

Lung Cancer Risk Among Smokers of Menthol Cigarettes

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Background Menthol cigarettes, preferred by African American smokers, have been conjectured to be harder to quit and to contribute to the excess lung cancer burden among black men in the United States. However, data showing an association between smoking menthol cigarettes and increased lung cancer risk compared with smoking nonmenthol cigarettes are limited. The Food and Drug Administration is currently considering whether to ban the sale of menthol cigarettes in the United States.

Methods We conducted a prospective study among 85806 racially diverse adults enrolled in the Southern Community Cohort Study during March 2002 to September 2009 according to cigarette smoking status, with smokers classified by preference for menthol vs nonmenthol cigarettes. Among 12373 smokers who responded to a follow-up questionnaire, we compared rates of quitting between menthol and nonmenthol smokers. In a nested case-control analysis of 440 incident lung cancer case patients and 2213 matched control subjects, using logistic regression modeling we computed odds ratios (ORs) and accompanying 95% confidence intervals (CIs) of lung cancer incidence, and applied Cox proportional hazards modeling to estimate hazard ratios (HRs) of lung cancer mortality, according to menthol preference.

Results Among both blacks and whites, menthol smokers reported smoking fewer cigarettes per day; an average of 1.6 (95% CI = 1.3 to 2.0) fewer for blacks and 1.8 (95% CI = 1.3 to 2.3) fewer for whites, compared with nonmenthol smokers. During an average of 4.3 years of follow-up, 21% of participants smoking at baseline had quit, with menthol and nonmenthol smokers having equal odds of quitting (OR = 1.02, 95% CI = 0.89 to 1.16). A lower lung cancer incidence was noted in menthol vs nonmenthol smokers (for smokers of <10, 10–19, and ≥20 cigarettes per day, compared with never smokers, OR = 5.0 vs 10.3, 8.7 vs 12.9, and 12.2 vs 21.1, respectively). These trends were mirrored for lung cancer mortality. In multivariable analyses adjusted for pack-years of smoking, menthol cigarettes were associated with a lower lung cancer incidence (OR = 0.65, 95% CI = 0.47 to 0.90) and mortality (hazard ratio of mortality = 0.69, 95% CI = 0.49 to 0.95) than nonmenthol cigarettes.

Conclusions The findings suggest that menthol cigarettes are no more, and perhaps less, harmful than nonmenthol cigarettes.

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Menthol cigarettes account for a sizeable majority of cigarettes smoked by African American smokers but only a minority among whites (1). Incidence rates of lung cancer have long been known to be higher among black men compared with white men for reasons that are not yet clear (2,3). Smoking prevalence has historically been slightly higher among black men compared with white men, but the number of cigarettes smoked per day is generally lower (1,4), so that differential smoking amounts do not readily explain the racial disparity in lung cancer risk. The use of menthol cigarettes has been hypothesized as a contributor to this disparity, although empirical evidence for a higher cancer risk among menthol vs nonmenthol cigarettes has been surprisingly limited (5–11). There have been some suggestions that mentholation may affect cigarette smoking behavior (eg, inhalation), dependency, and/or biology, and that menthol smokers have lower quit rates than nonmenthol smokers

that could contribute to higher total exposures to carcinogenic compounds in tobacco smoke (12,13). However, the number of studies examining these various issues has not been large, and further information on potential hazards associated with menthol cigarettes is needed as the Food and Drug Administration is presently deliberating whether to impose a ban on the sale of menthol cigarettes in the United States.

Herein we present results from the Southern Community Cohort Study (SCCS), a prospective study implemented to examine racial disparities in cancer and other chronic diseases (14,15). The SCCS is uniquely positioned to evaluate smoking patterns and associated risks among blacks and whites of similar socioeconomic status. Smoking prevalence at enrollment was exceptionally high, and both menthol and nonmenthol cigarette use was common. The initial follow-up period of up to 8 years accrued sufficient numbers of incident lung cancer cases and deaths to

estimate associations between menthol and nonmenthol users. Further, the follow-up data enabled us to assess smoking quit rates by cigarette type. The resultant information from this well-characterized population adds to the scientific evidence from which policies regarding smoking reduction and cancer prevention can be evaluated.

Participants and Methods

Study Population and Data Collection

The SCCS is an ongoing prospective cohort study designed to evaluate disparities in cancer and other chronic diseases. During March 2002, to September 2009, 85 806 adults aged 40–79 years residing in 12 southern states (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia) were enrolled in the SCCS. Two-thirds of the participants self-reported their race as African American and the remainder predominantly as non-Hispanic white. Study details are provided elsewhere (14,15); in brief, recruitment was partially achieved from mailings to age-, sex-, and race-stratified random samples of the general population, but took place predominantly (approximately 85%) at community health centers (CHCs), institutions which provide primary health services in medically underserved areas, where trained study interviewers administered a computer-assisted personal interview to collect baseline data on demographic characteristics and potential cancer risk factors, including tobacco use history, and personal and family medical history, among others. The SCCS was reviewed and approved by institutional review boards at Vanderbilt University and Meharry Medical College. Written informed consent was obtained from all study participants.

Cigarette smokers were defined as those who reported smoking at least 100 cigarettes in their lifetime. Current smokers were those who answered “Yes” to “Do you smoke now?” and menthol smokers were those who answered “Yes” to “Are the cigarettes you usually smoke menthol?” Packs were computed by dividing the reported number of cigarettes smoked per day by 20, which is the number of cigarettes in a pack. Pack-years of smoking were computed by multiplying packs by the number of years smoked (derived from the age reported starting and quitting smoking for former smokers, or the age starting smoking and current age for current smokers). Persons with missing information on smoking characteristics (<3% of the cohort) were excluded from the analyses.

In November 2008 (coincident with the latter part of participant recruitment), we began attempting to recontact participants to update information using a brief follow-up questionnaire administered by mail or telephone. Still ongoing, this activity is currently about 60% complete, with respondents to the follow-up survey tending more often to be women, older, and of higher income and education level than nonrespondents. The follow-up questionnaire assessed the current smoking status of participants using the question, “What is your current cigarette smoking status?” For participants who were current smokers at baseline, those reporting themselves to be nonsmokers in the follow-up questionnaire were classified as quitting, and the remainder as continuing smokers.

CONTEXT AND CAVEATS

Prior knowledge

It is not clear whether mentholated cigarettes, preferred by African Americans, contribute to the higher burden of lung cancer in this population. It has been suggested that mentholation is more hazardous, affects smoking behavior, and also makes it harder to quit smoking. The Food and Drug Administration is currently considering a ban on the sale of menthol cigarettes in the United States.

Study design

Prospective study using participants from the ongoing Southern Community Cohort Study analyzed quitting rates between menthol and nonmenthol smokers after an average follow-up of 4.3 years. Race (black, white, other) was self-reported. A nested case-control analysis within this cohort assessed the risks of lung cancer incidence and mortality based on menthol preference.

Contribution

Menthol and nonmenthol smokers showed equal odds of quitting. Both lung cancer incidence and mortality were lower in menthol smokers compared with nonmenthol smokers, even after adjusting for pack-years of smoking.

Implications

Results do not support claims that menthol cigarettes are responsible for a greater lung cancer burden in African Americans and in fact raise the possibility of a lesser threat compared with nonmenthol cigarettes.

Limitations

Some misclassification of cigarette type may have occurred because detailed history of menthol vs nonmenthol use was not available.

From the Editors

Lung Cancer Incidence and Mortality Ascertainment

A total of 463 incident lung cancers (*International Classification of Diseases-Oncology* [ICD-O-3] codes C340–C349) diagnosed after entry into the SCCS were identified via linkage with state cancer registries operating in the 12-state study area and/or from National Death Index (NDI) mortality records, with 60 (13%) cases identified solely from NDI. The cohort was followed for mortality via linkage to both the Social Security Administration and the NDI through December 31, 2008. We identified 320 deaths attributed to lung cancer (ICD-10 codes C33, C34).

Statistical Analysis

Quitting Smoking. We assessed quitting smoking in two ways, retrospectively based on information on quitting provided by the participants at entry into the cohort, and prospectively by computing quit rates ascertained from the follow-up interviews for persons who were current smokers at entry into the cohort. From the baseline data, we identified those who reported themselves as former smokers who had quit smoking before their entry into the cohort. Then, among ever-smokers, unconditional logistic regression analyses were used to compute odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) associated with being a former smoker (ie, ORs and CIs of quitting smoking before cohort enrollment) according to menthol vs nonmenthol

status and pack-years of smoking. Additional variables included in these models were age (continuous), sex, annual household income (<\$15,000, \$15,000–\$24,999, and >\$25,000), education (<9 years, 9–11 years, high school, some college, and college graduate or higher), recruitment source (CHC or general population), and body mass index (continuous, kg/m²). The association between menthol status and quitting was found to be modified by race, with statistically significant interaction ($P < .001$) detected using the likelihood ratio test, and thus race-specific odds ratios are presented.

Unconditional logistic regression analyses also were used in prospective analyses to compute odds ratios and 95% confidence intervals for quitting during the follow-up period, with covariates included for time elapsed between the baseline and follow-up questionnaires, age, sex, race, income, education, recruitment source, body mass index, pack-years of smoking at entry into the cohort, and type of cigarette (menthol or nonmenthol). We also assessed models with cigarettes smoked per day and duration of smoking as separate variables instead of combined in pack-years, but results were nearly identical and not presented.

Lung Cancer Incidence. The state cancer registries had variable time periods of complete cancer ascertainment, and we could not accurately determine censoring end dates within each state cancer registry (eg, some cancers occurring in 2009 may have been listed within a state registry, but not all cancers diagnosed in 2008 may have yet been recorded). This uncertainty in exact end dates for cancer incidence follow-up dictated a nested case-control analysis rather than a proportional hazards time-to-event modeling of relative risks for incident lung cancer. Thus, corresponding to each lung cancer case patient ($N = 463$), we selected five participants using incidence density sampling, who were alive and had not been diagnosed with lung cancer as of the date of the case patient's cancer diagnosis, as control subjects ($N = 2315$). The control subjects were matched with the case patients for age (within 1 year, although relaxed to within 6 years for 5% of the control subjects to allow five to be chosen), sex, race (black, white, and other), recruitment source, and recruitment site. Conditional logistic regression models were used to estimate odds ratios and 95% confidence intervals for lung cancer risk in smoking groups defined by baseline smoking status, cigarettes smoked per day, and menthol vs nonmenthol cigarette smoking. Matching factors were accounted for in the conditional analysis, and additional covariates included education, income, ever use of other tobacco products (pipes, cigars, chewing tobacco, and snuff; yes or no), first-degree family history of lung cancer (yes or no), and having health insurance (yes or no). In two separate subanalyses, one restricted to current smokers and one to former smokers, we calculated odds ratios for lung cancer incidence by menthol vs nonmenthol status, using unconditional logistic regression with adjustment for matching factors, a continuous variable representing pack-years of smoking, and inclusion of the other covariates mentioned above.

Lung Cancer Mortality. Cox proportional hazards models were used to estimate hazard ratios (HRs) and accompanying 95% confidence intervals for lung cancer mortality among cohort members in the various baseline smoking groups relative to never smokers. Age was used as the time variable, and covariates mirrored those

used for the incident lung cancer analysis, plus sex, race, and recruitment source. We also conducted analyses restricted to current smokers at cohort entry, estimating the hazard ratio for lung cancer death by menthol vs nonmenthol status, with adjustment for pack-years of smoking. The proportionality assumptions of the Cox models, that hazard ratios remained relatively constant over time, were assessed by computing hazard ratios separately for the first 3 years of follow-up vs subsequent years, with generally similar patterns observed.

For base rates lower than 10%, the odds ratios are good estimates of relative risks, which was the case for lung cancer incidence and mortality in this study. All statistical analyses were conducted using SAS/STAT software, version 9.2 (SAS Institute, Inc, Cary, NC) and STATA software, version 10 (StataCorp, College Station, TX). All tests of statistical significance were two-sided and P values less than .05 were considered to be statistically significant.

Results

Characteristics of the Study Population

Among the 85 806 participants enrolled in the SCCS, we excluded 2414 (2.8%) with missing baseline smoking information. Baseline smoking characteristics of the 54 777 African American (blacks) and 24 945 white SCCS participants are shown in Table 1. Data for other racial groups are not presented in Table 1, but these individuals were included in the analyses of quit rates and lung cancer incidence and mortality. Prevalence of current smoking was high—33% for black women, 36% for white women, 57% for black men, and 41% for white men. Among current smokers, 86% of blacks smoked menthol cigarettes compared with only 23% of whites, whereas among former smokers, the racial difference was slightly smaller (78% for blacks vs 31% for whites). Menthol smokers tended to be younger in age than nonmenthol smokers, especially among blacks, with a mean age difference of 3.8 years (95% CI = 3.6 to 4.0). Menthol and nonmenthol smokers tended to be similar with respect to income and education level, except among current smokers who were white women, among whom a higher percentage of menthol vs nonmenthol (33% vs 25%) smokers had some college or higher education. On average, black men smoked 10.4 (95% CI = 10.0 to 10.8) fewer cigarettes per day than white men, and black women smoked 7.2 (95% CI = 6.8 to 7.5) fewer cigarettes per day than white women. Within each race-sex group, menthol cigarette users smoked statistically significantly fewer cigarettes per day than nonmenthol users. Among black ever-smokers, menthol users smoked an average of 1.6 (95% CI = 1.3 to 2.0) fewer cigarettes per day than nonmenthol users; among white ever-smokers, menthol users smoked an average of 1.8 (95% CI = 1.3 to 2.3) fewer cigarettes per day than nonmenthol users.

Quitting Smoking Rates Among Menthol vs Nonmenthol Smokers

Overall, 35% of ever-smokers had quit smoking by the time they enrolled in the SCCS. For blacks, once age and other covariates were adjusted for, the prevalence of having quit smoking among menthol users was equal to that for nonmenthol users (adjusted OR = 1.03, 95% CI = 0.96 to 1.11), but among the whites, menthol

Table 1. Characteristics of cigarette smoking among African American and white Southern Community Cohort Study (SCCS) participants*

Smoking status at entry into SCCS	Type of cigarette	Age, y	Characteristic(sample size, cpd,smoking duration)	Black men (n = 22 820)	Black women (n = 31 957)	White men (n = 9678)	White women (n = 15 267)		
Never smoker	—	40–49	No.	2595	6716	828	1793		
			50–59	No.	1672	5311	901	2243	
			>60	No.	853	3288	752	1906	
		Former smoker	Menthol	40–49	No.	1350	1924	148	415
					Mean No. of cpd	14.6	13.8	24.2	19.0
					≥20 cpd, %	36	33	58	49
				50–59	Mean duration, y	18.2	16.6	17.8	16.5
					No.	1454	1,844	271	528
					Mean No. of cpd	16.7	14.4	25.6	20.7
				>60	≥20 cpd, %	43	34	67	52
					Mean duration, y	23.2	20.9	23.5	19.3
					No.	774	1,175	300	500
			Nonmenthol	40–49	Mean no. of cpd	17.9	13.3	25.5	19.6
					≥20 cpd, %	47	32	69	49
					Mean duration, y	30.0	26.6	28.0	24.5
				50–59	No.	131	176	499	622
					Mean No. of cpd	14.9	12.0	24.7	20.8
					≥20 cpd, %	38	27	68	56
>60	Mean duration, y	18.1	14.8	18.7	17.7				
	No.	340	445	792	885				
	Mean No. of cpd	18.5	16.3	26.9	22.3				
Current smoker	Menthol	40–49	≥20 cpd, %	48	38	71	58		
			Mean duration, y	23.2	22.6	23.9	21.2		
			No.	635	620	1,198	909		
		50–59	Mean No. of cpd	19.6	13.6	27.5	21.1		
			≥20 cpd, %	54	35	73	57		
			Mean duration, y	29.5	27.6	29.0	26.0		
		>60	No.	6821	5818	410	812		
			Mean No. of cpd	12.3	11.6	20.6	18.0		
			≥20 cpd, %	27	24	63	54		
Mean duration, y	27.6		26.7	30.0	29.0				
50–59	No.		3631	2621	262	485			
	Mean No. of cpd		12.3	11.1	20.6	17.1			
	≥20 cpd, %	27	21	64	49				
>60	Mean duration, y	36.5	34.1	38.0	35.1				
	No.	668	596	80	147				
	Mean No. of cpd	11.7	9.3	21.3	17.8				
Nonmenthol	40–49	≥20 cpd, %	28	16	70	54			
		Mean duration, y	47.0	44.3	51.0	45.5			
		No.	701	466	1,725	2,091			
	50–59	Mean no. of cpd	13.2	13.0	22.0	19.1			
		≥20 cpd, %	32	31	68	56			
		Mean duration, y	28.6	27.5	29.7	29.2			
	>60	No.	763	639	1099	1292			
		Mean no. of cpd	14.2	12.2	22.9	19.3			
		≥20 cpd, %	35	29	68	57			
Nonmenthol	40–49	Mean duration, y	37.9	35.8	39.1	36.6			
		No.	432	318	413	639			
		Mean No. of cpd	12.2	11.2	21.4	18.1			
Nonmenthol	50–59	≥20 cpd, %	27	21	65	57			
		Mean duration, y	48.4	45.5	49.6	46.1			
		No.	432	318	413	639			

* Analysis among the 79 722 African American (black) and white SCCS participants with known smoking histories; excluded from the table are 3670 (4.4%) cohort members with baseline smoking data who are of other or unknown race. Other race participants are included in the analyses shown in Tables 2 and 3. cpd = cigarettes per day.

users were statistically significantly more likely to have quit than nonmenthol users (adjusted OR = 1.55, 95% CI = 1.41 to 1.70). Among SCCS participants who have thus far completed prospective follow-up, 7886 and 4487 reported being current smokers of menthol and nonmenthol cigarettes, respectively, at baseline

enabling prospective determination of quit rates. After an average 4.3 (range 1–8) years of follow-up, 21% of these smokers reported that they had quit smoking. The odds of quitting were inversely related to pack-years smoked, increased with age and income, and did not differ statistically significantly by sex, race, or type of cigarette

smoked (data not shown). The odds of quitting smoking during follow-up were similar among menthol compared with nonmenthol smokers (adjusted OR = 1.02, 95% CI = 0.89 to 1.16).

Lung Cancer Incidence Among Menthol vs Nonmenthol smokers

In the nested case-control analysis, because of the matched design, the incident lung cancer case patients and the corresponding control subjects were identical with respect to age (mean age = 57 years), sex (52% men), and recruitment source (90% CHC), but education and income tended to be lower in case patients vs control subjects (45% vs 34% less than high school; 68% vs 60% <\$15,000 annual income). Table 2 shows the adjusted odds ratios for incident lung cancer in relation to baseline smoking status. Former smokers at entry to the cohort had a fourfold increase in lung cancer incidence compared with never smokers (OR = 4.4, 95% CI = 2.8 to 6.9). The risk for current smokers was substantially higher and differed by cigarette type. Depending on the amount smoked, the odds of incident lung cancer increased 10.3-, 12.9-, and 21.1-fold among nonmenthol smokers and 5.0-, 8.7-, and 12.2-fold among menthol smokers, of less than 10, 10-19, and 20 or more cigarettes per day, respectively, compared with never smokers. In each category of cigarettes smoked per day (<10, 10-19, ≥20 cigarettes), lung cancer incidence was higher among nonmenthol than menthol smokers. In analyses restricted to current smokers at baseline and adjusted for pack-years of smoking, the overall risk of lung cancer associated with menthol cigarette type was lower compared with nonmenthol (OR = 0.65, 95% CI = 0.47 to 0.90). Lower risks of lung cancer incidence associated with mentholated cigarettes were observed among both blacks (OR = 0.52, 95% CI = 0.34 to 0.78) and whites (OR = 0.84, 95% CI = 0.43 to

1.64), and men (OR = 0.77, 95% CI = 0.49 to 1.23) and women (OR = 0.43, 95% CI = 0.24 to 0.75), with no statistically significant differences (ie, no effect modification) by race ($P = .52$) or sex ($P = .45$). Similarly, in analyses restricted to former smokers, the pack-years adjusted lung cancer incidence odds ratio associated with menthol compared with nonmenthol smokers was 0.72 (95% CI = 0.43 to 1.21). Results were not affected by exclusion of lung cancer cases (13%) identified only through mortality records (data not shown).

Lung Cancer Mortality Among Menthol vs Nonmenthol Smokers

Trends in risk of lung cancer mortality in association with cigarette smoking were similar to the trends noted above for lung cancer incidence, with the mortality hazard ratios close to the incidence odds ratios shown above. Lung cancer mortality rates were increased 10- to 16-fold among nonmenthol smokers and fivefold to 14-fold among menthol smokers compared with never smokers (Table 3). Among current smokers, the pack-years-adjusted risk of lung cancer mortality was statistically significantly lower for users of menthol compared with nonmenthol cigarettes (HR of mortality = 0.69, 95% CI = 0.49 to 0.95).

Discussion

This large prospective study of African American and non-African American men and women with high smoking rates revealed that use of menthol cigarettes was associated with substantial increases in the risk of lung cancer incidence and mortality, but that the relative risks for lung cancer associated with menthol cigarettes were lower than those associated with nonmenthol cigarettes. Furthermore, menthol smokers tended to smoke fewer cigarettes

Table 2. Lung cancer incidence in relation to menthol and non menthol cigarette smoking*

Baseline smoking status, type of cigarette, cpd†	OR(95% CI)‡
Never smoker	1.0 (Referent)
Current, nonmenthol, ≥20 cpd	21.1 (12.2 to 36.5)
Current, nonmenthol, 10-19 cpd	12.9 (7.3 to 23.0)
Current, nonmenthol, <10 cpd	10.3 (5.5 to 19.3)
Current, menthol, ≥20 cpd	12.2 (7.2 to 20.8)
Current, menthol, 10-19 cpd	8.7 (5.2 to 14.7)
Current, menthol, <10 cpd	5.0 (2.9 to 8.6)
Former smoker	4.4 (2.8 to 6.9)

* A matched nested case-control study of lung cancer incidence in relation to menthol and nonmenthol cigarette smoking. Analysis included 440 incident lung cancer case patients and 2213 individually matched control subjects after excluding 23 (5.0%) of 463 identified lung cancer case patients and 102 (4.4%) of 2315 control subjects in the final multivariable model because of incomplete data on one or more model covariates. OR = odds ratio; CI = confidence interval; cpd = cigarettes per day.

† Self-reported smoking status at entry into the cohort.

‡ Odds ratios and 95% confidence intervals were estimated from conditional logistic regression matched on age (mostly within 1 year), sex, race (black, white, and other), and recruitment source (community health centers, general population), and adjusted for education (<9, 9-11, 12, >12 years, and college or beyond), household income (<\$15,000, \$15,000-\$24,999, and ≥\$25,000), ever use of noncigarette tobacco products (yes, no), health insurance status (yes, no), first-degree family history of lung cancer (yes, no), and body mass index (continuous).

Table 3. Lung cancer mortality in relation to menthol and non menthol cigarette smoking*

Baseline smoking status, type of cigarette, cpd†	HR(95% CI)‡
Never smoker	1.0 (Referent)
Current, nonmenthol, ≥20 cpd	16.1 (9.2 to 28.3)
Current, nonmenthol, 10-19 cpd	14.2 (7.8 to 25.8)
Current, nonmenthol, <10 cpd	9.9 (5.0 to 19.6)
Current, menthol, ≥20 cpd	13.9 (7.9 to 24.3)
Current, menthol, 10-19 cpd	8.3 (4.6 to 14.9)
Current, menthol, <10 cpd	4.6 (2.4 to 8.7)
Former smoker	4.7 (2.8 to 8.0)

* Cox proportional hazards analysis of lung cancer mortality among the Southern Community Cohort Study participants. Analysis included 305 deaths attributed to lung cancer after excluding 15 (4.7%) of the 320 identified deaths in the final multivariable model because of incomplete data on one or more model covariates. HR = hazard ratio; CI = confidence interval; cpd = cigarettes per day.

† Self-reported smoking status at entry into the cohort.

‡ Hazard ratios and 95% confidence intervals from Cox proportional hazards model with age used as the time variable, and adjusted for sex, race (black, white, other), recruitment source (community health centers, general population), education (<9, 9-11, 12, >12 years, college or beyond), household income (<\$15,000, \$15,000-\$24,999, ≥\$25,000), ever use of noncigarette tobacco products (yes, no), health insurance status (yes, no), first-degree family history of lung cancer (yes, no), and body mass index (continuous).

per day than nonmenthol smokers, and the likelihood of quitting smoking (both before study enrollment, and during follow-up) was the same or higher among menthol than nonmenthol smokers. The findings provide important new evidence that does not support claims that menthol cigarettes impart a greater lung cancer burden than nonmenthol cigarettes. Cigarette smoking remains the leading cause of premature death in the United States, but undue emphasis on reduction of menthol relative to other cigarettes may distract from the ultimate health prevention message that smoking of any cigarettes is injurious to health.

Previous research on lung cancer risk associated with smoking menthol cigarettes has not been extensive, but results have generally been consistent with our observations in the SCCS. Three case-control studies (5–8) of lung cancer [one reported in initial (5) and later stages (6)] and two prospective studies (9,10) have examined the relative impacts on lung cancer of menthol vs nonmenthol cigarettes. Only one, a cohort study involving 318 lung cancer cases in a 1979–1991 follow-up of smokers in a northern California health plan (9), reported a higher risk with menthols, but only among men and not women; the others, including a large multicenter case-control study with over 3400 lung cancer patients (6) estimated lung cancer relative risks to be the same or slightly less among menthol compared with nonmenthol smokers. Combining the multicenter study (6) data across sex and race groups, the overall odds of lung cancer can be shown to be statistically significantly lower among menthol compared with nonmenthol smokers (OR = 0.79, 95% CI = 0.65 to 0.96). Similarly, in the SCCS population, we found relative risks of 0.65 (incidence) and 0.69 (mortality) associated with menthol vs. nonmenthol cigarette type on lung cancer risk, with little indication of heterogeneity across race or sex groups.

Lower quit rates have been reported for menthol than nonmenthol cigarette smokers participating in smoking cessation trials (16, 17), in prospective (18) and cross sectional (19) surveys at health clinics, in a prospective follow-up for coronary artery disease (20), and in some recent subgroup analyses of large national databases (21,22). However, in two other smoking cessation trials (10,23), in two large population surveys (24,25), and in alternative analyses of one of the large national databases (26), negligible differences by cigarette type were found in the prevalence or rates of quitting. In the SCCS cohort, we evaluated quitting before entry into the cohort and during follow-up. Both analyses provided no evidence of a reduced tendency to quit among menthol smokers.

A recent national survey found menthol cigarettes to be preferred by 83% of African American but only by 23% of white smokers (1), figures almost identical to those observed in this study. In the SCCS, both black and white menthol smokers smoked an average of 1.6–1.8 fewer cigarettes per day than nonmenthol smokers of the same race and were less likely to smoke more than a pack per day. Lower consumption among menthol smokers has been reported previously (21,22,24–26), with menthol smokers having a nearly 30% reduced odds of heavy smoking (>20 cigarettes) reported in the largest survey (25). The lower relative risks of lung cancer we observed among menthol compared with nonmenthol smokers were adjusted for pack-years of consumption and thus independent of amounts smoked.

The limitations of our study include lack of detail in the histories of menthol vs nonmenthol use, in particular, the inability to

distinguish those who may have switched from one cigarette type to another. Hence, we could not identify exclusive menthol or nonmenthol users or estimate the years spent in smoking each type. However, tendencies to switch between menthols and nonmenthols have been consistently reported to be very low, especially among African Americans (27). Small percentages of smokers may not accurately report the menthol vs nonmenthol nature of the cigarettes they smoke, although the discrepancies appear to be less for adult than adolescent smokers (5). Such misclassifications of cigarette type, however, would tend to attenuate rather than enhance differences between the smoking groups. We also relied on self-report of smoking status (never, former, and current smoker). However, in a sample of SCCS participants, we assessed serum cotinine levels, and misclassification was low (4% for self-reported never smokers and 6% for self-reported former smokers based on a serum cotinine cutoff of 15 ng/mL) (L. B. Signorello, unpublished data). Although we stratified our analysis by categories based on cigarettes per day, some residual confounding may still exist because within the cigarettes per day categories the numbers of cigarettes smoked per day are slightly higher for nonmenthol than menthol smokers; however, the statistically significantly lower lung cancer odds ratios and hazard ratios for menthol vs nonmenthol smokers persisted when we directly adjusted for pack-years of consumption.

The strengths of this study include its size, with systematically obtained data on nearly 86000 adults, its inclusion of large numbers of both blacks and nonblacks of similar socioeconomic status, and its prospective design, where data on smoking and other variables were obtained before the onset of lung cancer, thus minimizing the potential for recall bias that can affect retrospective case-control studies. In addition, ongoing follow-up data collection enabled us to ascertain updated smoking status on large numbers of participants and prospectively evaluate quitting behavior in this heavy-smoking cohort.

The study findings are timely as deliberations are ongoing regarding the potential ban of the sale of menthol cigarettes in the United States. These data indicate that rates of lung cancer are no higher among menthol vs nonmenthol smokers, and raise the possibility they may in fact be lower, and that smoking cessation rates appear not to differ greatly between menthol and nonmenthol cigarette smokers. These findings should inform any decision-making process by the Food and Drug Administration to single out menthol cigarettes as uniquely more harmful than nonmenthol cigarettes.

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