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Lung Cancer Risk in White and Black Americans

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PURPOSE: To test whether differences in smoking-related lung cancer risks in blacks and whites can explain why lung cancer incidence is greater in black males than in white males but about equal in black and white females, given that a greater proportion of blacks are smokers, but smoke far fewer cigarettes per day than do whites.
METHODS: A hospital-based case-control study was conducted between 1984 and 1998 that included interviews with 1,710 white male and 1,321 white female cases of histologically confirmed lung cancer, 254 black male and 163 black female cases, and 8,151 controls. Relative risks were estimated via odds ratios using logistic regression, adjusted for age, education, and body mass index.
RESULTS. We confirmed prior reports that smoking prevalence is higher but overall dosage is lower among blacks. Overall ORs were similar for blacks and whites, except among the heaviest smoking males (21+ cigarettes per day or 37.5 pack–years), in whom ORs for blacks were considerably greater than for whites. Long-term benefits of cessation were similar for white and black ex-smokers. Smokers of menthol flavored cigarettes were at no greater risk for lung cancer than were smokers of unflavored brands.
CONCLUSIONS. Lung cancer risks were similar for whites and blacks with similar smoking habits, except possibly for blacks who were very heavy smokers; this sub-group is unusual in the general population of African American smokers. Explanations of racial disparities in lung cancer risk may need to account for modifying factors including type of cigarette (yield, mentholation), diet, occupation, and host factors such as ability to metabolize mainstream smoke carcinogens.
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INTRODUCTION

Lung cancer rates in the US show substantial unexplained racial variability. SEER incidence rates have been reported higher for blacks than whites in every year since 1973, with rate differentials between 34% and 67%. (1, 2). The prevalence of cigarette smoking has been considerably higher in black than in white males since 1950. It was slightly higher in black than in white females from 1962 until 1992, after which the rates have been nearly equal (3–6). The seeming

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Selected Abbreviations and Acronyms

AHF = American Health Foundation
BMI = body mass index
CDC = Centers for Disease Control and Prevention
CI = confidence interval
CPD = cigarettes per day
NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone
OR = odds ratio
PY = pack-years
SEER = surveillance, epidemiology and end results

consistency between smoking and lung cancer rates is weakened, however, by substantial differences in the number of cigarettes smoked per day (CPD). In 1991, 29.2% of adult blacks currently smoked cigarettes compared with 25.5% of whites, but blacks smoked on average 15.0 CPD while whites smoked 21.0 CPD. (7). Comparable differences have been reported in many other studies (5, 8–10).

Few analytic studies have addressed this anomaly. Schwartz and Swanson (11) concluded that racial differences in incidence could be "entirely explained" by smoking habits, based on an epidemiological study of over 5500 cases diagnosed in Detroit area hospitals in 1984 to 1987. Nevertheless, their conclusion did not apply to persons under 55 years of age, and was based on large numbers of proxy interviews, which might have affected the precision of reported ORs.

Although smoking is the overwhelming cause of lung cancer, other host and environmental factors may also modify risk. Modifying factors that have been studied include diet (12, 13), genetic polymorphisms in metabolizing genes (14–18) as well as more general familial factors (19, 20), metabolism differences (21, 22), occupation (23), and non-biological factors such as social class (24) and education (25). The hypothesis that the strong preference for menthol flavored cigarettes among black smokers may also partly explain risk differences has led to conflicting results among investigators, with no association reported by our group (26), and a positive association reported for men but not women by Sidney et al. (27).

To better delineate smoking-related risks for lung cancer between racial groups, it is important to make direct assessments of risk in relation to smoking habits as an essential backdrop for interpreting the impact of other risk factors, including those observed in metabolic and molecular studies. To address these issues we examined smoking habits and lung cancer risk in black and white Americans.

METHODS

Between 1984 and 1998 the American Health Foundation performed a hospital-based case-control study in the three major New York City cancer centers plus other hospitals in New York, Philadelphia, Washington DC, and other US cities (see Acknowledgments). Only incident cases were selected, defined as persons diagnosed with lung cancer for the first time during the 12 months preceding interview (most within 2 months). All cases were confirmed by histopathology. Adenocarcinomas were more common in women (46% of cases) than in men (37%), but differed little by race. Controls were selected from the daily admission rosters and frequency matched to cases on the basis of sex, age (±5 y), hospital, and year of interview. Eligible control diagnoses excluded tobacco-related diseases such as coronary heart disease, stroke, peripheral vascular disease, chronic obstructive pulmonary disease, gastric ulcer, cirrhosis of the liver, and cancers of the mouth, larynx, esophagus, bladder, kidney, pancreas, or liver (28). Control patients for studies of other tobacco-related cancers besides lung were being interviewed at the same time as cases, so that a large control pool of patients with non-tobacco-related diseases was available. Approximately half of male controls had benign or malignant diseases including benign prostatic hypertrophy (9%), prostate cancer (8%), colon-rectum cancer (11%); bone and joint diseases (5%); kidney stones, nephritis, and other kidney diseases (8%); abscesses (2%); sprains, strains, and fractures including hip, and a wide variety of other non-malignant conditions requiring hospitalization. Forty percent of female controls had cancers which included breast (15%), colon-rectum (7%), ovary (4%), connective tissue (2%), and melanoma (2%); other female controls were hospitalized for osteoarthritis (5%), fractures including hip (5%), genital prolapse (2%), abscesses (2%) and a wide variety of other non-malignant conditions. After providing written informed consent using a form approved by the Institutional Review Board of each hospital, every subject was interviewed by an AHF-trained interviewer using a structured questionnaire that elicited information on demographic variables, smoking history, and other possible risk factors. Approximately 85% of eligible patients who were approached agreed to be interviewed.

The 15-year accrual interval was chosen because it included large numbers of black and white patients who were recruited with a uniform protocol and interviewed under similar circumstances. The present analysis overlaps and extends earlier reports (26, 29) that included patients interviewed between 1977 and 1991. This is a significant extension, since it makes use of data obtained via face to face interviews with 11,599 patients (4192 interviewed after 1991), of whom 3448 were cases and 8151 were controls. It includes 417 black cases, 254 of whom were male (121 interviewed after 1991) and 163 female (81 interviewed after 1991).

Distributions of demographic and smoking variables were compared using chi-square tests. Means of continuous variables were compared between groups using *t*-tests. Odds ratios for lung cancer were computed using unconditional

logistic regression, with age at diagnosis entered as a continuous covariate and smoking parameters as indicator variables (30). Educational level and BMI (body mass index, computed as weight in kg five years prior to diagnosis divided by the square of height in cm) were considered to be potentially confounding variables, based upon prior reports from our group (31). Therefore, indicator variables for education (3 levels) and BMI (3 levels) were included in the logistic regression models in addition to smoking dosage.

A goal of this study was to evaluate the hypothesis that the risk of lung cancer differs between blacks and whites for equivalent exposure to tobacco smoke. Dosage was modeled in current smokers using categories of CPD or cumulative pack-years, and duration of smoking habit. Risk among ex-smokers was estimated in relation to years since quit. Since race is a matching variable by design, it was not appropriate to test the regression coefficients of the main effects in blacks versus whites for equality. Rather, a model was constructed that included a main effect for race (0 for white and 1 for black) along with interaction terms for race with each dosage variable and the covariates age, BMI, and education to control for potential confounding. The interaction of race with each of the dosage terms was then tested against zero. This is equivalent to a Wald's test for equality of the race term for the same dosage variable in separate stratified analyses for blacks or whites. A significantly non-zero value of the regression coefficient for the race-dosage interaction is interpreted as evidence of a black–white difference in lung cancer risk for given levels of tobacco smoke exposure.

There was initial concern that dosages might have varied during the 15-year study period. However, the average number of cigarettes smoked per day did not change significantly over time among men, or among black females. White women reduced their cigarette intake by an average of 2.1 CPD between 1984 to 1991 and 1992 to 1998 ($p < 0.01$). In an ANOVA that included time period, sex, and race effects, only the sex and race effects were significant, but not time period. The distributions of CPD within each sex-race group were also remarkably consistent over time. Therefore, a uniform categorization of CPD was used for the entire 15-year period, and no period adjustment was made. Because men smoke more cigarettes per day than do women, different groupings of CPD were used for men and for women, using gender-specific tertiles based on distributions among blacks.

RESULTS

Characteristics of the patient population are shown in Table 1. The average ages in the four sub-groups ranged between 56.9 and 61.7 years; the age distribution was somewhat younger in black compared with white men. Ed-

TABLE 1. Population characteristics of lung cancer cases and hospital controls by gender

	Male					Female			
	White		Black			White		Black	
	Cases (n = 1710)	Controls (n = 4491)	Cases (n = 254)	Controls (n = 440)		Cases (n = 1321)	Controls (n = 2862)	Cases (n = 163)	Controls (n = 358)
	%	%	%	%		%	%	%	%
Age					Age				
<40	2.1	4.3	2.0	6.4	<40	2.0	3.6	4.9	4.8
40–49	9.7	13.3	11.4	16.1	40–49	12.4	12.5	8.0	13.7
50–59	26.3	26.6	31.1	34.1	50–59	25.7	25.4	30.1	34.9
60–69	39.1	38.6	38.2	35.0	60–69	35.7	35.8	42.3	34.4
70+	22.9	17.3	17.3	8.4	70+	24.2	22.7	14.7	12.3
Mean(SD)	61.7(9.8)	59.6(10.5)	60.6(9.5)	56.9(10.3)	Mean(SD)	61.4(10.2)	60.7(10.9)	60.2(9.4)	58.0(10.2)
Education years					Education years				
<12	21.1	15.3	48.0	39.8	<12	14.2	12.9	42.9	36.6
=12	30.4	26.3	26.4	26.6	=12	43.0	34.2	31.3	26.5
>12	48.5	58.3	25.6	33.6	>12	42.9	52.9	25.8	36.9
Mean(SD)	13.4(3.5)	14.3(3.6)	11.4(3.3)	11.9(3.2)	Mean(SD)	13.2(2.7)	13.8(3.2)	11.6(2.6)	12.2(3.1)
Body mass index (kg/cm^2)					Body mass index				
≤23.54	23.2	17.4	40.3	23.7	≤21.50	36.4	30.8	34.7	25.2
23.55–26.67	38.8	38.8	31.5	32.3	21.51–23.96	34.2	32.6	25.7	27.0
26.68+	38.0	43.8	28.2	44.1	23.97+	29.5	36.7	39.5	47.9
Mean(SD)	26.2(3.8)	26.9(0.1)	25.0(4.0)	26.9(0.2)	Mean(SD)	24.0(4.2)	25.6(5.8)	25.5(5.3)	28.3(6.5)

ucation level differed by disease status and race: cases had fewer years of education than controls and blacks of either gender in general had significantly fewer years in education compared with whites. The mean BMI was significantly lower in cases than controls within each of the four sex-race groups ($p < 0.05$). White females tended to be leaner than black females, regardless of disease status.

The distribution of smoking variables is shown in Table 2. As expected, cases were far more likely than controls to be current smokers, to have begun smoking at an earlier age, and to have smoked for a longer period of time. Cases who were current smokers consumed more CPD, and ex-smokers had quit more recently compared with controls for all sex-race groups. Cigarette consumption by females was less intense than by males. Smoking prevalence was higher among blacks than whites–especially in males—in both cases and controls. Among current smokers, however, blacks smoked significantly fewer CPD than did whites: 10.7 fewer among male controls ($p < 0.001$) and 5.8 fewer among female controls ($p < 0.001$). The lower levels of CPD among blacks translated into substantially smaller numbers of pack-years (18 pack–years (PY) for black male controls and 8.7 PY for black female controls).

There was no difference between blacks and whites in age at onset of smoking among male cases, but among female cases blacks began smoking on average 1.4 years later than whites (19.2 versus 17.8 y, $p < 0.01$). The percentage of ex-smokers was higher for whites than for blacks, while black ex-smokers on average had quit smoking more recently than white ex-smokers had. Cessation patterns for females were similar though less pronounced than for males. White male cases who were ex-smokers had quit on average 2.8 y. longer than black male cases ($p < 0.05$), while a smaller difference of 1.7 year in the same direction was seen among female cases, which was not statistically significant.

TABLE 2. Distribution of smoking variables by gender and race

	Male					Female			
	White		Black			White		Black	
	Cases (n = 1710)	Controls (n = 4491)	Cases (n = 254)	Controls (n = 440)		Cases (n = 1321)	Controls (n = 2862)	Cases (n = 163)	Controls (n = 358)
	%	%	%	%		%	%	%	%
Smoking status					Smoking status				
Non-smoker	3.5	29.8	2.4	25.5	Non-smoker	9.2	50.5	6.8	49.7
Ex-smoker	49.8	49.5	33.1	36.4	Ex-smoker	37.6	33.0	30.7	23.2
Current smoker	46.7	20.7	64.6	38.2	Current smoker	53.1	16.6	62.6	27.1
Current smoker					Current smoker				
Cigarettes per day					Cigarettes per day				
1–19	10.8	25.7	26.2	62.5	1–10	9.4	28.5	24.5	50.5
20	26.6	27.3	39.0	22.6	11–20	38.9	39.8	47.1	37.1
21–30	19.0	17.8	15.9	8.3	21+	51.6	31.7	28.4	12.4
31+	43.7	29.2	18.9	6.6					
Mean(SD)	32.6(15.5)	26.6(15.3)	24.4(14.1)	15.9(11.4)	Mean(SD)	27.6(13.2)	20.8(12.8)	20.2(10.1)	15.0(9.2)
Pack-years					Pack-years				
≤20	4.6	13.6	9.2	41.0	≤14	4.1	19.3	14.1	30.2
20–37.5	16.3	24.8	32.5	33.7	14–31.5	20.3	29.5	28.3	37.5
37.5–55	27.6	29.8	27.6	16.9	31.5–48	32.6	27.6	39.4	19.8
55+	51.6	31.8	30.7	8.4	48+	43.1	23.6	18.2	12.5
Mean(SD)	61.8(30.8)	47.6(27.7)	48.0(31.4)	29.6(23.0)	Mean(SD)	48.1(23.5)	34.4(22.2)	36.4(22.7)	25.7(17.2)
Smoking duration in years					Smoking duration in years				
<40	39.6	55.1	43.6	63.7	<40	45.3	63.5	51.0	68.0
40+	60.4	44.9	56.4	36.3	40+	54.7	36.5	49.0	32.0
Mean(SD)	41.7(10.2)	37.0(11.6)	42.2(10.9)	34.6(12.2)	Mean(SD)	40.5(9.9)	34.8(12.3)	38.9(10.4)	35.1(11.1)
Age at onset of smoking					Age at onset of smoking				
Mean(SD)	16.4(3.9)	17.7(5.1)	16.3(4.1)	18.4(5.8)	Mean(SD)	17.8(3.9)	20.7(7.8)	19.2(5.6)	20.8(6.8)
Cigarette preference					Cigarette preference				
Menthol cigarette	15.5	18.9	40.8	49.0	Menthol cigarette	13.5	23.7	41.6	51.8
Non-menthol cigarette	84.5	81.1	59.2	51.0	Non-menthol cigarette	86.5	76.3	58.4	48.2
Ex-smokers					Ex-smokers				
Years since quit					Years since quit				
1–10	50.9	30.9	67.9	45.0	1–5	33.5	18.6	48.0	26.5
11–20	27.5	28.6	16.7	32.5	6–15	38.7	32.5	22.0	37.4
21+	21.6	40.5	15.5	22.5	16+	27.8	48.9	30.0	36.1
Mean(SD)	13.2(10.4)	18.6(11.4)	10.4(9.8)	14.1(11.1)	Mean(SD)	11.8(9.9)	17.6(12.1)	10.1(9.0)	14.6(11.2)

ORs for lung cancer in relation to overall smoking habits and intensity are shown in Table 3. Among current smokers, the OR for lung cancer among white males was comparable to that among black males (21.0 vs. 18.2), and the OR among white females was comparable to that among black females (19.3 vs. 17.2). The ORs among ex-smokers were similar for white and black males (7.9 and 8.1, respectively). None of the black–white differences in smoking habit ORs were statistically significant.

Classical dose-response patterns were observed in all four sex–race combinations using either CPD or PY. The 95% confidence intervals for ORs for blacks and whites overlapped for each specific dosage category. However, for dosages of 20 or more CPD and 37.5 or more PY, the ORs for black males greatly exceeded those for white males. For example, among current smokers of 20 CPD, the OR for black males was 34.2 (95% CI 13.3–88.3), which was nearly 75% higher than the value of 20.0 (14.4–27.6) for white males. At the highest dosage (21+ CPD) the OR for black males was 42.2 (15.9–111.9), nearly 50% higher than for white males (29.8; 22.1–40.2). At the same dosage the OR for black females (42.9; 17.0–108.4) was 28% higher than for white females (33.6; 25.4–44.4). For cumulative dosages above 20 PY, ORs for black males considerably exceeded those for white males, with the ORs at 37.5 PY and above nearly twice as great in black males. The interaction term between PY and race was statistically significant ($p < 0.05$). However, there were no black–white differences in PY related ORs for females. OR estimates of risk related to duration of smoking habit were likewise similar in blacks and whites.

Smoking cessation effects are also shown in Table 3. Using non-smokers as the reference, ORs decreased as the smoking cessation period expanded. Among men, the ORs were comparable between whites and blacks, and the term for interaction of race with years of cessation was not statis-

TABLE 3. Odds ratios (adjusted for age at diagnosis, BMI and education years) for lung cancer in relation to smoking habits

	Male			Female	
	White	Black		White	Black
	OR(95%CI)	OR(95%CI)		OR(95%CI)	OR(95%CI)
Smoking status			Smoking status		
Non-smoker	1.0	1.0	Non-smoker	1.0	1.0
Ex-smoker	7.9(6.0–10.3)	8.1(3.4–19.4)	Ex-smoker	6.3(5.1–7.9)	9.3(4.5–19.2)
Current smoker	21.0(15.8–27.8)	18.2(7.6–43.4)	Current smoker	19.3(15.4–24.2)	17.2(8.7–33.7)
Current smokers			Current smokers		
Cigarettes per day			Cigarettes per day		
Non-smoker	1.0	1.0	Non-smoker	1.0	1.0
1–19	8.4(5.9–12.1)	7.5(3.0–18.7)	1–10	6.2(4.4–8.8)	8.3(3.8–18.2)
20	20.0(14.4–27.6)	34.2(13.3–88.3)	11–20	19.1(14.6–25.0)	21.3(10.0–45.2)
21+	29.8(22.1–40.2)	42.2(15.9–111.9)	21+	33.6(25.4–44.4)	42.9(17.0–108.4)
Interaction p-value[a]	0.182		Interaction p-value[a]	0.868	
Pack-years			Pack-years		
Non-smoker	1.0	1.0	Non-smoker	1.0	1.0
≤20	6.3(4.0–9.9)	4.7(1.7–13.0)	≤14	3.4(2.1–5.4)	7.7(3.2–18.2)
20.0–37.5	12.1(8.6–17.0)	16.7(6.6–41.9)	14.0–31.5	10.6(7.8–14.2)	9.7(4.5–20.9)
37.5–55.0	15.7(11.6–21.4)	28.3(10.8–74.1)	31.5+	22.7(17.9–28.8)	23.9(11.6–49.1)
55.0+	28.3(21.1–37.9)	54.7(19.4–153.9)			
Interaction p-value[a]	0.035		Interaction p-value[a]	0.636	
Smoking duration in years			Smoking duration in years		
Non-smoker	1.0	1.0	Non-smoker	1.0	1.0
<40	15.8(11.5–21.8)	16.1(6.7–45.7)	<40	13.4(10.2–17.6)	14.6(6.9–30.9)
40+	25.1(18.6–33.8)	20.1(8.7–54.7)	40+	24.7(19.1–32.0)	20.7(9.6–44.7)
Interaction p-value[a]	0.277		Interaction p-value[a]	0.408	
Ex-smokers			Ex-smokers		
Years since quit			Years since quit		
Non-smoker	1.0	1.0	Non-smoker	1.0	1.0
1–10	14.5 (10.9–19.5)	13.7 (5.9–37.5)	1–5	10.1 (7.9–13.0)	11.0 (5.0–24.2)
11–20	7.8 (5.8–10.6)	4.2 (1.6–12.7)	6–15	6.7 (4.8–9.4)	6.5 (2.0–20.7)
21+	3.7 (2.8–5.1)	3.9 (1.4–12.3)	16+	3.4 (2.6–4.4)	7.2 (2.9–17.5)
Interaction p-value[a]	0.888		Interaction p-value[a]	0.221	

[a] p-value for term representing interaction between race and indicated dosage variable.

tically significant. A small difference in ORs was observed between white and black female ex-smokers with more than 15 years of cessation. However, risk estimates among female ex-smokers did not differ significantly between whites and blacks.

There were only small racial differences in self-reported depth of inhalation or the amount of each cigarette smoked: 36% of white male and 27% white female smokers reported that they inhaled deeply, compared with 35% of black males and 24% of black females. Furthermore, 81% of white males and 71% white females smoked at least two thirds of each cigarette, compared with 81% of black males and 75% of black females (data not shown in Tables).

Among current smokers, 45.1% of male and 46.5 of female blacks smoked menthol cigarettes, compared with 17.3% of male and 17.6% of female whites. ORs among smokers of menthol cigarettes were practically the same as among smokers of non-menthol cigarettes (Table 4).

DISCUSSION

Our data show few differences in lung cancer risk between blacks and whites in both men and women. In current smokers, relative risk estimates were similar between blacks and whites when stratified by amount and duration of smoking, and in ex-smokers by years since smoking cessation. Higher risks were observed among black men compared with white men for the heaviest smokers (e.g., 21 or more CPD, 37.5 or more PY), but these differences were not statistically significant. A significant interaction was found between dosage and race in men only ($p < 0.05$), which was due largely to the differences among blacks in the 55+ PY category. While our data are thus consistent with differences in risk among the heaviest smokers, it should be noted that most blacks smoke fewer than one pack per day (32) (as do the controls in this study) and that the observed increased risk thus occurred among a relatively small group of black smokers. Further studies would be needed to confirm this possible increase in risk.

The validity of our findings depends in part on the extent of bias in this case-control design, which may be gauged to some extent by comparison with smoking habits in the general population. Our data are consistent with national survey data on smoking habits (32), which show a higher prevalence of cigarette smoking in black compared with white males, but a significantly smaller daily consumption among regular smokers. The observed brand distributions in our patient population were not unusual, and the prevalence of menthol smokers differed by only a few percent from those reported in a case-control study by Carpenter et al. (33). Although risks among ex-smokers did not differ between whites and blacks, we noted substantial differences in cessation patterns that are consistent with the limited number of black ex-smokers. Among the controls, white males had quit on average 4.5 years earlier than black males ($p < 0.001$) and white females had quit 3.0 years earlier than black females ($p < 0.05$). Ex-smokers made up a significantly greater percentage of ever-smokers among whites compared with blacks (71% vs. 49% for males, 67% vs. 46% for females, both $p < 0.001$). Few population data are available against which these cessation rates may be compared, but they are consistent with patterns recently reported by Gilpin and Pierce (34) who used cross-sectional data gathered from a succession of National Health Interview Surveys conducted between 1965 and 1992. They reported generally lower cessation among African Americans aged 35 to 50 years compared with whites in the same age group.

Previous studies have shown that smoking habits are related to socioeconomic status (SES), which in turn is strongly correlated with lung cancer risk (5). Baquet et al. have shown that adjustment of rates for SES tends to reduce racial differences in risk (24). We adjusted all smoking-related ORs for education. Nevertheless, there were still large social class differences between whites and blacks as measured by educational level. These educational differences between lung cancer cases and controls in general are consistent with many earlier reports from our group (9, 28, 29).

The lower socioeconomic status of blacks may have resulted in limited access to health care and manifested as late presentation with severely advanced disease. Among black lung cancer patients, 81.3% presented with stage III and IV, compared with 58.7% among white cases. If the severity of lung cancer increases with the intensity of cigarette smoking, an underestimate of lung cancer risk in blacks with heavy cigarette consumption might result due to undersampling of severe black lung cancer cases. However,

TABLE 4. Odds ratios for lung cancer in current smokers according to preference for menthol cigarettes adjusted for age, education (3 levels), BMI (3 levels), and pack-years (4 levels for males and 3 levels for females)

	Males		Females	
	White	Black	White	Black
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Non-menthol	1.00	1.00	1.00	1.00
Menthol	0.83(0.63–1.09)	1.34(0.79–2.29)	0.61(0.44–1.06)	0.79(0.41–1.54)

within each CPD or PY category, ORs did not differ by stage, suggesting that underestimation has not occurred.

Cigarette brands favored by black smokers might differ in toxicity from those smoked by the majority of whites, and it has been suggested that the greater preference for menthol flavored cigarettes among black smokers may contribute to their higher lung cancer rates (35). This preference may be the result of racially targeted advertising by the tobacco industry. Hoffman–Goetz et al. (36) examined popular magazines whose readership is principally black, and noted that in 8 years only 6 of 84 articles on cancer specifically addressed lung cancer, while the same magazines carried nearly 1500 tobacco advertisements. While black smokers in our study were more likely to choose menthol than non-menthol brands (Table 2), our data provide no evidence that menthol cigarettes per se produce greater lung cancer risk than do non-menthol brands (Table 4). This is consistent with a 1991 report by Kabat and Hebert (26) based on 588 male and 456 female cases (those data overlap the present study), as well as with the study by Carpenter et al. (33) based on 337 cases. By contrast, Sidney et al. (27) concluded that increased lung cancer risk was associated with menthol cigarette smoking in male but not female smokers. However, Ahiyevich (37) found no significant differences in puff volume between black and white women who smoked either menthol or nonmenthol cigarettes. Experimental data show no increase in NNK-induced adduct formation in NNK-treated rats that were administered menthol in their drinking water (NNK is a tobacco-specific nitrosamine, which experimentally produces lung adenocarcinoma in rodents), further supporting our conclusion that menthol does not play a role in risk for lung cancer. Menthol is the only one of many flavoring agents added to cigarettes which is used to differentiate brands from one another (38, 39); little is known of possible health effects of other additives.

We adjusted for age, education, and body mass, which Kabat et al. (31) showed to be inversely related to lung cancer risk, and used BMI five years prior diagnosis to reduce bias introduced by weight loss due to the cancer itself. Other exposures or lifestyle situations such as occupational exposures also influence lung cancer risk (40), but occupational lung cancer studies among blacks are rare. Using data from National Health Interview Surveys, Sterling (23) observed that more blacks than whites held jobs with potential carcinogenic exposures. We recently reported elevated lung cancer risks among black males exposed to asbestos and coal dust, and among black females exposed to paint and gas fumes (41). In the present study, there were no significant differences between blacks and whites in the proportions of occupations known to be associated with higher lung cancer risk. However, the number of different occupations and exposures was large, and there was little statistical power to examine risk with respect to specific occupations; such investigations are more efficiently performed in cohorts of workers occupationally exposed to lung carcinogens (42).

Metabolic mechanisms undoubtedly play a role in determining lung cancer risk. Richie and colleagues reported significant higher levels of urinary NNAL, NNAL-Gluc, and total NNAL in black compared with white smokers of similar CPD, and significant lower urinary NNAL-Gluc:NNAL ratios in blacks (21). We recently measured higher levels of both plasma and urinary cotinine, plasma thiocyanate, and total NNAL in black compared with white smokers on a per-cigarette basis. (43) Glucuronidation is one of the major detoxification mechanisms for NNAL and its parent metabolite, NNK; differences in glucuronidative capacity may contribute to the differences in susceptibility to lung cancer between blacks and whites. Perez-Stable et al. (22) proposed that higher levels of cotinine per cigarette smoked by blacks compared with whites could be explained by slower clearance of cotinine and higher intake of nicotine per cigarette by blacks.

Molecular epidemiologic studies have examined the role of polymorphisms in genes coding for enzymes that activate or detoxify mainstream tobacco smoke carcinogens like NNK, or polycyclic aromatic hydrocarbons like benzo[a]pyrene, but few have directly compared the risk associated with these polymorphisms in blacks versus whites. Associations were recently reported between the presence of the GSTM1 (0/0) genotype and increased risk for oral cancer (which like lung cancer is also tobacco-related) in blacks but not whites (44, 45), in a pattern that was linked to smoking dose. As in the present study, the biggest racial difference in risk was in heavier smokers. Although a significant association has not been observed for the GSTM1 null polymorphism and lung cancer risk in either blacks (16, 46) or whites (47), a significant association was reported among Japanese (48), supporting the need to examine polymorphic profiles for other metabolizing enzyme genes.

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