Menthol Cigarettes, Smoking Cessation, Atherosclerosis, and Pulmonary Function

The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: African American smokers are more likely to experience tobacco-related morbidity and mortality than European American smokers, and higher rates of menthol cigarette smoking may contribute to these disparities.

Methods: We prospectively measured cumulative exposure to menthol and nonmenthol cigarettes and smoking cessation behavior (1985-2000), coronary calcification (2000), and 10-year change in pulmonary function (1985-1995) in African American and European American smokers recruited in 1985 for the Coronary Artery Risk Development in Young Adults Study.

Results: We identified 1535 smokers in 1985 (972 menthol and 563 nonmenthol); 89% of African Americans preferred menthol vs 29% of European Americans (P<.001). After adjustment for ethnicity, demographics, and social factors, we found nonsignificant trends in menthol smokers toward lower cessation (odds ratio [OR], 0.71; 95% confidence interval [CI], 0.49-1.02; P=.06) and recent quit-tempt (OR, 0.77; 95% CI, 0.56-1.06; P=.11) rates and a significant increase in the risk of relapse (OR, 1.89; 95% CI, 1.17-3.05; P=.009). Per pack-year of exposure, however, we found no differences from menthol in tobacco-related coronary calcification (adjusted OR, 1.27; 95% CI, 1.01-1.60 for menthol cigarettes and 1.33; 95% CI, 1.06-1.68 for nonmenthol cigarettes per 10-pack-year increase; P=.75 for comparison) or 10-year pulmonary function decline (adjusted excess decline in forced expiratory volume in 1 second, 84 mL; 95% CI, 32-137 for menthol cigarettes and 80 mL; 95% CI, 30-129 for nonmenthol cigarettes, per 10-pack-year increase; P=.88 for comparison).

Conclusion: Menthol and nonmenthol cigarettes seem to be equally harmful per cigarette smoked in terms of atherosclerosis and pulmonary function decline, but menthol cigarettes may be harder to quit smoking.

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provides a unique opportunity to evaluate the long-term effects of smoking menthol cigarettes. The CARDIA Study has collected detailed longitudinal data on smoking habits during 15 years of follow-up in a large cohort of young African American and European American men and women in 4 US cities. The CARDIA Study also measured pulmonary function directly on 2 occasions 10 years apart and coronary calcification (a marker for atherosclerosis) at the year 15 examination. To determine whether menthol cigarettes are harder to quit smoking or more harmful than nonmenthol cigarettes, we measured the association between menthol cigarette exposure and smoking cessation behavior, coronary calcification, and pulmonary function decline in CARDIA smokers.

STUDY DESIGN AND SAMPLE

The CARDIA Study is a longitudinal study of risk factors for coronary artery disease in 5115 African American and European American women and men aged 18 to 30 years and healthy at the time of enrollment in 1985. After informed consent was obtained from participants and approval was provided by the institutional review board at each site (Oakland; Chicago, Ill; Minneapolis, Minn; and Birmingham), participants underwent a baseline examination and then follow-up examinations at years 2, 5, 7, 10, and 15, with 74% retention of the surviving cohort at year 15 (2000). Details of the study design, recruitment, and procedures have been published elsewhere. For this investigation, we identified CARDIA smokers and measured associations between menthol/nonmenthol exposure and smoking cessation behaviors during follow-up, the prevalence of coronary calcification in 2000, and changes in pulmonary function test results between 1985 and 1995.

MENTHOL PREFERENCE AND EXPOSURE

Current smoking, number of cigarettes smoked per day, and menthol preference (“Is [your current brand of cigarettes] mentholated or nonmentholated?”) were assessed at each CARDIA examination. These data, along with data on past years of smoking at baseline, were used to estimate cumulative exposure to cigarettes in terms of pack-years. We partitioned pack-year exposure into menthol pack-years and nonmenthol pack-years, assuming that participants smoked only menthol or nonmenthol cigarettes at any one time.

OUTCOME MEASURES

The following smoking cessation behaviors were assessed at each examination: not currently smoking, recent quit attempts (“Have you [tried, made any attempts] to quit smoking in the past [2, 3, 5] years?”), and cessation if recent quit attempt (successful smoking cessation among participants who reported a recent quit attempt). We also examined longitudinal patterns of cessation behavior, including sustained smoking cessation (no current smoking the past 2 times they were examined in The CARDIA Study) and documented relapse (baseline smokers who reported no current smoking at a subsequent examination and then current smoking the final time they were examined).

Coronary calcification was measured in consenting CARDIA participants in 2000. Participants underwent computed tomography scanning using an electron beam scanner (GE Imatron C-150; GE Healthcare, Chalfont St Giles, England) or a multidetector scanner (GE LightSpeed; GE Healthcare; or Siemens V2 series; Siemens AG, Munich, Germany). A committee of expert cardiologists, radiologists, and a physicist developed a scanning protocol to standardize scan acquisition across these slightly different technologies. Two scans were obtained for each participant using a hydroxyapatite model for standardization. Scans were electrocardiographically gated at 80% (GE Imatron) or 50% (GE LightSpeed and Siemens V2) of the R-R interval, with an image thickness of 3 (GE Imatron) or 2.5 (GE LightSpeed and Siemens V2) mm, and completed within 100 (GE Imatron), 520 (GE LightSpeed), or 360 (Siemens V2) milliseconds. Specialized image-processing software was used to identify all potential calcific foci composed of at least 4 adjacent pixels (an area ≥ 1.87 mm²) with a density greater than 130 Hounsfield units. Each potential focus was then confirmed or deleted by a blinded cardiovascular radiologist based on knowledge of coronary artery anatomy, and the presence or absence of coronary calcium was determined. Between- and within-reader reproducibility was high.

Pulmonary function testing was performed in 1985 and in 1995 using a Collins Survey 8-L water-sealed spirometer and an Eagle II microprocessor (Warren E. Collins Inc, Braintree, Mass). Trained technicians performed frequent calibrations of the instruments and coached participants through 3 to 5 trials of forced expiration to obtain 3 trials meeting minimal quality standards (no clear errors in execution) and showing reproducibility of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) within 5% and 100 mL, respectively. Among the multiple exploratory trials recorded for each participant, we used maximum FVC, maximum FVC, and maximum midexpiratory flow (MMEF, defined as the average flow between the points at which 25% and 75% of the total FVC has been expired) for analyses per CARDIA protocol. The primary outcome was the change in FEV₁ between the 1985 and 1995 examinations; secondary analyses examined change in FVC and MMEF.

OTHER COVARIATES

Sex, ethnicity, and date of birth were recorded at baseline. Educational grade attained, family income, current alcohol consumption (number of drinks per week), physical activity level (Likert-type scale), and marital, employment, and insurance status were measured by means of self-report at each examination (except income is not available from the baseline examination). Glucose intolerance (defined by the use of diabetes mellitus medication or by a fasting blood glucose level >110 mg/dL [>6.1 mmol/L]), systolic and diastolic blood pressure, plasma levels of low- and high-density lipoprotein cholesterol and triglycerides, and body mass index (calculated as weight in kilograms divided by the square of height in meters) were measured directly.

STATISTICAL ANALYSIS

For the first 3 cessation behavior outcomes (not currently smoking, recent quit attempt, and cessation if recent quit attempt), we performed repeated-measures analyses using logistic models that included each examination of each participant as a separate observation, and we used robust estimates of standard errors to take into account clustering by participant. For the longitudinal cessation pattern analyses (sustained smoking cessation and documented relapse outcomes), we used logistic regression with 1 observation per participant.

We used logistic regression to assess the independent contributions of menthol and nonmenthol exposure to the risk of having coronary calcium. We simultaneously estimated odds ratios (ORs) for each additional 10-pack-year increase in cumu-
ative lifetime exposure to menthol and nonmenthol cigarettes. To compare the putative effects of menthol vs nonmenthol cigarettes, we used Wald tests of the null hypothesis that the coefficients for menthol and nonmenthol exposure were equal.

For the pulmonary function analysis, we used linear regression to assess the independent contributions of menthol and nonmenthol exposure to change in pulmonary function (FEV1, FVC, and MMEF) in the 10 years between 1985 and 1995. We simultaneously estimated coefficients for each additional 10-pack-year increase in the interval exposure (during the same 10 years) to menthol and nonmenthol cigarettes. To compare the putative effects of menthol vs nonmenthol cigarettes, we used Wald tests of the null hypothesis that the coefficients for menthol and nonmenthol exposure were equal. For each regression, we present a series of models sequentially adjusting for demographic and socioeconomic factors, habits, and potential mediators related to each outcome.

Of the original 5115 CARDIA participants, 74% reported for the 2000 examination. To take into account differential dropout we estimated visit-specific probabilities of participating in any given examination using smoking status, age, sex, ethnicity, education, income, and marital status measured at the previous examination. We used these probabilities, inverted, as probability weights in all the models except the sustained smoking cessation and documented relapse analyses (in which the outcome is not tied to a particular CARDIA examination). We also performed unweighted analyses and found nearly identical results in every case. All the analyses were executed using Stata 8.0 statistical software (StataCorp, College Station, Tex).

### STUDY SAMPLE AND MENTHOL PREFERENCE

Of 5115 CARDIA participants enrolled in 1985, 1544 reported current smoking; 972 current smokers (63%) preferred menthol cigarettes and 563 (36%) nonmenthol. Menthol preference was unknown for 9 smokers (0.6%). Menthol preference was stable (11%-12% switched preference during follow-up) and was strongly related to ethnicity, with 89% of African Americans preferring menthol compared with only 29% of European Americans (P < .001). Baseline menthol preference was also associated with younger age, female sex, lower educational level, unemployment, lower alcohol intake, higher body mass index, and fewer cigarettes smoked per day (Table 1).

### SMOKING CESSATION BEHAVIOR

Baseline menthol smokers were more likely to still be smoking during follow-up examinations than baseline nonmenthol smokers (69% vs 54% in 2000; P < .001). However, stratification by ethnicity attenuates this association; as African Americans are more likely to smoke menthol cigarettes and less likely to quit smoking during follow-up (Figure 1). Before adjustment, menthol smokers were less likely to be noncurrent smokers at follow-up examinations (OR, 0.61; 95% confidence interval [CI], 0.49-0.76); after adjustment, the association is weaker (OR, 0.90; 95% CI, 0.68-1.19) (Table 2).

Among smokers who tried to quit, menthol seemed unrelated to quitting (adjusted OR, 1.00; 95% CI, 0.71-1.42), but menthol was associated with a lower likelihood of trying to quit in the first place (adjusted OR, 0.77; 95% CI, 0.56-1.06; P = .11). In longitudinal analyses, menthol smokers were less likely to exhibit sustained smoking cessation (adjusted OR, 0.71; 95% CI, 0.49-1.02; P = .06) and nearly twice as likely to relapse after an examination during which they reported no current smoking (adjusted OR, 1.89; 95% CI, 1.17-3.05; P = .009) (Table 2). Results were similar among African Americans and European Americans and after additional adjustment for cigarettes smoked daily at baseline.

### CORONARY CALCIFICATION

The prevalence of coronary calcification (14% overall in these smokers) was strongly associated with cumulative exposure to tobacco smoke, but the association seemed to be equivalent among baseline menthol smokers and nonmenthol smokers (Figure 2). Logistic models showed no difference in the associations between menthol and nonmenthol exposure and coronary calcification before or after adjustment for demographics, socioeconomic status, or other habits. Further adjustment for physiologic mediators of coronary disease led to attenuation in each smoking–coronary calcium association consistent with partial mediation by those measured factors (Table 3). Results were similar in African Americans and European Americans.

### PULMONARY FUNCTION DECLINE

The FEV1 declined by an average of 180 mL between 1985 and 1995 in CARDIA smokers, and the magnitude of decline was strongly associated with interval exposure to to-
bacco smoke among menthol and nonmenthol smokers (Figure 3 and Table 4). Regression models showed no detectable difference in the magnitude of association between menthol- and nonmenthol-associated decline in FEV1, FVC, or MMEF before or after adjustment. European Americans tended to have larger declines associated with menthol cigarettes (P = .05 for FEV1), whereas African Americans showed the opposite tendency (P = .35 for FEV1).

In this longitudinal analysis of smoking behavior across 15 years, we looked for differences between menthol and nonmenthol smokers in smoking cessation behavior, coronary calcification, and pulmonary function decline. We found some evidence that menthol smokers are less likely to attempt cessation, more likely to relapse after successfully quitting, and less likely to report sustained smoking cessation but not with recent quit attempts or relapse after quitting; interactions between menthol preference and cigarettes per day were not significant. European American smokers were less likely to report recent quit attempt or relapse after quitting, and found no relationship between current (vs former) smoking and menthol preference. Menthol inhibits the metabolism of nicotine, leading to higher levels of nicotine per cigarette smoked, and menthol smokers tend to show higher levels of addiction in terms of time to first cigarette in the morning despite lower volume and frequency of puffs and lower numbers of cigarettes smoked per day seen in the present study and others. These findings suggest that menthol cigarettes may be harder to quit smoking, but uncertainty about this point remains, in part because of the difficulty and large sample sizes required to tease apart the effects of ethnicity and menthol preference, which are highly correlated.

### Table 2. Smoking Cessation Behaviors According to Baseline Menthol Preference: The CARDIA Study, 1985-2000

<table>
<thead>
<tr>
<th>Measure of Cessation*</th>
<th>Examinations or Participants, No.</th>
<th>Unadjusted†</th>
<th>Adjusted for Age, Sex, and Ethnicity</th>
<th>Also Adjusted for Social Factors‡</th>
<th>Also Adjusted for Cigarettes per Day at Baseline§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not currently smoking</td>
<td>6655</td>
<td>0.61 (0.49-0.76)</td>
<td>0.84 (0.64-1.10)</td>
<td>0.90 (0.68-1.19)</td>
<td>0.90 (0.68-1.19)</td>
</tr>
<tr>
<td>Recent quit attempt</td>
<td>6636</td>
<td>0.63 (0.65-1.05)</td>
<td>0.74 (0.54-1.01)</td>
<td>0.77 (0.56-1.06)</td>
<td>0.77 (0.57-1.06)</td>
</tr>
<tr>
<td>Cessation if recent quit attempt</td>
<td>4062</td>
<td>0.66 (0.50-0.87)</td>
<td>0.96 (0.68-1.36)</td>
<td>1.00 (0.71-1.42)</td>
<td>0.98 (0.69-1.39)</td>
</tr>
<tr>
<td>Sustained smoking cessation</td>
<td>1260</td>
<td>0.45 (0.34-0.60)</td>
<td>0.63 (0.44-0.90)</td>
<td>0.71 (0.49-1.02)</td>
<td>0.70 (0.48-1.03)</td>
</tr>
<tr>
<td>Documented relapse</td>
<td>597</td>
<td>1.87 (1.28-2.74)</td>
<td>1.99 (1.24-3.21)</td>
<td>1.89 (1.17-3.05)</td>
<td>1.89 (1.17-3.05)</td>
</tr>
</tbody>
</table>

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval.

*The 3 repeated-measures analyses (not currently smoking, recent quit attempt, and cessation if recent quit attempt) use current smoking status and covariates from each examination for each participant. For the repeated-measures outcomes, the number of examinations analyzed is shown. For the 2 nonrepeated-measures outcomes (sustained smoking cessation and documented relapse), the number of participants analyzed is shown. See the “Methods” section for details.

†Repeated-measures analyses are also adjusted for examination, clustering within participant, and differential loss to follow-up using inverse probability weighting (see the “Methods” section). Analyses without inverse probability weighting showed nearly identical results.

‡Social factors include educational level, marital status, employment, and health insurance status. Covariates are either examination specific (in repeated-measures analyses) or at baseline.

§A higher number of cigarettes smoked per day at baseline was associated with lower rates of noncurrent smoking, cessation if recent quit attempt, and sustained cessation but not with recent quit attempts or relapse after quitting; interactions between menthol preference and cigarettes per day were not significant for any outcomes, although the study was somewhat underpowered for this analysis.

**COMMENT**
Smoking is known to be a major risk factor for coronary artery disease, and the present findings demonstrate a strong dose-response relationship with coronary calcification, a marker of atherosclerosis. Per cigarette, however, menthol and nonmenthol exposure seem to be equally harmful. Previous studies of menthol vs nonmenthol cigarette smoking show no effects of mentholation on blood pressure or heart rate, although one study showed a small difference in heart rate associated with menthol candy/tea ingestion. We are unaware of any previous studies of menthol and atherosclerosis. Although the present study does not rule out a difference in thrombosis or other nonatherosclerotic mechanisms leading to coronary events, we found no evidence that it plays a role in coronary heart disease disparities between African Americans and European Americans.

Pulmonary function decline and obstructive lung disease are also known to be strongly associated with tobacco smoke exposure, and the present study demonstrated this dose-response relationship. Per cigarette, however, menthol and nonmenthol exposure again seem to be equally harmful. There are few published studies of menthol and pulmonary function and no previous longitudinal studies of menthol and pulmonary function in humans, to our knowledge. One tobacco industry-funded study of rats exposed to menthol and nonmenthol cigarette smoke for 13 weeks showed histopathologic changes consistent with smoking that seemed to be equivalent between menthol- and nonmenthol-exposed rats. Another industry document hints at “an adverse effect on the respiratory function” associated with mentholation of cigarettes without providing details, but several small trials of menthol vapor inhalation (not in a cigarette) suggest improved mucociliary clearance, less airway reactivity, fewer wheezing episodes and less need for bronchodilator dosing, bronchodilation, and “easier breathing” among patients with asthma, chronic obstructive lung disease, or acute upper respiratory tract illness. Menthol seems unlikely to be a contributor to the pulmonary function decline associated with tobacco smoke exposure.

This study is limited somewhat by sample size, particularly when we attempt to tease apart the effects of ethnicity and menthol preference. The limited numbers of European American menthol smokers (n=189) and African American nonmenthol smokers (n=95) make ethnicity-specific analyses and (to a lesser extent) adjusted analyses somewhat imprecise. Inherent random variation and measurement error also limit precision and bias measures of association toward the null so that we could have missed small differences between menthol and nonmenthol cigarettes. Loss to follow-up in this cohort may theoretically bias results, but selection bias does not occur with-

![Figure 2. Age-adjusted prevalence of coronary calcification among baseline menthol and nonmenthol smokers, The Coronary Artery Risk Development in Young Adults Study, 2000.](image)

| Table 3. Cumulative Exposure to Menthol and Nonmenthol Cigarettes and the Prevalence of Coronary Calcification: The CARDIA Study, 2000 |
|---------------------------------|------------------|-----------------|-----------------|-----------------|
| Type of Cigarette Exposure*      | Unadjusted       | Adjusted for Age, Sex, and Ethnicity | Also Adjusted for Socioeconomic Status and Habits§ | Also Adjusted for Physiologic Mediators of Coronary Artery Disease† |
| Menthol cigarettes, per 10-pack-year increase | 1.53 (1.24-1.89) | 1.35 (1.09-1.67) | 1.27 (1.01-1.60) | 1.16 (0.91-1.47) |
| Nonmenthol cigarettes, per 10-pack-year increase | 1.51 (1.25-1.82) | 1.38 (1.11-1.71) | 1.33 (1.06-1.68) | 1.23 (0.98-1.55) |
| P value comparing strength of association¶ | .91 | .87 | .75 | .67 |

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval.

*Cumulative tobacco exposure was partitioned into menthol and nonmenthol exposure based on menthol preference at each examination (see the “Methods” section). Odds ratios are estimated per 10-pack-years of cigarette exposure, equivalent to 1 pack per day. For example, we could interpret the first result in this table as follows: “Smoking menthol cigarettes at a rate of 1 pack per day for 10 years (or 2 packs per day for 5 years) is associated, on average, with a 1.53-fold increase in the odds of having coronary calcification.”

*All models, including the “unadjusted model,” are adjusted for both measures of cumulative exposure to cigarettes (menthol and nonmenthol) and for differential loss to follow-up using inverse probability weighting (see the “Methods” section). Analyses are restricted to smoking participants attending each CARDIA examination with nonmissing coronary calcium scores (n=838). Analyses including all smoking participants with nonmissing coronary calcium scores (n=1033) without weighting for differential follow-up show nearly identical results.

†Socioeconomic status indicators included education and income, measured in 2000.

‡Habits included alcohol consumption and exercise, measured in 2000.

§Physiologic mediators of coronary artery disease included body mass index, glucose intolerance, systolic and diastolic blood pressure, plasma levels of low- and high-density lipoprotein cholesterol, and triglycerides, measured in 2000.

¶P values refer to Wald tests of the null hypothesis that the coefficients for menthol and nonmenthol exposure were equal. For example, for the unadjusted analysis, P=.91 refers to a test comparing 1.53 (the odds ratio for menthol) and 1.51 (the odds ratio for nonmenthol).
Figure 3. Ten-year change in forced expiratory volume in 1 second (FEV₁) in relation to interval pack-year exposure to cigarette smoke among baseline menthol and nonmenthol smokers, The Coronary Artery Risk Development in Young Adults Study, 1985-1995.

### Table 4. Interval Exposure to Menthol and Nonmenthol Cigarettes and 10-Year Decline in Pulmonary Function: The CARDIA Study, 1985-1995

<table>
<thead>
<tr>
<th>Measure of Pulmonary Function and Type of Cigarette Exposure*</th>
<th>Unadjusted†</th>
<th>Adjusted for Age, Sex, and Ethnicity</th>
<th>Also Adjusted for Socioeconomic Status‡ and Habits§</th>
<th>Also Adjusted for Body Mass Index∥</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol cigarettes, per 10–pack-year increase</td>
<td>106 (59 to 153)</td>
<td>89 (40 to 137)</td>
<td>84 (32 to 137)</td>
<td>84 (33 to 134)</td>
</tr>
<tr>
<td>Nonmenthol cigarettes, per 10–pack-year increase</td>
<td>94 (49 to 139)</td>
<td>90 (43 to 137)</td>
<td>80 (30 to 129)</td>
<td>84 (34 to 134)</td>
</tr>
<tr>
<td>P value comparing strength of association¶</td>
<td>.64</td>
<td>.96</td>
<td>.88</td>
<td>.99</td>
</tr>
<tr>
<td>FVC, mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol cigarettes, per 10–pack-year increase</td>
<td>112 (53 to 170)</td>
<td>82 (23 to 141)</td>
<td>60 (−2 to 122)</td>
<td>59 (2 to 115)</td>
</tr>
<tr>
<td>Nonmenthol cigarettes, per 10–pack-year increase</td>
<td>103 (44 to 161)</td>
<td>96 (34 to 158)</td>
<td>73 (11 to 135)</td>
<td>79 (19 to 139)</td>
</tr>
<tr>
<td>P value comparing strength of association¶</td>
<td>.79</td>
<td>.71</td>
<td>.74</td>
<td>.56</td>
</tr>
<tr>
<td>MMEF, mL/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menthol cigarettes, per 10–pack-year increase</td>
<td>201 (76 to 326)</td>
<td>178 (50 to 307)</td>
<td>195 (62 to 328)</td>
<td>195 (61 to 328)</td>
</tr>
<tr>
<td>Nonmenthol cigarettes, per 10–pack-year increase</td>
<td>69 (−47 to 185)</td>
<td>120 (−5 to 244)</td>
<td>124 (−12 to 259)</td>
<td>124 (−12 to 260)</td>
</tr>
<tr>
<td>P value comparing strength of association¶</td>
<td>.06</td>
<td>.43</td>
<td>.35</td>
<td>.35</td>
</tr>
</tbody>
</table>

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; MMEF, maximal midexpiratory flow.

*The predictors herein are interval tobacco exposures (partitioned into menthol and to nonmenthol pack-years based on menthol preference at each examination); ie, the number of pack-years of exposure accumulated during the 10 years between pulmonary function tests (1985-1995). Regression coefficients are given in terms of decline per 10 pack-years of cigarette exposure, equivalent to 1 pack per day during the 10 interval years. For example, we could interpret the first result in this table as follows: “Smoking menthol cigarettes at a rate of 1 pack per day for 10 years is associated, on average, with an excess decline of 106 mL in FEV₁.”

†All models, including the “unadjusted model,” are adjusted for both measures of cumulative exposure to cigarettes (menthol and nonmenthol) and for differential loss to follow-up using inverse probability weighting (see the “Methods” section). Analyses are restricted to smoking participants attending all the CARDIA examinations until 1995 with nonmissing pulmonary function tests (n = 982 for FEV₁ and FVC and n = 844 for MMEF). Analyses including all smoking participants with nonmissing pulmonary function tests (n = 1212 for FEV₁ and FVC and n = 1042 for MMEF) without weighting for differential follow-up were nearly identical.

‡Socioeconomic status indicators included education and income, measured in 1995.

§Habits included alcohol consumption and exercise, measured in 1995.

∥Body mass index (calculated as weight in kilograms divided by the square of height in meters) was measured in 1995.

¶P values refer to Wald tests of the null hypothesis that the coefficients for menthol and nonmenthol exposure were equal. For example, for the unadjusted FEV₁ analysis, P = .64 refers to a test comparing 106 mL (the estimate for menthol) and 94 mL (the estimate for nonmenthol).
out differential effects simultaneously by menthol preference and the outcome, and sensitivity analyses show essentially no differences between analyses with and without inverse probability weighting despite the fact that we could predict dropout with some accuracy. Some investigators have raised concerns that individuals may switch to menthol cigarettes when they develop preclinical disease. This could theoretically bias the coronary calcification or pulmonary function results (but not the cessation results, which use only baseline menthol preference); however, this tendency would lead to a bias toward finding more harm from menthol, which is essentially a conservative bias in relation to these conclusions. There is also a concern that other cigarette characteristics (tar, nicotine content, or other additives) could be different in menthol cigarettes and thereby confound our results; we cannot adjust directly for these other characteristics owing to limited data in The CARDIA Study. We note, however, that the most popular menthol (Newport and Kool) and non-menthol (Marlboro and Camel) cigarette brands are similar at least in terms of tar and nicotine content. Finally, this analysis does not address lung cancer, nonatherosclerotic heart disease, or other potential harms from cigarette smoking that may be facilitated or amplified by the presence of menthol. Ischemic heart disease and chronic rette smoking that may be facilitated or amplified by the presence of menthol. Ischemic heart disease and chronic airway obstruction, however, are the 2 most common causes of smoking-attributable mortality in the United States after lung cancer.

In summary, the preference for mentholated cigarettes among US smokers is highly associated with ethnicity and seems to be relatively stable across time. Mentholation of cigarettes does not seem to explain disparities in ischemic heart disease and obstructive pulmonary disease between African Americans and European Americans in the United States but may partially explain lower rates of smoking cessation among African American smokers. It is possible, therefore, that switching from menthal cigarettes to nonmenthol cigarettes might facilitate subsequent smoking cessation, especially in African Americans, and thereby reduce tobacco-related heart disparities. At a policy level, regulation of tobacco additives, such as menthol, has been proposed as a way to reduce tobacco addiction in the United States and as one step in a long-term strategy designed to replace tobacco with “clean” sources of nicotine to reduce the health consequences of nicotine addiction in the United States. Our results provide some support for this strategy, although the primary goal of public health officials, physicians, and patients should be to reduce all tobacco smoke exposure regardless of menthol content.

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Previous Presentation: An abstract containing a preliminary analysis of these data was presented at the American Heart Association’s 45th Annual Conference on Cardiovascular Disease Epidemiology and Prevention; May 2, 2005; Washington, DC.

REFERENCES


