α3β4 receptors from desensitization, trapping receptors in the desensitized state. The degree of desensitization increased with menthol concentration. The authors proposed that menthol augments the desensitization effects of nicotine at sensory receptors in the bronchial airways, thereby reducing its irritant effects, encouraging greater exposure to nicotine and tobacco smoke. Further, by augmenting desensitization of α3β4 nicotinic acetylcholine receptors in the brain, menthol may reduce the amount of nicotine required to desensitize overactive receptors, some of which would have been up-regulated as a result of chronic nicotine administration. Alternatively, menthol may blunt the symptoms of nicotine withdrawal (e.g. mice null for β4 receptor subunits demonstrated fewer withdrawal symptoms), which may offset any increase in symptoms resulting from up-regulation of α4β2 receptor subtypes. These effects may contribute to addiction to menthol cigarettes, but further research is required fully to understand the biological mechanisms associated with its effects.

6.6 Nicotine metabolism and bioavailability

Menthol inhibits the oxidative metabolism of nicotine to cotinine and glucuronidation of nicotine (TPSAC, 2011; Abobo, 2012; FDA, 2013a). The effect is, however, small, and TPSAC (2011) concluded that it is unlikely to have a significant effect on smoking behaviour or the development of addiction. Limited evidence suggests that menthol inhibits the glucuronidation of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol in smokers (Muscat et al., 2009; TPSAC, 2011). Race or ethnicity may play a role in the effects of menthol on

metabolism, as African Americans, Asians, Hispanics and people of mixed ethnicity have slower nicotine metabolic rates than whites (Benowitz et al., 2009; Rubinstein et al., 2013; Fagan et al., 2015a).

Menthol has been shown to enhance transdermal and transbuccal absorption of other drugs (Ahijevych & Garrett, 2004; Ferris Wayne & Connolly, 2004). It has been suggested that inhaled menthol also increases the permeability of the lung to drugs, thereby increasing pulmonary absorption of the constituents of smoke[13] (Ahijevych & Garrett, 2004). Squier et al. (2010) observed that menthol enhances penetration of *N*-nitrosonornicotine and nicotine through oral mucosa, even after short exposure. The practical implication is increased oral exposure of users of menthol-flavoured cigarettes and non-combusted tobacco to carcinogens.

Zuo et al. (2015) studied whether menthol increases the rate of accumulation of nicotine in the brain during smoking. They used PET scans to compare the effects of smoking a single menthol or non-menthol cigarette in a balanced cross-over design. Smoking menthol cigarettes was associated with a steeper initial slope in men, while women had faster brain nicotine accumulation than men in both conditions with a variety of measures. Overall, the results did not provide strong support for a role of menthol in enhancing brain nicotine accumulation.

6.7 Genetic differences

People who can taste "bitterness" are less likely to become smokers, suggesting that the bitter taste makes smoking more aversive (TPSAC, 2011). Nicotine contributes to the unpleasant bitterness of cigarette smoke, while menthol offsets it, suggesting that menthol might interact with genetically determined taste sensitivity to facilitate smoking. Menthol could allow smokers who are genetically more sensitive to bitterness to better tolerate tobacco smoke (TPSAC, 2011). Oncken et al. (2015) found an association between menthol cigarette preference and the frequency and distribution of the PAV haplotypes.

In the study by Zuo et al. (2015) described above, women reported stronger sensations in the back of the mouth, throat and windpipe and had higher ratings

[13] Clark PI, Babu S, Sharma E. Menthol cigarettes: What do we know? Background paper presented to WHO. November 2008.

of liking of and satisfaction with menthol cigarettes, suggesting greater sensitivity to and a preference for the sensory effects of menthol, which might contribute to the popularity of menthol cigarettes among women.

6.8 Summary

The evidence suggests a variety of mechanisms by which menthol might contribute to the initiation and persistence of cigarette smoking. Reduced irritation may lessen aversion to initial self-administration of nicotine in novice smokers and tobacco users, thereby facilitating continued tobacco use, leading to addiction (TPSAC, 2011). These effects may interact significantly with a genetic sensitivity that would otherwise present obstacles to tobacco use. Increased sensory stimulation from menthol may support greater conditioned reinforcement of nicotine use and substitute for the lower impact of low-delivery products. Respiratory effects or increased transbuccal permeability might contribute to deeper inhalation or more complete absorption of nicotine and other smoke constituents. Slower rates of nicotine metabolism may increase its bioavailability, although the evidence indicates that this mechanism is not a significant contributory factor to the extent of dependence on menthol cigarettes. Most promising are recent findings on the effects of menthol on nicotinic acetylcholine receptors (Ton et al., 2015; Wickham, 2015). Although more study is needed, the findings suggest that menthol modulates the effects of nicotine on the airway and brain in a way that enhances addiction to menthol cigarettes.

7. Health outcomes

Industry documents suggest that tobacco companies have conducted little research on the potential disease-inducing effects of menthol and did not pursue studies that suggested adverse effects (Salgado & Glantz, 2011). Evaluation of health outcomes includes studies of biomarkers of exposure, differences in the ways that menthol cigarettes are smoked, the toxicity of smoke from menthol cigarettes and comparisons of the risks of smoking menthol and non-menthol cigarettes in human populations.

7.1 Biomarkers of exposure

While some studies show that smoking menthol cigarettes modulates exposure to or the metabolism of nicotine, the findings are inconsistent. Brinkman and colleagues (2012) in the cross-over study described above found no differences in urine levels of cotinine but higher levels of nicotine in the mouths of people who smoked menthol cigarettes. Ashley et al. (2012) observed that the level of nicotine in the mouth was higher when smoking cigarettes with natural menthol than those with synthetic menthol. Jones et al. (2013a) found higher serum cotinine levels among menthol smokers; however, this difference was erased after adjustment for race/ethnicity. Benowitz et al. (2010) found higher plasma and urine nicotine levels in smokers of non-menthol cigarettes. Other authors found no difference between smokers of menthol and non-menthol products (Caraballo et al., 2011; Muscat et al., 2012; Jones et al., 2013a; Strasser et al., 2013; FDA, 2013b).

Although it has been suggested that menthol in tobacco smoke interferes with the metabolism of toxicants, increasing their accumulation in the body, the evidence is limited (Hoffman, 2011; Heck, 2009; Muscat et al., 2009). Brinkman et al. (2012)

found that the smoke of a menthol cigarette had a higher concentration of NNK (39%) than a non-menthol cigarette and that smokers of menthol cigarettes had a higher daily mouth level of NNK (52%) than smokers of non-menthol cigarettes but no significant difference in the levels of urinary biomarkers for nicotine (NNAL or pyrene). Furthermore, no difference in urinary NNAL was observed (Benowitz et al., 2010; Sardar et al., 2012; Rostron, 2013).

The FDA (2013b) concluded from the evidence that menthol in cigarettes is probably not associated with changes in any known biomarkers of exposure. Other studies have had mixed results. In a representative sample of adult smokers in the USA, those who smoked menthol cigarettes had a higher blood concentration of cadmium but not cotinine, lead or NNAL (Jones et al., 2013a). In a population study in the USA in 2014 of the association between biomarker concentrations and menthol cigarette use by race or ethnic group, NNAL concentrations were lower in all smokers of menthol than non-menthol cigarette smokers and in white smokers.

7.2 Smoking behaviour and topography

TPSAC (2011) reviewed studies of smoking behaviour and topography, including the number of puffs per cigarette, the average puff volume, the total puff volume, time to first cigarette and nicotine and CO levels before and after smoking a cigarette. The presence of menthol did not appear to increase inhalation of smoke from a cigarette (discussed in section 5 above). Although some studies suggested that menthol selectively enhances absorption of CO, it is difficult to generalize this finding. No studies were found on the effect of menthol cigarettes on inhalation parameters by novice, light or intermittent smokers.

7.3 Toxicity

The levels of smoke constituents in menthol and non-menthol cigarettes show little difference and no consistent difference (TPSAC, 2011; Bodnar et al., 2012). Internal industry documents suggest that high levels of menthol increase the amounts of tar and fine particles in cigarette smoke, and the increased particle formation was suggested to facilitate transfer of additive materials to the particle phase of the smoke to a greater extent than most other tobacco constituents. Smoke

generated from cigarettes to which menthol was added also delivered higher levels of formaldehyde and lead than smoke from control cigarettes (Lee & Glantz, 2011).

Gordon et al. (2011) assessed exposure to toxicants from a commercial non-menthol brand that was mentholated at four levels. Menthol in total particulate matter increased linearly with the added menthol concentration, but the amounts of nicotine, TSNAs, polycyclic aromatic hydrocarbons, cotinine and quinoline in the cigarettes remained essentially unchanged. In commercial Camel Crush cigarettes, the yield of volatile organic compounds appeared to increase in the presence of menthol. In a cross-over study, Brinkman and colleagues (2012) found no difference in the amount of fine particulate matter in menthol and non-menthol test cigarettes, although significantly larger masses of ultrafine particulate and fine particulate benzo[*a*]pyrene were collected from the menthol cigarettes.

Few studies have been conducted on whether menthol alters the toxicity of smoke. Fowler et al. (2012) found that treatment of rodent and human cells with menthol was cytotoxic but not genotoxic as measured by micronucleus induction. In a study of exposure of plant and human cell cultures to menthol and non-menthol cigarette smoke, cell death was significantly enhanced by mentholated smoke. Menthol alone was inert, suggesting that it contributed synergistically to cell death initiated by compounds in smoke (Noriyasu et al., 2013).

7.4 Cancer risk

Most of the studies reviewed by the FDA (2013a) and TPSAC (2011) showed no difference in the cancer risk of menthol and non-menthol cigarette smokers. Methodological limitations were identified, as none of the studies was designed to address the relative risks associated with smoking menthol cigarettes. Two studies reported that smokers of menthol cigarettes had a reduced risk for lung cancer (Blot et al., 2011; Rostron, 2012), but neither study accounted for differences in the design of the mentholated cigarettes, which had little or no filter ventilation, while the non-menthol cigarettes were more highly ventilated. A meta-analysis of data from 13 published studies on cancer mortality indicated that menthol cigarette use is associated with a lower risk for cancer than non-menthol cigarette use (Jones et al., 2013b). Although the cancer rates of Black and white smokers in the USA are significantly different, the difference does not appear to be attributable to use of menthol cigarettes (Kabat et al., 2012).

7.5 Non-cancer disease risk

Neither the FDA (2013a) nor TPSAC (2011) found that menthol cigarette smokers had higher risks for non-cancer disease than non-menthol cigarette smokers. More recent studies provide an indication of possible risk. Park et al. (2015) found that, although menthol cigarette smokers were not at higher risk for chronic obstructive pulmonary disease, they were more likely to experience severe exacerbation of such disease during longitudinal follow-up. Menthol cigarette smokers were twice as likely to have hypertension, a higher body mass index and abdominal obesity, and double the odds of moderate-to-high risk for cardiovascular disease (Míguez-Burbano et al., 2014). A meta-analysis of data from five studies indicated an increased risk for cardiovascular disease (Jones et al., 2013b). The evidence on the risk for stroke of menthol cigarette smokers in the USA is conflicting. An increased risk was found in one study (Vozoris, 2012), particularly among women and non-African Americans, but no increase was seen in a second study (Rostron, 2014). The risk for stroke was not increased among African-American menthol cigarette smokers, and the association with peripheral artery disease was similar for smokers of non-menthol and menthol cigarettes (Jones, 2013c).

7.6 Summary

Several reviews have commented on the shortcomings of the available epidemiological, clinical and laboratory research on menthol cigarettes (Clark & Gardiner, 2011; TPSAC, 2011; Besaratinia & Tommasi, 2015), and it is difficult to draw meaningful conclusions. There is no strong evidence that use of menthol cigarettes increases the delivery or toxicity of smoke or biomarkers of exposure to nicotine or toxicants. The finding of Noriyasu and colleagues (2013) that menthol alone is inert but increases cell death initiated by other smoke components deserves further investigation, as do potential differences in the delivery of fine and ultrafine particulate. Although there is little evidence that menthol cigarette smokers are at increased risk for cancer, recent studies support concern about the risks for non-cancer diseases, particularly of the cardiovascular system, and further investigation is warranted.

8. Effects on smoking behaviour, dependence and quitting

Menthol increases the harm of smoking primarily by increasing initiation and by reducing cessation by some groups of smokers. The main measures of these effects include differences in the rates of experimentation, progression from experimentation to long-term use and dependence, the strength of dependence, difficulty in quitting or more frequent relapse after cessation. Menthol may also increase the use of other harmful substances.

8.1 Initiation

Age is a significant predictor of the use of menthol products (TPSAC, 2011; FDA, 2013a; FDA, 2013b). Younger smokers are more likely than older smokers to smoke menthol cigarettes, and a higher proportion of younger than older adolescent smokers smoke menthol cigarettes (Hersey et al., 2006; Fernander et al., 2010; Hersey et al., 2010; Lawrence et al., 2010; Rock et al., 2010; Giovino et al., 2015). These observations suggest a role of menthol in initiation; however, the cross-sectional nature of these data limits the conclusions that can be drawn.

Self-reported age at first cigarette and age at starting regular smoking are similar for menthol and non-menthol cigarette smokers (TPSAC, 2011; Rosenbloom et al., 2012; Faseru et al., 2013). A national survey of adolescents, however, indicated that the longer the delay of initiation, the more likely an individual was to smoke menthol cigarettes (Fernander et al., 2010). A study by the tobacco industry (Curtin et al., 2014a) of self-reported age at initiation in four US national surveys found no difference between menthol and non-menthol cigarette smokers. The results

for adolescent smokers were inconclusive: the mean age at first cigarette smoked was reported to be about 9 months older and the mean age at first regular smoking 2–3 months younger than the overall rates.

Some studies indicate that more smokers of a few cigarettes (who might represent experimenters) smoke menthol cigarettes than non-menthol cigarettes (TPSAC, 2011). Less established smokers (< 1 year of smoking) are more likely to use menthol cigarettes than more established smokers (Hersey et al., 2006). In a cohort study in the USA, a larger proportion of students who recognized Newport (the leading menthol cigarette brand) at baseline initiated smoking. Although Newport was third in brand recognition, it was the only brand that was associated with future smoking behaviour (Dauphinee et al., 2013). These findings indicate that menthol cigarettes encourage experimentation by new or novice smokers.

8.2 Switching

More frequent switching from menthol to non-menthol cigarettes suggests that menthol cigarettes serve as a starter product, which could explain some of the observed age trends in menthol cigarette smoking. Switching between menthol and non-menthol cigarettes is uncommon for all smokers, regardless of race, indicating that they do not find menthol and non-menthol cigarettes close substitutes (Tauras et al., 2010). Non-menthol cigarettes are less frequently used as a substitute for menthol cigarettes than the reverse, and both young adult and African-American smokers in particular are less responsive to price with respect to switching between menthol and non-menthol cigarettes (Tauras et al., 2010). On the basis of reviews of unpublished data, TPSAC (2011) concluded that, at least in some populations of smokers, more menthol cigarette smokers switch to non-menthol cigarettes. The results for adolescents were inconclusive.

Kasza et al. (2014) found a very low prevalence of switching between menthol and non-menthol cigarettes in a representative US sample (3% switched to menthol and 8% switched to non-menthol cigarettes). Significantly more smokers switched from menthol to non-menthol cigarettes than from non-menthol to menthol cigarettes, confirming the findings of TPSAC (2011). Reversion to menthol cigarettes was more common than reversion to non-menthol cigarettes, particularly among Black smokers. Villanti et al. (2012) studied smokers aged 16–24 years in a cohort study and found that 15% of smokers of menthol cigarettes at baseline had switched to

non-menthol cigarettes and 7% of smokers of non-menthol cigarettes at baseline had switched to menthol cigarettes. Initiation with menthol cigarettes is a highly significant predictor of current menthol cigarette use at 1 year (Rath et al., 2015).

8.3 Progression to regular use

Evidence of the role of menthol in the progression to regular use was limited until recently. Delnevo et al. (2015) examined self-reported changes in the past year among young adults aged 18–34 years and found that menthol cigarette use nearly doubled the odds of increased smoking. Similarly, among US middle- and high-school students, initiating smoking with menthol cigarettes was strongly associated with progression to established smoking in a 3-year longitudinal cohort study (Nonnemaker et al., 2013). A survey of Canadian students in grades 9–12 found that menthol cigarette smokers smoked more cigarettes per day and had significantly greater odds for reporting their intent to continue smoking than non-menthol cigarette smokers (Azagba et al., 2014). The results were similar when separate analyses were conducted for established and experimental smokers. Together, these studies suggest that young people who start by smoking menthol cigarettes are at greater risk for progression to regular smoking.

8.4 Strength of addiction

Adolescent menthol cigarette smokers are more dependent on nicotine than adolescent non-menthol cigarette smokers, with higher measures of dependence (Hersey et al., 2006; Hersey et al., 2010), smoking urgency (e.g. needing a cigarette within 1 h) and craving or feeling irritable or restless after not smoking (Muilenburg & Legge, 2008; Hersey et al., 2010; TPSAC, 2011). Adolescent smokers who initiated smoking with menthol cigarettes had higher nicotine dependence scores (Nonnemaker et al., 2013), and menthol cigarette use was associated with a shorter time to needing a cigarette among both smokers who reported using a regular brand and among established smokers (Hersey et al., 2010). In New Zealand, differences by demographic and socioeconomic status in menthol cigarette preference among adolescent smokers were consistent with patterns found in the USA; however, there was no significant correlation between menthol cigarette preference and loss of autonomy, which is a measure of dependence (Li et al., 2012).

Adult menthol cigarette smokers are more likely to smoke their first cigarette within 5 min of waking (Fagan et al., 2010; Rosenbloom et al., 2012; D'Silva et al., 2012; Curtin et al., 2014b) and are more likely to wake at night to smoke (Bover et al., 2008; Gandhi et al., 2009) than non-menthol cigarette smokers. No difference was found between menthol and non-menthol cigarette smokers for many other standard measures of dependence (Brody et al., 2012; Faseru et al., 2013; Reitzel et al., 2013b; Curtin et al., 2014b). Smoking a menthol cigarette was not associated with a higher mean serum cotinine concentration than smoking a non-menthol cigarette in either Black or white smokers (Carabello et al., 2011; Muscat et al., 2012). In a study of adult menthol and non-menthol cigarette smokers, no difference was found in either the Fagerstrom test of nicotine dependence or the "heaviness of smoking" measure of dependence (Frost-Pineda et al., 2014). Female menthol cigarette smokers showed signs of greater dependence than female non-menthol cigarette smokers (Rosenbloom et al., 2012).

The evidence regarding daily consumption of menthol and non-menthol cigarette smokers is inconclusive, about half of the studies indicating no difference (TPSAC, 2011; Rosenbloom et al., 2012; FDA, 2013a) and most of the others showing that more non-menthol cigarettes are smoked per day (Fagan et al., 2010; Stahre et al., 2010; Wang et al., 2010; TPSAC, 2011; FDA, 2013a). Comparisons by race or ethnicity gave inconclusive results, some studies indicating a lower smoking rate only among white menthol cigarette smokers and others finding the reverse (TPSAC, 2011). Lawrence et al. (2010) found that 52% of menthol and 42% of non-menthol cigarette smokers smoked fewer than 10 cigarettes per day. In a cross-over study, participants who switched between menthol and non-menthol cigarettes smoked fewer menthol cigarettes per day (Brinkman et al., 2012).

These conflicting results for different measures of dependence among adult smokers suggest that the usual measures may not adequately describe the experience of menthol cigarette smokers. In a study of native Hawaiian, Filipino and white cigarette smokers aged 18–35 years, no significant differences were found on several scales of dependence; however, menthol cigarette smokers reported greater difficulty in refraining from smoking in places where it was forbidden, had greater difficulty in giving up the first cigarette in the morning and had higher subscale scores for social and environment goads in the Wisconsin Inventory of Smoking Dependence Motives, after control for covariates (Fagan et al., 2015b).

8.5 Intention to quit or seek treatment

Most studies indicate similar or higher rates of quit attempts among menthol cigarette smokers (Levy et al., 2011a), especially among Blacks (Kahende et al., 2011; Reitzel et al., 2013b), while others suggest that menthol cigarette use is associated with fewer quit attempts in some populations (Kahende et al., 2011; D'Silva et al., 2012). Black menthol cigarette smokers were more likely to have made a quit attempt than white non-menthol cigarette smokers (Kahende et al., 2011) and were more confident about quitting than Black non-menthol cigarette users (Reitzel et al., 2013a). Fagan et al. (2015a) found that more dependent menthol cigarette smokers were more likely to have tried to quit smoking in the past 12 months but were less likely to have tried to quit several times.

No published studies were found on the effect of menthol cigarettes on cessation among adolescent smokers. Menthol cigarette smokers aged 18–34 years were more likely to report intention to quit, but no difference was found between menthol and non-menthol cigarette users in ever attempting to quit (Rath et al., 2015).

8.6 Cessation outcomes and relapse rates

Both TPSAC (2011) and the FDA (2013a) raised concern about the quality of the data available on cessation outcomes. No studies were found that were designed specifically to evaluate the role of menthol cigarettes in cessation. Population surveys of differences in menthol cigarette smoking by racial or ethnic group indicate that non-whites, particularly African Americans, who smoke menthol cigarettes have lower quit rates than non-whites who smoke non-menthol cigarettes (Foulds et al., 2010; TPSAC, 2011). The results on quit rates among white menthol and non-menthol cigarette smokers were inconclusive (Foulds et al., 2010; TPSAC, 2011). Menthol cigarette smokers were less likely to be former smokers (Delnevo et al., 2011). The analysis by the FDA (2013a) of the 2006–2007 Tobacco Use Supplement to the Current Population Survey in the USA indicated that use of menthol cigarettes makes cessation more difficult. Reitzel et al. (2011) found that women who quit smoking during or immediately before pregnancy were more likely to relapse postpartum if they had smoked menthol cigarettes.

Rojewski et al. (2014) investigated whether use of menthol cigarettes predicted smoking cessation outcomes among smokers who had sought treatment. Menthol

cigarette smokers had lower quit rates and gained significantly more weight than non-menthol cigarette smokers who quit. In a randomized double-blind trial of the efficacy of bupropion in promoting cessation in adult African-American smokers of ≤ 10 cigarettes per day who were seeking treatment, smokers of non-menthol cigarettes were more likely to remain abstinent throughout treatment (Faseru et al., 2013). In a cohort study in the USA, menthol cigarette use was not significantly associated with smoking abstinence; however, a significant difference was found by race: white menthol cigarette smokers were five times less likely than white non-menthol cigarette smokers to remain abstinent (Reitzel et al., 2013b). In other studies, fewer menthol cigarette smokers attempted cessation, after control for treatment (Smith et al., 2014) or the tobacco control environment (Lewis et al., 2014). In contrast, an analysis by the tobacco industry (Sulsky et al., 2014) of data from several surveys identified no consistent difference between menthol and non-menthol cigarette smokers in success in quitting.

TPSAC (2011) found little evidence of an effect of menthol cigarette use on the effectiveness of cessation medication, particularly in studies in which medications were recommended (Foulds et al., 2006; Gandhi et al., 2009). Okuyemi et al. (2012) found no significant effect of menthol cigarette smoking on the pharmacokinetics of bupropion and its metabolites at steady state. Faseru et al. (2013) found that, while smoking menthol cigarettes was negatively associated with quitting, it did not affect the response to pharmacotherapy.

8.7 Effects on use of other tobacco products and of drugs

Emerging evidence suggests that menthol cigarette use may increase the use of other tobacco products and of drugs, particularly among adolescents. Among high-school students in the USA, menthol cigarette use increases the odds for use of marijuana use beyond that associated with regular cigarette smoking (Kong et al., 2013). Menthol use was also a significant correlate for use of little cigars (Cohn et al., 2015). Students in grades 7–12 in Canada who smoked menthol cigarettes were significantly more likely to participate in binge drinking and to use marijuana than non-menthol cigarette smokers (Azagba & Sharaf, 2014). The presence of menthol did not significantly reduce the urge to smoke after short-term use of e-cigarettes (D'Ruiz, 2015).

Winhusen et al. (2013) assessed the association between menthol cigarette use and dependence on cocaine and methamphetamines. Cocaine-dependent participants who smoked menthol cigarettes were significantly more likely to report that cigarettes prolonged their cocaine high than non-menthol cigarette smokers and were less likely to abstain from stimulants during active treatment. No difference was found between methamphetamine-dependent menthol and non-menthol smokers. There were significantly more white menthol cigarette smokers among the cocaine-dependent participants (37%) than the methamphetamine-dependent participants (18%).

8.8 Summary

Menthol cigarette smoking is most common among younger smokers, and these cigarettes appear to promote experimentation among new or novice smokers. Most smokers who begin smoking menthol cigarettes continue to smoke them after progressing to regular use. Menthol cigarettes more often support progression to regular use than non-menthol cigarettes among adolescent and young adult smokers. Adolescent menthol cigarette smokers are more dependent on nicotine than those who smoke non-menthol cigarettes. The results of comparisons of measures of dependence among adult smokers are conflicting. The common observation that menthol cigarette smokers smoke fewer cigarettes per day yet score higher on specific measures of dependence (particularly time to first cigarette and waking at night to smoke) may indicate that menthol cigarettes have different physiological effects from non-menthol cigarettes, as described in section 6. Menthol cigarette smokers have similar or more frequent intentions to quit as non-menthol cigarette smokers, and young, highly dependent and Black menthol cigarette smokers more often intend to quit. Growing evidence indicates that menthol cigarette smokers are less successful in quitting than those who smoke non-menthol cigarettes and are more likely to relapse after quitting. Menthol cigarette smoking does not appear to affect the efficacy of pharmacotherapy, but it can increase the reinforcing effects of other stimulants such as cocaine (Winhusen et al., 2013) and is a significant risk factor among adolescents for using other drugs, including alcohol (Azagba & Sharaf, 2014) and marijuana (Kong et al., 2013; Azagba & Sharaf, 2014).

9. Regulation of menthol

Articles 9 and 10 of the WHO FCTC address the regulation of tobacco product contents and emissions. To support countries in implementing these articles, the Conference of the Parties issued partial guidelines on the restriction or prohibition of ingredients used to increase palatability, including sugars, sweeteners and flavouring agents that mask the harshness of tobacco products (WHO, 2010). No specific recommendations have yet been issued with respect to menthol.

9.1 Existing regulatory control

On the basis of the partial guidelines, many governments have regulated or banned specific additives in tobacco products to decrease their attractiveness, particularly to adolescents. In 2012, the Brazilian regulatory authority approved a ban on all flavour additives, including menthol, in all tobacco products (ANVISA, 2012), although this ban remains suspended by an injunction from a higher court. The Tobacco Control Legal Consortium (2015) summarized regulations on flavours, including menthol, in various countries. Canada amended its Tobacco Act in 2009 to ban the use of additives that have flavouring properties or enhance flavour; however, the act excludes menthol. Five provinces (Alberta, Ontario, Quebec, New Brunswick and Nova Scotia) have since enacted regulations prohibiting use of all flavourings, including menthol. The Nova Scotia and Alberta bans are in force but are currently being challenged in court; the ban in New Brunswick was in force as of January 2016, the ban in Quebec will be in force as of May 2016, and that in Ontario will be in force as of January 2017. Ethiopia banned the sale and distribution of all flavoured tobacco products, including with menthol, as of 21 September 2015. In Chile, a bill banning the sale of menthol tobacco

products passed the Senate but requires the consent of the other house and the President's signature. The European Union will ban tobacco products (starting with cigarettes and roll-your-own tobacco) with flavours as of May 2016, with a transitional period until May 2020 for products with a market share > 3% (i.e. menthol cigarettes); the use of flavourings in capsules will be banned as of May 2016. Turkey will ban menthol in cigarettes and hand-rolled tobacco at the manufacturer level as of 1 January 2019 and at the retail level as of 20 May 2020. The ban applies to any quantity of menthol, including low levels in cigarettes that are not marketed as menthol cigarettes. In the USA, the FDA banned use of "characterizing" flavours (e.g. strawberry, grape, orange, cherry and coffee) in cigarettes in 2009. Menthol was excluded from the ban; the FDA continues to deliberate on whether to regulate this flavour.

9.2 Support for regulation

In a representative survey in Australia in 2013, 76% of participants supported or strongly supported a measure banning additives (all flavours) in order to make tobacco products less attractive to young people, while only 5% opposed the measure (Australian Institute of Health and Welfare, 2013). The majority of smokers (59%) in a representative sample of adults in the USA opposed a ban on menthol, which represents more than twice the proportion (24%) that opposed a reduction in nicotine. Smokers were significantly less supportive than non-smokers, and African-American smokers were more supportive of removing menthol than non-African-American smokers (Bolcic-Jankovic & Biener, 2014). Another survey in the USA also found significantly more support for reducing nicotine than for banning menthol (67% versus 19%) (Fix et al., 2011). Pearson et al. (2012) found little support for banning menthol in the US population as a whole (20%) and among menthol cigarette smokers (13%). These findings indicate that the US public requires more education on menthol cigarettes. US smokers who support removal of menthol are significantly more likely to prefer that removal be done gradually over a period of years rather than immediately (Bolcic-Jankovic & Biener, 2014).

The results of surveys in other regions would be useful.

9.3 Challenges to regulation

Despite the considerable evidence assembled by the TPSAC (2011) and the FDA (2013a), a ban on menthol in the USA has encountered significant challenges. Proposals to ban menthol in cigarettes raised concern about the disproportionate impact on racial or ethnic populations who prefer these products. The tobacco industry has attempted to put the science on menthol use and health effects into question (Heck, 2009; Heck, 2010; Wang et al., 2010). In addition, the tobacco industry challenged the composition of the TPSAC, which resulted in a legal decision that three members of the Advisory Council should be precluded from participating in the panel because they were expert witnesses in tobacco-related litigation, which was ruled to be a violation of conflict of interest provisions. As a result, the FDA could not use any of the conclusions in the TPSAC (2011) report. The ruling has been appealed; a final decision has yet to be issued.

Similar industry activities were reported in other jurisdictions.

9.4 Potential effects of a menthol ban

In Brazil, the ban on additives was faced with multiple legal injunctions and a huge volume of documents provided by the industry, opposing the ban. The tobacco industry and its front groups requested exceptions for a number of additives, all of which then required further independent analysis. The constitutionality of ANVISA itself was also challenged.[14] In the European Union, in a massive lobby against the directive on tobacco products, more than 100 lobbyists were hired, and the Health Commissioner was eventually forced to resign.

Regulators must also be aware of potential trade issues. In June 2010, Indonesia filed a complaint with the World Trade Organization, challenging the US ban on "characterizing" flavours. Indonesia argued that the provision resulted in less favourable treatment of an imported Indonesian product (clove cigarettes) than of a "like" domestic product (menthol cigarettes).

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[14] Figueiredo VC. Flavored cigarettes: perceptions, use and regulatory responses in Brazil. Presentation at the 4th Latin American and Caribbean Conference on Tobacco or Health. Center for Studies on Tobacco and Health. National School of Public Health; 2014 (http://www.tobaccoorhealthlac.org/files/Cigarrillos_con_saborizantes-VALESKA_CARVALHO.pdf).

In a survey in the USA in 2014, 66% of young adult menthol cigarette smokers reported that they would quit smoking if menthol cigarettes were no longer sold, while 18% said they would switch to non-menthol cigarettes, and 16% said they would switch to some other tobacco product. More Black menthol cigarette smokers (79%) reported an intention to quit than other menthol cigarette smokers who indicated concurrent use of other tobacco products (Wackowski et al., 2014). Earlier surveys indicated that two of five US adult menthol cigarette smokers would quit smoking altogether rather than switch to non-menthol cigarettes (Pearson et al., 2012; Wackowski & Delnevo, 2015).

A smoking simulation model based on data from the Tobacco Use Supplement to the 2003 Current Population Survey in the USA projected that a ban on menthol would result in a reduction in smoking prevalence of 10% overall and 25% for Blacks (Levy et al., 2011b).

A survey in 2015 included the option of switching to menthol e-cigarettes in the event of a ban on menthol cigarettes (Wackowski et al., 2015); 15% of menthol cigarette smokers said they would switch to menthol e-cigarettes. No significant differences were found by gender, age or current e-cigarette use, but higher percentages of Black (23%) and white (18%) menthol cigarette smokers said they would switch to mentholated e-cigarettes as compared with Hispanics. The percentage of menthol cigarette smokers who reported that they would quit smoking and not use any other product (28%) was lower than that found in previous studies, suggesting that the introduction of e-cigarettes could change outcomes in the event of a ban on menthol.

There is little basis for predicting the unintended consequences of a menthol ban, such as use of contraband products or post-marketing mentholation of products. A survey in the USA found that 25% of menthol cigarette smokers (< 11% of all smokers) would seek illegal menthol products, while 35% reported that they would quit (O'Connor et al., 2012). Arguments about the introduction of contraband products have been made by sources with a vested interest in the profitability of the tobacco industry; the scenarios presented are hypothetical, and none is based on factual evidence. No information is available about changes in the circulation of contraband products in regions where regulations have been implemented.

9.5 Summary

Following Brazil's passage of a menthol ban, Ethiopia, Turkey, the European Union, a number of provinces in Canada, and other health authorities are considering or have begun enactment of regulations targeting menthol. Legal and scientific challenges from the tobacco industry present important obstacles to regulation. Lack of public support for a menthol ban is another obstacle in some countries; significant public education may be necessary to publicize the negative impact of menthol cigarettes on public health. Limited data from surveys suggest that a ban on menthol would reduce overall tobacco use, as many current menthol cigarette smokers indicated that they would quit smoking if menthol cigarettes were no longer available.

10. Conclusions

Although this document suggests several areas for research, prompt elimination of menthol should not be delayed. There is already sufficient evidence to ban the use of menthol in cigarettes: a number of studies indicate that eliminating menthol from cigarettes would have significant public health benefits. Therefore, countries should be encouraged to prohibit menthol and its analogues, precursors or derivatives in cigarettes. Furthermore, in accordance with the partial guidelines for implementation of Articles 9 and 10, countries are also encouraged to consider eliminating menthol in other tobacco products.

The main conclusions of this advisory note are listed below.

- The prevalence of menthol cigarette use differs substantially among countries. The rates of use approach 50% in some countries but are negligible in others.

- Evidence from several countries indicates that menthol cigarettes are smoked more often by youth, young adults and women. The rates of menthol cigarette use in some countries are higher among racial or ethnic minorities and other vulnerable populations, including smokers with psychiatric disorders.

- Marketing contributes to the greater use of menthol cigarettes by youth and women and some other populations, with tailored advertising and proposal of products with different amounts of menthol or menthol capsules.

- Consistent with these marketing themes and the unique sensory effects of menthol, smokers in all the countries for which data are available have positive perceptions about menthol cigarettes, such as their "smoothness" or "mildness" and implicit health benefits or reduced health risks.

- Menthol cigarettes promote experimentation and progression to regular use to a greater extent than non-menthol cigarettes among youth.

- Adolescent menthol cigarette smokers are more dependent than those who smoke non-menthol cigarettes. The results of studies of the dependence of adult menthol and non-menthol cigarette smokers are inconclusive, but certain important measures (time to first cigarette, waking at night to smoke) are consistently more prevalent in menthol cigarette smokers.

- The rate of intention to quit among menthol cigarette smokers is similar to or higher than that of non-menthol cigarette smokers, but they are less successful in quitting.

11. Recommendations

- In view of the weight of the evidence, a ban on menthol in cigarettes is recommended, which should include menthol analogues, precursors and derivatives.

- In accordance with the partial guidelines for implementation of Articles 9 and 10, countries also should consider prohibiting menthol in products other than cigarettes.

- In countries in which menthol has little or no market penetration, use of menthol in tobacco products should be banned pre-emptively.

- Where a ban has not been implemented, countries should draw public attention to the negative effects of menthol, ensure that it plays no part in any tobacco promotional activities, and seek the support of all relevant stakeholders to move towards a ban.

- Surveillance should include monitoring of menthol product use and evaluation of the effects of a ban on menthol.

- Countries should consider making cessation services accessible, as stated in Article 14, to facilitate quitting smoking of menthol cigarettes and use of other tobacco products.

12. References

Abobo CV, Ma J, Liang D (2012) Effect of menthol on nicotine pharmacokinetics in rats after cigarette smoke inhalation. Nicotine Tob Res 14:801–808.

Ahijevych K, Garrett BE (2004) Menthol pharmacology and its potential impact on cigarette smoking behavior. Nicotine Tob Res 6(Suppl.1):S17–S28.

Ai J, Taylor KM, Lisko JG, Tran H, Watson CH, Holman MR (2015) Menthol content in US marketed cigarettes. Nicotine Tob Res doi:10.1093/ntr/ntv162 [Epub ahead of print].

Allen B, Cruz TB, Leonard E (2010) Development and validation of a scale to assess attitudes and beliefs about menthol cigarettes among African-American smokers. Eval Health Prof 33:414–436.

Alsharari SD, King JR, Nordman JC, Muldoon PP, Jackson A, Zhu AZ, et al. (2015) Effects of menthol on nicotine pharmacokinetic, pharmacology and dependence in mice. PLoS One 10;10.

Anderson SJ (2011) Marketing of menthol cigarettes and consumer perceptions: a review of tobacco industry documents. Tob Control 20(Suppl.2):ii20–ii28.

ANVISA (Brazilian Health Surveillance Agency) (2012) News. Anvisa approves the withdrawal of flavored cigarettes. Brasilia (http://portal.anvisa.gov.br/wps/portal/anvisa-ingles/anvisaingles/News/!ut/p/c4/04_SB8K8xLLM9MSSzPy8xBz9CP0os3hfRw8jD0NnA3cLSw83A-08jS18nMwNnAxN3I_2CbEdFAHlqbj8!/?WCM_PORTLET=PC_7_MAH2H1C0G89HF0I29MB60C0441020591_WCM&WCM_GLOBAL_CONTEXT=/wps/wcm/connect/anvisa+ingles/anvisa/news/anvisa+approves+the+withdrawal+of+flavored+cigarettes).

Ashley M, Dixon M, Sisodiya A, Prasad K (2012) Lack of effect of menthol level and type on smokers' estimated mouth level exposures to tar and nicotine and perceived sensory characteristics of cigarette smoke. Regul Toxicol Pharmacol 63:381–390.

Ashoor A, Nordman JC, Veltri D, Yang KH, Al Kury L, Shuba Y, et al. (2013) Menthol binding and inhibition of α7-nicotinic acetylcholine receptors. PLoS One 8:e67674.

Australian Institute of Health and Welfare (2015) National Drug Strategy Household Survey, 2013. Canberra: Australian National University (http://www.aihw.gov.au/data/).

Azagba S, Sharaf MF (2014) Binge drinking and marijuana use among menthol and non-menthol adolescent smokers: findings from the youth smoking survey. Addict Behav 39:740–743.

Azagba S, Minaker LM, Sharaf MF, Hammond D, Manske S (2014) Smoking intensity and intent to continue smoking among menthol and non-menthol adolescent smokers in Canada. Cancer Causes Control 25:1093–1099.

Bautista DM, Siemens J, Glazer JM, Tsuruda PR, Basbaum AI, Stucky CL, et al. (2007) The menthol receptor TRPM8 is the principal detector of environmental cold. Nature 448:204–208.

Benowitz NL, Hukkanen J, Jacob P 3rd (2009) Nicotine chemistry, metabolism, kinetics and biomarkers. Handb Exp Pharmacol 192:29–60.

Benowitz NL, Dains KM, Dempsey D, Havel C, Wilson M, Jacob P 3rd (2010) Urine menthol as a biomarker of mentholated cigarette smoking. Cancer Epidemiol Biomarkers Prev 19:3013–3019.

Besaratinia A, Tommasi S (2015) The lingering question of menthol in cigarettes. Cancer Causes Control 26:165–169.

Blot WJ, Cohen SS, Aldrich M, McLaughlin JK, Hargreaves MK, Signorello LB (2011) Lung cancer risk among smokers of menthol cigarettes. J Natl Cancer Inst 103:810–816.

Bodnar JA, Morgan WT, Murphy PA, Ogden MW (2012) Mainstream smoke chemistry analysis of samples from the 2009 US cigarette market. Regul Toxicol Pharmacol 64:35–42.

Bessac BF, Jordt SE (2008) Breathtaking TRP channels: TRPA1 and TRPV1 in airway chemosensation and reflex control. Physiology (Bethesda) 23:360–370.

Bolcic-Jankovic D, Biener L (2014) Public opinion about FDA regulation of menthol and nicotine. Tob Control 24:e241–e245.

Bover MT, Foulds J, Steinberg MB, Richardson D, Marcella SW (2008) Waking at night to smoke as a marker for tobacco dependence: patient characteristics and relationship to treatment outcome. Int J Clin Pract 62:182–190.

Brennan E, Gibson L, Momjian A, Hornik RC (2015) Are young people's beliefs about menthol cigarettes associated with smoking-related intentions and behaviors? Nicotine Tob Res 17:81–90.

Brinkman MC, Chuang JC, Gordon SM, Kim H, Kroeger RR, Polzin GM, et al. (2012) Exposure to and deposition of fine and ultrafine particles in smokers of menthol and nonmenthol cigarettes. Inhal Toxicol 24:255–269.

Brody AL, Mukhin AG, La Charite J, Ta K, Farahi J, Sugar CA, et al. (2013) Up-regulation of nicotinic acetylcholine receptors in menthol cigarette smokers. Int J Neuropsychopharmacol 16:957–966.

Buday T, Brozmanova M, Biringerova Z, Gavliakova S, Poliacek I, Calkovsky V, et al. (2012) Modulation of cough response by sensory inputs from the nose – role of trigeminal TRPA1 versus TRPM8 channels. Cough 8:11.

Caraballo RS, Asman K (2011) Epidemiology of menthol cigarette use in the United States. Tob Induced Dis 9(Suppl.1):S1.

Caraballo RS, Holiday DB, Stellman SD, Mowery PD, Giovino GA, Muscat JE, et al. (2011) Comparison of serum cotinine concentration within and across smokers of menthol and nonmenthol cigarette brands among non-Hispanic black and non-Hispanic white US adult smokers, 2001-2006. Cancer Epidemiol Biomarkers Prev 2011;20:1329–1340.

Cardello AV, Wise PM (2008) Taste, smell and chemesthesis in product experience. In: Schifferstein R, Hekkert P, editors. Product experience. Amsterdam: Elsevier; 91–103.

Castro FG (2004) Physiological, psychological, social, and cultural influences on the use of menthol cigarettes among Blacks and Hispanics. Nicotine Tob Res 6(Suppl.1):S29–S41.

Celebucki CC, Wayne GF, Connolly GN, Pankow JF, Chang EI (2005) Characterization of measured menthol in 48 US cigarette sub-brands. Nicotine Tob Res 7:523–531.

Chen C, Isabelle LM, Pickworth WB, Pankow JF (2010) Levels of mint and wintergreen flavorants: smokeless tobacco products vs. confectionery products. Food Chem Toxicol 48:755–763.

Chen C, Luo W, Isabelle LM, Gareau KD, Pankow JF (2011) The stereoisomers of menthol in selected tobacco products. A brief report. Nicotine Tob Res 13:741–745.

Clark PI, Gardiner P (2011) Menthol should not be given a free pass based on studies of biomarkers of toxicity. Cancer Epidemiol Biomarkers Prev 20:1269–1271.

Cohn A, Cobb CO, Niaura RS, Richardson A (2015) The other combusted products: prevalence and correlates of little cigar/cigarillo use among cigarette smokers. Nicotine Tob Res 17:1473–1481.

Connolly GN, Behm I, Osaki Y, Wayne GF (2011) The impact of menthol cigarettes on smoking initiation among non-smoking young females in Japan. Int J Environ Res Public Health 8:1–14.

Cruz TB, Wright LT, Crawford G (2010) The menthol marketing mix: targeted promotions for focus communities in the United States. Nicotine Tob Res 12(Suppl.2):S147–S153.

Curtin GM, Sulsky SI, Van Landingham C, Marano KM, Graves MJ, Ogden MW, et al. (2014a) Measures of initiation and progression to increased smoking among current menthol compared to non-menthol cigarette smokers based on data from four US Government surveys. Regul Toxicol Pharmacol 70:446–456.

Curtin GM, Sulsky SI, Van Landingham C, Marano KM, Graves MJ, Ogden MW, et al. (2014b) Primary measures of dependence among menthol compared to non-menthol cigarette smokers in the United States. Regul Toxicol Pharmacol 69:451–466

Dauphinee AL, Doxey JR, Schleicher NC, Fortmann SP, Henriksen L (2013) Racial differences in cigarette brand recognition and impact on youth smoking. BMC Public Health 13:170.

Davis S, McClave-Regan A, Rock V, Kruger J, Garrett B (2010) Perceptions of menthol cigarette use among US adults and adult smokers: findings from the 2009 Health Styles survey. Nicotine Tob Res 12(Suppl.2):S125–S135.

Delnevo CD, Gundersen DA, Hrywna M, Echeverria SE, Steinberg MB (2011) Smoking-cessation prevalence among US smokers of menthol versus non-menthol cigarettes. Am J Prev Med 41:357–365.

Delnevo CD, Villanti AC, Giovino GA. Trends in menthol and non-menthol cigarette consumption in the USA: 2000–2011. Tob Control 2014;23:e154–e155.

Delnevo CD, Villanti AC, Wackowski OA, Gundersen DA, Giovenco DP (2015) The influence of menthol, e-cigarettes and other tobacco products on young adults' self-reported changes in past year smoking. Tob Control doi: 10.1136/tobaccocontrol-2015-052325. [Epub ahead of print].

DiFranza JR, Clark DW, Pollay RW (2002) Cigarette package design: opportunities for disease prevention. Tob Induced Dis 1:97–109.

Dolka C, Piadé JJ, Belushkin M, Jaccard G (2013) Menthol addition to cigarettes using breakable capsules in the filter. Impact on the mainstream smoke yields of the Health Canada list constituents. Chem Res Toxicol 26:1430–1443.

D'Ruiz CD, Graff DW, Yan XS (2015) Nicotine delivery, tolerability and reduction of smoking urge in smokers following short-term use of one brand of electronic cigarettes. BMC Public Health 15:991.

D'Silva J, Boyle RG, Lien R, Rode P, Okuyemi KS (2012) Cessation outcomes among treatment-seeking menthol and nonmenthol smokers. Am J Prev Med 43(Suppl.3):S242–S248.

Eccles R (2000) Role of cold receptors and menthol in thirst, the drive to breathe and arousal. Appetite 2000;34:29–35.

Fagan P, Moolchan ET, Hart A Jr, Rose A, Lawrence D, Shavers VL, et al. (2010) Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns. Addiction 105(Suppl.1):55–74.

Fagan P, Moolchan ET, Pokhrel P, Herzog T, Cassel KD, Pagano I, et al. (2015a) Biomarkers of tobacco smoke exposure in racial/ethnic groups at high risk for lung cancer. Am J Public Health 105:1237–1245.

Fagan P, Pohkrel P, Herzog T, Pagano I, Vallone D, Trinidad DR, et al. (2015b) Comparisons of three nicotine dependence scales in a multiethnic sample of young adult menthol and non-menthol smokers. Drug Alcohol Depend 149:203–211.

Faseru B, Choi WS, Krebill R, Mayo MS, Nollen NL, Okuyemi KS, et al. (2011) Factors associated with smoking menthol cigarettes among treatment-seeking African American light smokers. Addict Behav 36:1321–1324.

Faseru B, Nollen NL, Mayo MS, Krebill R, Choi WS, Benowitz NL, et al. (2013) Predictors of cessation in African American light smokers enrolled in a bupropion clinical trial. Addict Behav 38:1796–1803.

FDA (Food and Drug Administration) (2013a) Preliminary scientific evaluation of the possible public health effects of menthol versus nonmenthol cigarettes. Silver Spring, Maryland: Center for Tobacco Products (http://www.fda.gov/downloads/UCM361598.pdf).

FDA (Food and Drug Administration) (2013b) Reference addendum: preliminary scientific evaluation of the possible public health effects of menthol versus nonmenthol cigarettes. Silver Spring, Maryland: Center for Tobacco Products (http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PeerReviewofScientificInformationandAssessments/UCM362600.pdf).

Fernander A, Rayens MK, Zhang M, Adkins S (2010) Are age of smoking initiation and purchasing patterns associated with menthol smoking? Addiction 105(Suppl.1):39–45.

Ferris WG, Connolly GN (2004) Application, function, and effects of menthol in cigarettes: a survey of tobacco industry documents. Nicotine Tob Res 6(Suppl.1):S43–S54.

Fix BV, O'Connor RJ, Fong GT, Borland R, Cummings KM, Hyland A (2011) Smokers' reactions to FDA regulation of tobacco products: findings from the 2009 ITC United States survey. BMC Public Health 11:941.

Foulds J, Gandhi KK, Steinberg MB, Richardson DL, Williams JM, Burke MV, et al. (2006) Factors associated with quitting smoking at a tobacco dependence treatment clinic. Am J Health Behav 30:400–412.

Foulds J, Hooper MW, Pletcher MJ, Okuyemi KS (2010) Do smokers of menthol cigarettes find it harder to quit smoking? Nicotine Tob Res 12(Suppl.2):S102–S109.

Fowler P, Smith K, Young J, Jeffrey L, Kirkland D, Pfuhler S, et al. (2012) Reduction of misleading ("false") positive results in mammalian cell genotoxicity assays. I. Choice of cell type. Mutat Res 742:11–25.

Frost-Pineda K, Muhammad-Kah R, Rimmer L, Liang Q (2014) Predictors, indicators, and validated measures of dependence in menthol smokers. J Addict Dis 33:94–113.

Gandhi KK, Foulds J, Steinberg MB, Lu SE, Williams JM (2009) Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic. Int J Clin Pract 63:360–367.

Giovino GA, Sidney S, Gfroerer JC, O'Malley PM, Allen JA, Richter PA, et al. (2004) Epidemiology of menthol cigarette use. Nicotine Tob Res 6(Suppl.1):S67–S81.

Giovino GA, Villanti AC, Mowery PD, Sevilimedu V, Niaura RS, Vallone DM, et al. (2015) Differential trends in cigarette smoking in the USA: is menthol slowing progress? Tob Control 24:28–37.

Gordon SM, Brinkman MC, Meng RQ, Anderson GM, Chuang JC, Kroeger RR, et al. (2011) Effect of cigarette menthol content on mainstream smoke emissions. Chem Res Toxicol 24:1744–1753.

Ha MA, Smith GJ, Cichocki JA, Fan L, Liu YS, Caceres AI, et al. (2015) Menthol attenuates respiratory irritation and elevates blood cotinine in cigarette smoke exposed mice. PLoS One 10:e0117128.

Hammond D, Parkinson C (2009) The impact of cigarette package design on perceptions of risk. J Public Health 31:345–353.

Hans M, Wilhelm M, Swandulla D (2012) Menthol suppresses nicotinic acetylcholine receptor functioning in sensory neurons via allosteric modulation. Chem Senses 37:463–469.

Heck JD (2009) Smokers of menthol and nonmenthol cigarettes exhibit similar levels of biomarkers of smoke exposure. Cancer Epidemiol Biomarkers Prev 18:622–629.

Heck JD (2010) A review and assessment of menthol employed as a cigarette flavoring ingredient. Food Chem Toxicol 48(Suppl.2):S1–S38.

Hersey JC, Nonnemaker JM, Homsi G (2010) Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. Nicotine Tob Res 12(Suppl.2):S136–S146.

Hersey JC, Ng SW, Nonnemaker JM, Mowery P, Yhomas KY, Vilsain MC, et al. (2006) Are menthol cigarettes a starter product for youth? Nicotine Tob Res 8:403–413.

Hickman NJ 3rd, Delucchi KL, Prochaska JJ (2014) Menthol use among smokers with psychological distress: findings from the 2008 and 2009 National Survey on Drug Use and Health. Tob Control 23:7–13.

Hoffman AC (2011) The health effects of menthol cigarettes as compared to non-menthol cigarettes. Tob Induced Dis 9(Suppl.1):S7.

Jones MR, Apelberg BJ, Tellez-Plaza M, Samet JM, Navas-Acien A (2013a). Menthol cigarettes, race/ethnicity, and biomarkers of tobacco use in US adults: the 1999–2010 National Health and Nutrition Examination Survey (NHANES). Cancer Epidemiol Biomarkers Prev 22:224–232.

Jones MR, Tellez-Plaza M, Navas-Acien A (2013b) Smoking, menthol cigarettes and all-cause, cancer and cardiovascular mortality: evidence from the National Health and Nutrition Examination Survey (NHANES) and a meta-analysis. PLoS One 8:e77941.

Jones MR, Apelberg BJ, Samet JM, Navas-Acien A (2013c) Smoking, menthol cigarettes, and peripheral artery disease in US adults. Nicotine Tob Res 15:1183–1189.

Kabat GC, Shivappa N, Hébert JR (2012) Mentholated cigarettes and smoking-related cancers revisited: an ecologic examination. Regul Toxicol Pharmacol 63:132–139.

Kabbani N (2013) Not so cool? Menthol's discovered actions on the nicotinic receptor and its implications for nicotine addiction. Front Pharmacol 4:95.

Kahende JW, Malarcher AM, Teplinskaya A, Asman KJ (2011) Quit attempt correlates among smokers by race/ethnicity. Int J Environ Res Public Health 8:3871–3888.

Kaleta D, Usidame B, Szosland-Fałtyn A, Makowiec-Dąbrowska T (2014) Use of flavoured cigarettes in Poland: data from the global adult tobacco survey (2009–2010). BMC Public Health 14:127.

Kamatou GP, Vermaak I, Viljoen AM, Lawrence BM (2013) Menthol: a simple monoterpene with remarkable biological properties. Phytochemistry 96:15–25.

Karashima Y, Damann N, Prenen J, Talavera K, Segal A, Voets T, et al. (2007) Bimodal action of menthol on the transient receptor potential channel TRPA1. J Neurosci 27:9874–9884.

Kasza KA, Hyland AJ, Bansal-Travers M, Vogl LM, Chen J, Evans SE, et al. (2014) Switching between menthol and nonmenthol cigarettes: findings from the US cohort of the International Tobacco Control Four Country Survey. Nicotine Tob Res 16:1255–1265.

King B, Yong HH, Borland R, Omar M, Ahmad AA, Sirirassamee B, et al. (2010) Malaysian and Thai smokers' beliefs about the harmfulness of 'light' and menthol cigarettes. Tob Control 19:444–450.

King B, White V, Balmford J, Cooper J, Borland R (2012) The decline of menthol cigarette smoking in Australia, 1980–2008. Nicotine Tob Res 14:1213–1220.

Klausner K (2011) Menthol cigarettes and smoking initiation: a tobacco industry perspective. Tob Control 20(Suppl.2):ii12–ii19.

Kong G, Singh N, Camenga D, Cavallo D, Krishnan-Sarin S (2013) Menthol cigarette and marijuana use among adolescents. Nicotine Tob Res 15:2094–2099.

Kreslake JM, Yerger VB (2010) Tobacco industry knowledge of the role of menthol in chemosensory perception of tobacco smoke. Nicotine Tob Res 12(Suppl.2):S98–S101.

Kreslake JM, Wayne GF, Alpert HR, Koh HK, Connolly GN (2008a) Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. Am J Public Health 98:1685–1692.

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 Tob Res 10:705–715.

Kuhn FJP, Kuhn C, Lückhoff A (2009) Inhibition of TRPM8 by icilin distinct from desensitization induced by menthol and menthol derivatives. J Biol Chem 284:4102–4111.

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

Lee YO, Glantz SA (2011) Menthol: putting the pieces together. Tob Control 20(Suppl.2):ii1–ii7.

Lee HJ, Pi SH, Kim Y, Kim HS, Kim SJ, Kim YS, et al. (2009) Effects of nicotine on antioxidant defense enzymes and RANKL expression in human periodontal ligament cells. J Periodontol 80:1281–1288.

Lee JG, Henriksen L, Rose SW, Moreland-Russell S, Ribisl KM (2015) A systematic review of neighborhood disparities in point-of-sale tobacco marketing. Am J Public Health 105:e8–e18.

Leffingwell JC (2015) Cool without menthol & cooler than menthol and cooling compounds as insect repellents. Canton, Georgia: Leffingwell & Associates (http://www.leffingwell.com/cooler_than_menthol.htm).

Levy DT, Pearson JL, Villanti AC, Blackman K, Vallone DM, Niaura RS, et al. (2011a) Modeling the future effects of a menthol ban on smoking prevalence and smoking-attributable deaths in the United States. Am J Public Health 101:1236–1240.

Levy DT, Blackman K, Tauras J, Chaloupka FJ, Villanti AC, Niaura RS, et al. (2011b) Quit attempts and quit rates among menthol and nonmenthol smokers in the United States. Am J Public Health 101:1241–1247.

Lewis M, Wang Y, Berg CJ (2014) Tobacco control environment in the United States and individual consumer characteristics in relation to continued smoking: differential responses among menthol smokers? Prev Med 65:47–51.

Li J, Paynter J, Arroll B (2012) A cross-sectional study of menthol cigarette preference by 14- to 15-year-old smokers in New Zealand. Nicotine Tob Res 14:857–863.

Lisko JG, Stanfill SB, Watson CH (2014) Quantitation of ten flavor compounds in unburned tobacco products. Anal Meth 6:4698–4704.

Marsh L, Mcgee R, Gray A (2012) A refreshing poison: one-quarter of young New Zealand smokers choose menthol. Aust N Z J Public Health 36:495–496.

Míguez-Burbano MJ, Vargas M, Quiros C, Lewis JE, Espinoza L, Deshratan A (2014) Menthol cigarettes and the cardiovascular risks of people living with HIV. J Assoc Nurses AIDS Care 25:427–435.

Millqvist E, Ternesten-Hasséus E, Bende M (2013) Inhalation of menthol reduces capsaicin cough sensitivity and influences inspiratory flows in chronic cough. Respir Med 107:433–438.

Minaker LM, Ahmed R, Hammond D, Manske S (2014) Flavored tobacco use among Canadian students in grades 9 through 12: prevalence and patterns from the 2010–2011 youth smoking survey. Prev Chronic Dis 11:E102.

Muilenburg JL, Legge JS Jr (2008) African American adolescents and menthol cigarettes: smoking behavior among secondary school students. J Adolesc Health 43:570–575.

Muscat JE, Chen G, Knipe A, Stellman SD, Lazarus P, Richie JP Jr (2009) Effects of menthol on tobacco smoke exposure, nicotine dependence, and NNAL glucuronidation. Cancer Epidemiol Biomarkers Prev 18:35–41.

Muscat JE, Liu HP, Stellman SD, Richie JP Jr (2012) Menthol smoking in relation to time to first cigarette and cotinine: results from a community-based study. Regul Toxicol Pharmacol 63:166–170.

Nonnemaker J, Hersey J, Homsi G, Busey A, Allen J, Vallone D (2013) Initiation with menthol cigarettes and youth smoking uptake. Addiction 108:171–178.

Noriyasu A, Konishi T, Mochizuki S, Sakurai K, Tanaike Y, Matsuyama K, et al. (2013) Menthol-enhanced cytotoxicity of cigarette smoke demonstrated in two bioassay models. Tob Induc Dis 11:18.

O'Connor RJ, Bansal-Travers M, Carter LP, Cummings KM (2012) What would menthol smokers do if menthol in cigarettes were banned? Behavioral intentions and simulated demand. Addiction 107:1330–1338.

Okuyemi KS, Faseru B, Reed GA, Cox LS, Bronars CA, Opole I, et al. (2012) Effects of menthol on the pharmacokinetics of bupropion among Black smokers. Nicotine Tob Res 14:688–693.

Oncken C, Feinn R, Covault J, Duffy V, Dornelas E, Kranzler HR, et al. (2015) Genetic vulnerability to menthol cigarette preference in women. Nicotine Tob Res 17:1416–1420.

Oxford Economics Ltd (2012) The influence of the availability of menthol cigarettes on youth smoking prevalence. A report for Philip Morris International. Oxford (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/229776/DE795779_Attachment_2_-_Oxford_Economics_The_influence_of_the_availability_of_ment.pdf).

Park SJ, Foreman MG, Demeo DL, Bhatt SP, Hansel NN, Wise RA, et al. (2015) Menthol cigarette smoking in the COPDGene cohort: relationship with COPD, comorbidities and CT metrics. Respirology 20:108–114.

Pearson JL, Abrams DB, Niaura RS, Richardson A, Vallone DM (2012) A ban on menthol cigarettes: impact on public opinion and smokers' intention to quit. Am J Public Health 102:e107–e114.

Pereira EJ, Sim L, Driver H, Parker C, Fitzpatrick M (2013) The effect of inhaled menthol on upper airway resistance in humans: a randomized controlled crossover study. Can Respir J 20:e1–e4.

Plevkova J, Kollarik M, Poliacek I, Brozmanova M, Surdenikova L, Tatar M, et al. (2013) The role of trigeminal nasal TRPM8-expressing afferent neurons in the antitussive effects of menthol. J Appl Physiol 115:268–274.

Pritchard WS, Houlihan ME, Guy TD, Robinson JH (1999) Little evidence that "denicotinized" menthol cigarettes have pharmacological effects: an EEG/heart-rate/subjective-response study. Psychopharmacology (Berl) 143:273–279.

PROPEL Centre for Population Health Impact (2014) Tobacco use in Canada: patterns and trends, Special supplement: flavoured tobacco use. Waterloo, Ontario: University of Waterloo (http://www.tobaccoreport.ca/2014/TobaccoUseinCanada_2014_FlavourSupplement.pdf).

Rath JM, Villanti AC, Williams VF, Richardson A, Pearson JL, Vallone DM (2015) Patterns of longitudinal transitions in menthol use among US young adult smokers. Nicotine Tob Res 17:839–846.

Reitzel LR, Nguyen N, Cao Y, Vidrine JI, Daza P, Mullen PD, et al. (2011) Race/ethnicity moderates the effect of prepartum menthol cigarette use on postpartum smoking abstinence. Nicotine Tob Res 13:1305–1310.

Reitzel LR, Li Y, Stewart DW, Cao Y, Wetter DW, Waters AJ, et al. (2013a) Race moderates the effect of menthol cigarette use on short-term smoking abstinence. Nicotine Tob Res 15:883–889.

Reitzel LR, Etzel CJ, Cao Y, Okuyemi KS, Ahluwalia JS (2013b) Associations of menthol use with motivation and confidence to quit smoking. Am J Health Behav 37:629–634.

Richardson A, Ganz O, Pearson J, Celcis N, Vallone D, Villanti AC (2014) How the industry is marketing menthol cigarettes: the audience, the message and the medium. Tob Control 24:594–600.

Rising J, Alexander L (2011) Marketing of menthol cigarettes and consumer perceptions. Tob Induced Dis 9(Suppl.1):S2–S2.

Rock VJ, Davis SP, Thorne SL, Asman KJ, Caraballo RS (2010) Menthol cigarette use among racial and ethnic groups in the United States, 2004–2008. Nicotine Tob Res 12(Suppl.2):S117–S124.

Rojewski AM, Toll BA, O'Malley SS (2014) Menthol cigarette use predicts treatment outcomes of weight-concerned smokers. Nicotine Tob Res 16(1):115–119.

Rosenbloom J, Rees VW, Reid K, Wong J, Kinnunen T (2012) A cross-sectional study on tobacco use and dependence among women: Does menthol matter? Tob Induced Dis 10:19.

Rostron B (2012) Lung cancer mortality risk for US menthol cigarette smokers. Nicotine Tob Res 14:1140–1144.

Rostron B (2013) NNAL exposure by race and menthol cigarette use among US smokers. Nicotine Tob Res 15:950–956.

Rostron B (2014) Menthol cigarette use and stroke risk among US smokers: a critical reappraisal. JAMA Intern Med 174:808–809.

Rubinstein ML, Shiffman S, Moscicki AB, Rait MA, Sen S, Benowitz NL (2013) Nicotine metabolism and addiction among adolescent smokers. Addiction 108:406–412.

Salgado MV, Glantz SA (2011) Direct disease-inducing effects of menthol through the eyes of tobacco companies. Tob Control 20(Suppl.2):ii44–ii48.

Sardar M, Wang J, Liang Q (2012) Metabolism of nicotine and 4-(methylnitrosamino)-l-(3-pyridyl)-1-butanone (NNK) in menthol and non-menthol cigarette smokers. Drug Metab Lett 6:198–206.

Smith SS, Fiore MC, Baker TB (2014) Smoking cessation in smokers who smoke menthol and non-menthol cigarettes. Addiction 109:2107–2117.

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 Tob Res 12:763–767.

Stahre M, Okuyemi KS, Joseph AM, Fu SS (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.

Strasser AA, Ashare RL, Kaufman M, Tang KZ, Mesaros AC, Blair IA (2013) The effect of menthol on cigarette smoking behaviors, biomarkers and subjective responses. Cancer Epidemiol Biomarkers Prev 22:382–389.

Substance Abuse and Mental Health Services Administration (2011) The national survey on drug use and health report: recent trends in menthol cigarette use. Rockville, Maryland: Center for Behavioral Health Statistics and Quality (http://www.samhsa.gov/data/sites/default/files/WEB_SR_088/WEB_SR_088/WEB_SR_088.htm).

Sulsky SI, Fuller WG, Van Landingham C, Ogden MW, Swauger JE, Curtin GM (2014) Evaluating the association between menthol cigarette use and the likelihood of being a former versus current smoker. Regul Toxicol Pharmacol 70:231–241.

Talavera K, Gees M, Karashima Y, Meseguer VM, Vanoirbeek JA, Damann N, et al. (2009) Nicotine activates the chemosensory cation channel TRPA1. Nature Neurosci 12:1293–1299.

Tauras JA, Levy D, Chaloupka FJ, Villanti A, Niaura RS, Vallone D, et al. (2020) Menthol and non-menthol smoking: the impact of prices and smoke-free air laws. Addiction 105(Suppl.1):115–123.

Thrasher JF, Abad-Vivero EN, Moodie C, O'Connor RJ, Hammond D, Cummings KM, et al. (2015) Cigarette brands with flavour capsules in the filter: trends in use and brand perceptions among smokers in the USA, Mexico and Australia, 2012–2014. Tob Control doi: 10.1136/tobaccocontrol-2014-052064 [epub ahead of print]

Tobacco Control Legal Consortium (2015) How other countries regulate flavored tobacco products. Saint Paul, Minnesota: Public Health Law Center, Mitchell Hamline School of Law (http://publichealthlawcenter.org/sites/default/files/resources/tclc-fs-global-flavored-regs-2015.pdf).

Ton HT, Smart AE, Aguilar BL, Olson TT, Kellar KJ, Ahern GP (2015) Menthol enhances the desensitization of human α3β4 nicotinic acetylcholine receptors. Mol Pharmacol 88:256–264.

TPSAC (Tobacco Products Scientific Advisory Committee) (2011) Menthol cigarettes and public health: review of the scientific evidence and recommendations. Rockville, Maryland: Center for Tobacco Products, Food and Drug Administration (http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf).

Unger JB, Allen B Jr, Leonard E, Wenten M, Cruz TB (2010) Menthol and non-menthol cigarette use among Black smokers in Southern California. Nicotine Tob Res 12:398–407.

Villanti AC, Giovino GA, Barker DC, Mowery PD, Sevilimedu V, Abrams DB (2012) Menthol brand switching among adolescents and young adults in the National Youth Smoking Cessation Survey. Am J Public Health 102:1310–1312.

Vozoris NT (2012) Mentholated cigarettes and cardiovascular and pulmonary diseases: a population-based study. Arch Intern Med 172:590–591.

Wackowski OA, Delnevo CD (2015) Young adults' risk perceptions of various tobacco products relative to cigarettes: results from the National Young Adult Health Survey. Health Educ Behav [Epub ahead of print].

Wackowski OA, Delnevo CD, Lewis MJ (2010) Risk perceptions of menthol cigarettes compared with nonmenthol cigarettes among New Jersey adults. Nicotine Tob Res 12:786–790.

Wackowski OA, Manderski MT, Delnevo CD (2014) Young adults' behavioral intentions surrounding a potential menthol cigarette ban. Nicotine Tob Res 16:876–880.

Wackowski OA, Delnevo CD, Pearson JL (2015) Switching to e-cigarettes in the event of a menthol cigarette ban. Nicotine Tob Res 17:1286–1287.

Wakefield M, Morley C, Horan JK Cummings KC (2002) The cigarette pack as image: new evidence from tobacco industry documents. Tob Control 11(Suppl.1):i73–i80.

Wang J, Roethig HJ, 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 57:24–30.

Wang T, Wang B, Chen H (2014) Menthol facilitates the intravenous self-administration of nicotine in rats. Front Behav Neurosci 8:437.

WHO (2010) Partial guidelines for implementation of Articles 9 and 10 of the WHO Framework Convention on Tobacco Control. Geneva (http://www.who.int/fctc/guidelines/Guideliness_Articles_9_10_rev_240613.pdf?ua=1).

Wickham RJ (2015) How menthol alters tobacco-smoking behavior: a biological perspective. Yale J Biol Med 88:279–287.

Willis DN, Liu B, Ha MA, Jordt SE, Morris JB (2011) Menthol attenuates respiratory irritation responses to multiple cigarette smoke irritants. FASEB J 25:4434–4444.

Wilson N, Weerasekera D, Peace J, Edwards R (2011) Smokers have varying misperceptions about the harmfulness of menthol cigarettes: national survey data. Aust N Z J Public Health 35:364–367.

Winhusen TM, Adinoff B, Lewis DF, Brigham GS, Gardin JG 2nd, Sonne SC, et al. (2013) A tale of two stimulants: mentholated cigarettes may play a role in cocaine, but not methamphetamine, dependence. Drug Alcohol Depend 133:845–851.

Wise PM, Preti G, Eades J, Wysocki CJ (2011) The effect of menthol vapor on nasal sensitivity to chemical irritation. Nicotine Tob Res 13:989–997.

Wise PM, Breslin PA, Dalton P (2012) Sweet taste and menthol increase cough reflex thresholds. Pulmon Pharmacol Ther 25:236–241.

Yerger VB (2011) Menthol's potential effects on nicotine dependence: a tobacco industry perspective. Tob Control 20(Suppl.2):ii29–ii36.

Young-Wolff KC, Hickman NJ 3rd, Kim R, Gali K, Prochaska JJ (2015) Correlates and prevalence of menthol cigarette use among adults with serious mental illness. Nicotine Tob Res 17:285–291.

Zuo Y, Mukhin AG, Garg S, Nazih R, Behm FM, Garg PK, et al. Sex-specific effects of cigarette mentholation on brain nicotine accumulation and smoking behavior. Neuropsychopharmacology 40:884–892.

Menthol is a flavouring agent commonly used in cigarettes and other tobacco products. Menthol cigarettes are used more frequently by younger smokers, women and ethnic minorities, and their use facilitates both initiation and continued smoking, leading to addiction. These issues have raised global concern.

To address this public health issue, the WHO Study Group on Tobacco Product Regulation (TobReg) has prepared this advisory note on menthol, which synthesizes recent studies on the prevalence and health effects of menthol in tobacco products. It provides evidence-based conclusions and recommendations for policy-makers and regulators, including for a ban on menthol (and its analogues, derivatives and precursors) in cigarettes.

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