Racial and Ethnic Variations in Lung Cancer Incidence and Mortality: Results From the Women's Health Initiative

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ABSTRACT

Purpose

This study aimed to evaluate racial/ethnic differences in lung cancer incidence and mortality in the Women's Health Initiative Study, a longitudinal prospective cohort evaluation of postmenopausal women recruited from 40 clinical centers.

Methods

Lung cancer diagnoses were centrally adjudicated by pathology review. Baseline survey questionnaires collected sociodemographic and health information. Logistic regression models estimated incidence and mortality odds by race/ethnicity adjusted for age, education, calcium/vitamin D, body mass index, smoking (status, age at start, duration, and pack-years), alcohol, family history, oral contraceptive, hormones, physical activity, and diet.

Results

The cohort included 129,951 women—108,487 (83%) non-Hispanic white (NHW); 10,892 (8%) non-Hispanic black (NHB); 4,882 (4%) Hispanic; 3,696 (3%) Asian/Pacific Islander (API); 534 (< 1%) American Indian/Alaskan Native; and 1,994 (1%) other. In unadjusted models, Hispanics had 66% lower odds of lung cancer compared with NHW (odds ratio [OR], 0.34; 95% CI, 0.2 to 0.5), followed by API (OR, 0.45; 95% CI, 0.27 to 0.75) and NHB (OR, 0.75; 95% CI, 0.59 to 0.95). In fully adjusted multivariable models, the decreased lung cancer risk for Hispanic compared with NHW women attenuated to the null (OR, 0.59; 95% CI, 0.35 to 0.99). In unadjusted models Hispanic and API women had decreased risk of death compared with NHW women (OR, 0.30 [95% CI, 0.15 to 0.62] and 0.34 [95% CI, 0.16 to 0.75, respectively]; however, no racial/ethnic differences were found in risk of lung cancer death in fully adjusted models.

Conclusion

Differences in lung cancer incidence and mortality are associated with sociodemographic, clinical, and behavioral factors. These findings suggest modifiable exposures and behaviors may contribute to differences in incidence of and mortality by race/ethnicity for postmenopausal women. Interventions focused on these factors may reduce racial/ethnic differences in lung cancer incidence and mortality.

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INTRODUCTION

Worldwide, lung cancer is a leading cause of cancer incidence and death.^{1,2} Disparities in lung cancer incidence and mortality have been previously reported in several cohort studies worldwide. These studies demonstrate the highest rates among non-Hispanic black (NHB) populations³⁻⁶ and the lowest rates among Hispanic^{7,8} and Asian populations.⁹⁻¹¹ Although these findings are consistent with those reported among men in the United States,^{3,4,12,13} these

discrepancies have not been as well-described among women.

The few studies among US women are inconsistent; some reported increased incidence and mortality among non-Hispanic white (NHW) women compared with other racial/ethnic groups^{4,14} and others showed increased incidence in NHB women.^{13,15,16} Some smaller-sample-size studies that adjusted for age, socioeconomic status, and smoking demonstrated similar incidences among NHW and NHB women.¹⁷⁻²² Other studies suggested that differences depend on pack-years smoked. For example, the Multi-Ethnic

Cohort study revealed an increased incidence among NHB women who smoke fewer than 30 cigarettes daily compared with NHW women, and that differences no longer persist in women who smoke more than 30 cigarettes daily.¹⁸ In this same study, consistent with other investigations,^{23,24} Japanese-American and Hispanic women had lower incidence than NHW women, which was thought to be due to decreased smoking rates.¹⁸ In the few studies that evaluated mortality, age-adjusted models demonstrated that mortality is similar among NHB and NHW women.^{3,25} However, one study demonstrated that NHB women younger than 65 years have decreased 5-year survival compared with NHW women.²⁶

Inconsistencies in the existing literature on racial and ethnic differences in lung cancer incidence and mortality may be due to the lack of inclusion of various risk factors. In this study, we sought to investigate the influence of sociodemographic, clinical, and behavioral risks on lung cancer incidence and mortality in the Women's Health Initiative (WHI). Our aim was to determine whether differences exist in lung cancer incidence and mortality among women by race/ethnicity in a prospective cohort.

METHODS

The WHI, a multiethnic, prospective, longitudinal cohort study of the major risk factors that affect postmenopausal women's health, includes observational study (OS) and clinical trial (CT) arms. The study design, described previously, included women at 40 US clinical centers.^{27,28} Postmenopausal women were eligible if they were age 50 to 79 years, were unlikely to relocate or die within 3 years, were without certain complicating conditions, and provided written consent. The CT arms evaluated effects of hormones, diet, and calcium and vitamin D supplementation, and women could choose to participate in one, two, or all three of the components. Women ineligible or unwilling to join the CT arms were invited to enroll on the OS, which examined association of baseline lifestyle, health, and risk factors on disease outcomes. Inclusion of the OS and CT arms provides an increased sample size that enhances the associations of behavioral patterns on lung cancer incidence and mortality.

Baseline Data Collection

Self-administered questionnaires were used to collect baseline demographic, medical, reproductive, and family history. Physical activity was obtained as metabolic equivalent of tasks (MET). Food intake was obtained by a semiquantitative food frequency questionnaire.

Behaviors such as smoking and alcohol use were also obtained through baseline questionnaires. Never smoking was defined as having smoked fewer than 100 cigarettes in a lifetime; past smokers was defined as those who had smoked 100 or more cigarettes but had not reported smoking at baseline; current smokers was defined as those who reported smoking at baseline. Additional information obtained from past smokers and current smokers included age of smoking initiation, cigarettes/day, years of smoking, and age of smoking cessation (past smokers only). Pack-years were calculated by multiplying cigarettes/day by the number of years smoked, divided by 20 (average cigarettes/pack). Nonsmokers were defined as having smoked zero pack-years; light smokers, fewer than 20 pack-years; and heavy smokers, 20 or more pack-years.

Information regarding hormone therapy use (defined as use of estrogen-containing agents for at least 3 months and additionally classified as estrogen alone or combination estrogen/progestin), oral contraceptives, and other medications, including dietary supplements, also was obtained. Information about race/ethnicity was self-reported as NHW, NHB, Hispanic, Asian/Pacific Islander (API), American Indian/Alaskan Native (AIAN), and other.

Follow-Up and Lung Cancer Ascertainment

Lung cancer diagnoses were collected annually for OS participants and semiannually for CT participants. Self-reports or next-of-kin (proxy) reports of lung cancer events were verified by centrally trained WHI physician adjudicators at the Clinical Centers after review of the medical and pathology records by using the Surveillance Epidemiology and End Results (SEER) coding system. Cancer-specific mortality was defined as lung cancer deaths and also was recorded if the patient had a lung cancer diagnosis and the cause of death was entered as other cancer if it was not specifically recorded as lung cancer. Participants were enrolled from 1993 until 1998, and follow-up lasted through 2009.

Statistical Analyses

Primary analyses were designed to address relationships between race/ethnicity and risk for incidence and mortality. Of secondary interest was the relationship between race/ethnicity and cancer subtype. We used logistic regression models to estimate odds ratios and 95% CIs for incidence and mortality by race/ethnicity because of the anticipated small cell sizes. The first model (model 1) was unadjusted; subsequent models were adjusted for age as a continuous covariate (model 2); adjusted additionally for smoking (model 3); and adjusted for all potential confounders at baseline (model 4), which were selected a priori on the basis of established and hypothesized risk factors. Potential confounders were included as covariates in the model; these included both smoking-related (age at initiation duration, pack-years, smoking status) and non-smoking-related (age, education, calcium and/or vitamin D supplementation, body mass index [BMI], alcohol use, OS or CT membership and random assignment status if enrolled in CT, family history of cancer, oral contraceptive use, hormone use, physical activity, and diet [fruit, vegetable, and meat

Fig 1. Cohort sample size flow chart, Women's Health Initiative. CT, clinical trial; OS, observational study.

Table 1. Baseline Characteristics by Race/Ethnicity

Covariate	No. (%) of Patients by Race/Ethnicity					
	White (n = 108,487)	Black (n = 10,892)	API (n = 3,696)	Hispanic (n = 4,882)	A/AN (n = 534)	Other (n = 1,460)
OS membership						
Yes	65,197 (60.1)	5,723 (52.5)	2,354 (63.7)	2,735 (56.0)	315 (59.0)	834 (57.1)
No	43,290 (39.9)	5,169 (47.5)	1,342 (36.3)	2,147 (44.0)	219 (41.0)	626 (42.9)
HT intervention						
Not randomized	91,134 (84.0)	8,878 (81.5)	3,241 (87.7)	3,729 (76.4)	437 (81.8)	1,209 (82.8)
E + P intervention	5,584 (5.1)	418 (3.8)	165 (4.5)	359 (7.4)	19 (3.6)	81 (5.5)
E + P control	5,488 (5.1)	440 (4.0)	155 (4.2)	303 (6.2)	21 (3.9)	71 (4.9)
E-alone control	3,152 (2.9)	598 (5.5)	65 (1.8)	250 (5.1)	24 (4.5)	54 (3.7)
E-alone intervention	3,129 (2.9)	558 (5.1)	70 (1.9)	241 (4.9)	33 (6.2)	45 (3.1)
CaD intervention						
Not randomized	84,692 (78.1)	8,414 (77.2)	3,052 (82.6)	3,727 (76.3)	417 (78.1)	1,159 (79.4)
Intervention	11,926 (11.0)	1,255 (11.5)	326 (8.8)	590 (12.1)	61 (11.4)	145 (9.9)
Control	11,869 (10.9)	1,223 (11.2)	318 (8.6)	565 (11.6)	56 (10.5)	156 (10.7)
DM intervention						
Not randomized	77,748 (71.7)	6,991 (64.2)	2,713 (73.4)	3,497 (71.6)	382 (71.5)	1,011 (69.2)
Intervention	12,306 (11.3)	1,580 (14.5)	376 (10.2)	561 (11.5)	62 (11.6)	180 (12.3)
Control	18,433 (17.0)	2,321 (21.3)	607 (16.4)	824 (16.9)	90 (16.9)	269 (18.4)
Age, years						
50-54	12,827 (11.8)	2,063 (18.9)	596 (16.1)	1,166 (23.9)	105 (19.7)	209 (14.3)
55-59	20,854 (19.2)	2,518 (23.1)	708 (19.2)	1,295 (26.5)	118 (22.1)	275 (18.8)
60-69	49,583 (45.7)	4,669 (42.9)	1,543 (41.7)	1,928 (39.5)	222 (41.6)	660 (45.2)
70-79	25,223 (23.2)	1,642 (15.1)	849 (23.0)	493 (10.1)	89 (16.7)	316 (21.6)
Education level						
High school graduate or less	22,816 (21.0)	2,639 (24.2)	766 (20.7)	2,017 (41.3)	164 (30.7)	374 (25.6)
Some post-secondary or more	85,671 (79.0)	8,253 (75.8)	2,930 (79.3)	2,865 (58.7)	370 (69.3)	1,086 (74.4)
Smoking status						
Never smoked	56,937 (52.5)	5,691 (52.2)	2,729 (73.8)	3,239 (66.3)	276 (51.7)	852 (58.4)
Past smoker	44,273 (40.8)	3,902 (35.8)	819 (22.2)	1,274 (26.1)	198 (37.1)	497 (34.0)
Current smoker	7,277 (6.7)	1,299 (11.9)	148 (4.0)	369 (7.6)	60 (11.2)	111 (7.6)
Alcohol use						
Nondrinker	9,985 (9.2)	1,951 (17.9)	1,408 (38.1)	958 (19.6)	92 (17.2)	225 (15.4)
Past drinker	18,047 (16.6)	3,541 (32.5)	764 (20.7)	1,116 (22.9)	137 (25.7)	307 (21.0)
< 1 drink/month	13,490 (12.4)	1,461 (13.4)	540 (14.6)	676 (13.8)	59 (11.0)	210 (14.4)
< 1 drink/week	22,710 (20.9)	1,995 (18.3)	553 (15.0)	1,028 (21.1)	97 (18.2)	314 (21.5)
1-6 drinks/week	30,159 (27.8)	1,474 (13.5)	335 (9.1)	881 (18.0)	106 (19.9)	290 (19.9)
≥ 7 drinks/week	14,096 (13.0)	470 (4.3)	96 (2.6)	223 (4.6)	43 (8.1)	114 (7.8)
Postmenopausal HT						
Never used	34,272 (31.6)	5,094 (46.8)	1,045 (28.3)	1,965 (40.2)	191 (35.8)	533 (36.5)
Past user	24,779 (22.8)	2,712 (24.9)	746 (20.2)	1,071 (21.9)	134 (25.1)	364 (24.9)
Current user	49,436 (45.6)	3,086 (28.3)	1,905 (51.5)	1,846 (37.8)	209 (39.1)	563 (38.6)
Oral contraceptive (ever used)						
Yes	45,660 (42.1)	4,194 (38.5)	1,337 (36.2)	2,074 (42.5)	226 (42.3)	534 (36.6)
No	62,827 (57.9)	6,698 (61.5)	2,359 (63.8)	2,808 (57.5)	308 (57.7)	926 (63.4)
Cancer in female relatives						
Yes	54,744 (50.5)	4,386 (40.3)	1,432 (38.7)	1,936 (39.7)	246 (46.1)	672 (46.0)
No	53,743 (49.5)	6,506 (59.7)	2,264 (61.3)	2,946 (60.3)	288 (53.9)	788 (54.0)
Cancer in male relatives						
Yes	39,912 (36.8)	3,407 (31.3)	1,259 (34.1)	1,183 (24.2)	164 (30.7)	481 (32.9)
No	68,575 (63.2)	7,485 (68.7)	2,437 (65.9)	3,699 (75.8)	370 (69.3)	979 (67.1)

(continued on following page)

Table 1. Baseline Characteristics by Race/Ethnicity (continued)

Covariate	No. (%) of Patients by Race/Ethnicity					
	White (n = 108,487)	Black (n = 10,892)	API (n = 3,696)	Hispanic (n = 4,882)	AIAN (n = 534)	Other (n = 1,460)
Calcium supplementation						
Yes	75,328 (69.4)	5,435 (49.9)	2,610 (70.6)	2,871 (58.8)	308 (57.7)	920 (63.0)
No	33,159 (30.6)	5,457 (50.1)	1,086 (29.4)	2,011 (41.2)	226 (42.3)	540 (37.0)
Vitamin D supplementation						
Yes	68,396 (63.0)	5,165 (47.4)	2,084 (56.4)	2,525 (51.7)	271 (50.7)	813 (55.7)
No	40,091 (37.0)	5,727 (52.6)	1,612 (43.6)	2,357 (48.3)	263 (49.3)	647 (44.3)
MET-h/week						
0	15,897 (14.7)	2,538 (23.3)	553 (15.0)	1,062 (21.8)	97 (18.2)	240 (16.4)
0-3	13,222 (12.2)	1,765 (16.2)	453 (12.3)	786 (16.1)	78 (14.6)	187 (12.8)
3-9	25,894 (23.9)	2,785 (25.6)	861 (23.3)	1,214 (24.9)	130 (24.3)	371 (25.4)
≥ 9	53,474 (49.3)	3,804 (34.9)	1,829 (49.5)	1,820 (37.3)	229 (42.9)	662 (45.3)
BMI, kg/m ²						
0-25	40,614 (37.4)	1,774 (16.3)	2,166 (58.6)	1,224 (25.1)	135 (25.3)	440 (30.1)
25-30	37,752 (34.8)	3,589 (33.0)	1,132 (30.6)	1,857 (38.0)	160 (30.0)	531 (36.4)
≥ 30	30,121 (27.8)	5,529 (50.8)	398 (10.8)	1,801 (36.9)	239 (44.8)	489 (33.5)
Age when started smoking, years						
< 20	30,033 (58.3)	2,518 (48.4)	332 (34.3)	717 (43.6)	129 (50.0)	308 (50.7)
≥ 20	21,517 (41.7)	2,683 (51.6)	635 (65.7)	926 (56.4)	129 (50.0)	300 (49.3)
Age when quit smoking, years*						
< 45	26,133 (59.0)	2,089 (53.5)	510 (62.3)	794 (62.3)	129 (65.2)	293 (59.0)
≥ 45	18,140 (41.0)	1,813 (46.5)	309 (37.7)	480 (37.7)	69 (34.8)	204 (41.0)
Mean (SD) daily medium servings of fruit	1.91 (1.22)	1.81 (1.38)	1.81 (1.24)	1.67 (1.34)	1.55 (1.14)	1.85 (1.36)
Mean (SD) daily medium servings of vegetables	2.25 (1.28)	1.78 (1.25)	2.00 (1.27)	1.6 (1.22)	1.91 (1.23)	2.1 (1.35)
Mean (SD) daily animal protein consumption, g	48.15 (23.69)	44.43 (32.66)	38.56 (24.79)	46.83 (31.9)	48.49 (44.69)	45.86 (27.83)
Mean (SD) physical activity (MET-h/week)	12.77 (13.65)	9.57 (12.62)	13.03 (14.09)	10.39 (13.62)	11.93 (14.93)	12.37 (14.1)
Mean (SD) pack-years	21.8 (21.87)	16.65 (16.69)	15.47 (17.26)	11.92 (15.16)	18.79 (19.97)	20.48 (20.83)
Mean (SD) years smoked	24.03 (13.99)	26.27 (13.38)	21.26 (14.1)	22.15 (13.83)	23.47 (15.27)	24.26 (13.95)
Mean (SD) quit rate	85.88 (0)	75.02 (0)	84.69 (0)	77.54 (0)	76.74 (0)	81.74 (0)

NOTE: All *P* values are < .001. Data are from the Women's Health Initiative observational study and clinical trial cohorts.

Abbreviations: AIAN, American Indian/Alaskan Native; API, Asian/Pacific Islander; BMI, body mass index; CaD, calcium and vitamin D; DM, dietary modification; E, estrogen; HT, hormone therapy; MET, metabolic equivalent; OS, observational study; P, progesterone; SD, standard deviation.

* *P* = .009.

consumptions)] characteristics. Because it is possible that race/ethnicity-specific risk is modified by smoking intensity, correlation between stage and race/ethnicity among incident cases was examined with Wald χ^2 tests. Models were fit with an interaction term between smoking intensity (heavy, light, nonsmoker) and race/ethnicity. These interactions were not significant, so they were dropped from final models.

In secondary analyses, we examined associations between histologic subtype and race/ethnicity, for which histologic subtype was defined as no cancer diagnosed, small-cell lung cancer, or non-small-cell lung cancer. Multinomial regression was used to explore associations between race/ethnicity and histology in a multivariable-adjusted model. Wald tests were used to assess relevant associations. For example, Wald tests were used to assess association between stage and race/ethnicity among incident cases and association between smoking dose and race/ethnicity on incidence and mortality. All analyses were conducted by using Statistical Analysis Systems (SAS) for Windows version 9.4. All tests were two tailed, and significance was defined as *P* less than .05 and a 95% CI that did not cross or include 1.

RESULTS

There were a total of 161,809 participants enrolled in either the OS (*n* = 93,676) or CT (*n* = 68,132) arms from October 1993 to December 1998. We excluded patients who had missing outcomes (*n* = 265 from OS; *n* = 148 from CT) and missing covariates (*n* = 16,253 from OS; *n* = 15,191 from CT). After exclusions, the total analytic cohort included 129,951 participants (Fig 1). Of these, there 108,487 (83%) were NHW; 10,892 (8%) were NHB; 3,696 (3%) were API; 4,882 (4%) were Hispanic; 534 (0.4%) were AIAN; and 1,460 (1%) women were classified as other race/ethnicity. Table 1 shows the demographic, health, and lifestyle characteristics of women by racial/ethnic group. NHW women represented the oldest racial/ethnic group. NHB, Hispanic, and AIAN women reported less postsecondary education than NHW women. NHW and AIAN women reported heavier alcohol use than other groups. NHW women reported the highest rates of cancer family history. Hispanic, NHB, and AIAN participants reported fewer METs and had higher BMIs than API and NHW women. NHW women reported the most daily fruit and vegetable servings and, along with AIAN participants, reported the most daily animal protein consumption.

API and Hispanic women had higher percentages of never-smoker statuses and lower proportions with a past smoking history than NHW women. NHB and AIAN women had the highest

proportion of current smoker status compared with other groups. Most women reported early ages at smoking initiation (younger than 20 years) and smoking cessation (younger than 45 years). Reported pack-year smoking history was greatest in NHW women followed by AIAN women; AIAN women, however, reported the longest duration of smoking. NHW women had the highest smoking cessation rates compared with other racial/ethnic groups; NHB women had the lowest smoking cessation rates.

In our analytic cohort, 1,044 women developed lung cancer; (NHW, *n* = 947; NHB, *n* = 71; API, *n* = 14; Hispanic, *n* = 14; AIAN, *n* = 4; other, *n* = 8). Of these, 613 women died at median 10.5 years of follow up (NHW, *n* = 550; NHB, *n* = 42; API, *n* = 7; Hispanic, *n* = 4; AIAN, *n* = 4).

Incidence odds ratios (ORs) are depicted in Table 2. In unadjusted models, women from racial/ethnic groups other than AIAN had statistically significant decreased lung cancer incidence compared with NHW women (*P* < .001). Hispanic women had 66% lower odds of incident lung cancer (OR 0.34; 95% CI, 0.2 to 0.5) compared with NHW women followed by API (OR, 0.45; 95% CI, 0.27 to 0.75) and NHB women (OR, 0.75; 95% CI, 0.59 to 0.95). When adjusted for age, there were no differences in incidence for NHB compared with NHW women; however, the lower incidence among Hispanic and API compared with NHW women continued to persist and was only slightly attenuated (OR, 0.40 [95% CI, 0.24 to 0.68] and 0.46 [95% CI, 0.27 to 0.77], respectively). In models additionally adjusted for smoking, Hispanic women continued to have lower incident odds than NHW women (OR, 0.47; 95% CI, 0.28 to 0.79). In fully adjusted multivariable models that took into account smoking and other sociodemographic factors, the decreased risk for Hispanic women compared with NHW women persisted but was additionally attenuated (OR, 0.59; 95% CI, 0.35 to 0.99). There were no statistically significant racial/ethnic differences in incidence by histologic subtypes in adjusted models (Table 3). Association between stage and race/ethnicity among incident cases was found to be statistically nonsignificant (*P* = .56; data not shown).

Table 4 demonstrates mortality ORs. In unadjusted models, Hispanic and API women had a decreased risk of lung cancer death compared with NHW women (OR, 0.30 [95% CI, 0.15 to 0.62] and 0.34 [95% CI, 0.16 to 0.75], respectively). The decreased risk of death was also demonstrated in age-adjusted models for Hispanic and API women (OR, 0.37 [95% CI, 0.18 to 0.76] and 0.36 [95%

Table 2. Lung Cancer Incidence OR Estimates From Logistic Regression Models

Race/ Ethnicity	Unadjusted		Age Adjusted		Age and Smoking Adjusted		Fully Adjusted	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
White	1.00 (Reference)	< .001	1.00 (Reference)	< .001	1.00 (Reference)	< .001	1.00 (Reference)	.26
Black	0.75 (0.59 to 0.95)		0.83 (0.65 to 1.05)		0.71 (0.56 to 0.91)		0.85 (0.66 to 1.09)	
API	0.45 (0.27 to 0.75)		0.46 (0.27 to 0.77)		0.68 (0.40 to 1.14)		0.74 (0.44 to 1.26)	
Hispanic	0.34 (0.20 to 0.57)		0.40 (0.24 to 0.68)		0.47 (0.28 to 0.79)		0.59 (0.35 to 0.99)	
AIAN	0.96 (0.38 to 2.44)		1.05 (0.42 to 2.68)		0.92 (0.36 to 2.36)		0.92 (0.36 to 2.36)	
Other	0.66 (0.34 to 1.31)		0.68 (0.34 to 1.34)		0.71 (0.36 to 1.40)		0.74 (0.38 to 1.47)	

NOTE. Estimates in fully adjusted model were adjusted for age, education, calcium supplementation, vitamin D supplementation, body mass index, age at start of smoking, duration of smoking habit, pack-years of exposure, smoking status, alcohol use, membership in observational study, hormone replacement therapy or dietary modification or calcium/vitamin D interventions, family history of cancer, oral contraceptive use, hormone use history, baseline physical activity, and diet (fruit, vegetable and meat consumption). Data are from the Women's Health Initiative observational study and clinical trial cohorts.

Abbreviations: AIAN, American Indian/Alaskan Native; API, Asian/Pacific Islander; OR, odds ratio.

Table 3. Lung Cancer OR Estimates From Multinomial Logistic Regression Model

Lung Cancer Histology	Fully Adjusted OR (95% CI) by Race/Ethnicity						P
	White	Black	Hispanic	API	AIAN	Other	
NSCLC	1.00 (Reference)	1.24 (0.85 to 1.80)	0.90 (0.51 to 1.56)	0.94 (0.53 to 1.68)	0.74 (0.23 to 2.41)	0.92 (0.44 to 1.90)	.44
SCLC	1.00 (Reference)	0.65 (0.30 to 1.38)	0.57 (0.16 to 1.97)	1.03 (0.30 to 3.59)	2.52 (0.71 to 8.87)	1.27 (0.37 to 4.40)	

NOTE. Estimates in model were adjusted for age, education, calcium supplementation, vitamin D supplementation, body mass index, age at start of smoking, duration of smoking habit, pack-years of exposure, smoking status, alcohol use, membership in observational study, hormone replacement therapy or dietary modification or calcium/vitamin D interventions, family history of cancer, oral contraceptive use, hormone use history, baseline physical activity, and diet (fruit, vegetable and meat consumption). Data are from the Women's Health Initiative observational study and clinical trial cohorts.

Abbreviations: AIAN, American Indian/Alaskan Native; API, Asian/Pacific islander; NSCLC, non-small-cell lung cancer; OR, odds ratio; SCLC, small-cell lung cancer.

CI, 0.16 to 0.77], respectively) and persisted for Hispanic women after additional adjustment for smoking (OR, 0.43; 95% CI, 0.21 to 0.89). In fully adjusted models, however, there were no significant racial/ethnic differences in risk of death.

Table 5 demonstrates incidence and mortality ORs of covariates from logistic regression models. Increasing age, duration of smoking as measured in years, heavy smoking, current smoking status (current *v* never), and family history of cancer were associated with an increased risk of incident lung cancer in fully adjusted models (Table 5). Similarly, in fully adjusted models for mortality, increasing age, duration of smoking as measured in years, heavy smoking, and current smoking status (current *v* never) were associated with increased risk of lung cancer mortality. BMI greater than 25 kg/m² and greater amount of vegetables consumed were associated with a decreased risk of lung cancer incidence and mortality.

DISCUSSION

In our study, with the WHI multiethnic cohort, we examined the influence of sociodemographic, clinical, and behavioral risks on differences in lung cancer incidence and mortality by race/ethnicity. We found that, after adjustment for age, Hispanic and API women had decreased lung cancer incidence and mortality than NHW women. Only Hispanic women, however, maintained the mortality advantage compared with NHW women after additional adjustment for smoking. Differences no longer persisted, however, after additional adjustment for other potential

confounders, including demographic, behavioral (including current smoking status, duration of smoking, diet, exercise, and vitamin and supplement use), and socioeconomic status factors. Our findings, which differ from studies that consistently demonstrate increased incidence and mortality for NHB men,^{14,29,30} highlight the importance of sex-specific investigations in lung cancer.

Our study is in agreement with previously described crude lung cancer incidence and mortality reports in the United States.¹⁴ Our results, which additionally adjust these crude rates for risk factors and potential confounders, are similar to other studies that demonstrate equivalent incidence among NHW and NHB women.^{31,32} Our results differ from population-based studies that have shown increased lung cancer incidence among NHB women after adjustment for age and smoking.^{13,15,16} Our results differ from those that show decreased incidence among API women compared with other racial/ethnic minorities but are consistent with those that demonstrate decreased incidence among Hispanics.^{18,33-35} Our observed decreased lung cancer incidence risk for Hispanic compared with NHW women in our fully-adjusted analysis warrants additional investigation.

Our results also differ from previous studies that demonstrate increased lung cancer mortality among NHW and NHB women^{16,36-38} and those that show decreased mortality among Hispanic and API women compared with other racial/ethnic groups.^{34,35} The findings, however, in previous literature on Hispanic and API women are conflicting, because some show decreased mortality among Hispanic and API women, whereas others do not corroborate these results.^{3,5,13,16,20} Our findings are

Table 4. Lung Cancer Mortality OR Estimates From Logistic Regression Models

Race/Ethnicity	Unadjusted		Age Adjusted		Age and Smoking Adjusted	Fully Adjusted	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	OR (95% CI)	P
White	1.00 (Reference)	< .001	1.00 (Reference)	< .001	1.00 (Reference)	1.00 (Reference)	.22
Black	0.77 (0.56 to 1.05)		0.86 (0.63 to 1.18)		0.74 (0.54 to 1.01)	0.86 (0.62 to 1.18)	
API	0.34 (0.16 to 0.75)		0.36 (0.16 to 0.77)		0.54 (0.25 to 1.17)	0.60 (0.28 to 1.31)	
Hispanic	0.30 (0.15 to 0.62)		0.37 (0.18 to 0.76)		0.43 (0.21 to 0.89)	0.52 (0.26 to 1.07)	
AIAN	1.66 (0.66 to 4.23)		1.85 (0.73 to 4.70)		1.62 (0.63 to 4.15)	1.59 (0.62 to 4.08)	
Other	0.61 (0.24 to 1.53)		0.62 (0.24 to 1.57)		0.66 (0.26 to 1.66)	0.68 (0.27 to 1.70)	

NOTE. Estimates in fully adjusted model were adjusted for age, education, calcium supplementation, vitamin D supplementation, body mass index, age at start of smoking, duration of smoking habit, pack-years of exposure, smoking status, alcohol use, membership in observational study, hormone replacement therapy or dietary modification or calcium/vitamin D interventions, family history of cancer, oral contraceptive use, hormone use history, baseline physical activity, and diet (fruit, vegetable and meat consumption). Data are from the Women's Health Initiative observational study and clinical trial cohorts.

Abbreviations: AIAN, American Indian/Alaskan Native; API, Asian/Pacific islander; OR, odds ratio.

Table 5. Covariate ORs From Incidence and Mortality Logistic Regression Models

Characteristic	Incidence OR (95% CI)	Mortality OR (95% CI)
OS membership		
No	1.00 (Reference)	1.00 (Reference)
Yes	0.99 (0.69 to 1.42)	0.90 (0.6 to 1.50)
HT membership		
Not randomized	1.00 (Reference)	1.00 (Reference)
E + P control	1.21 (0.83 to 1.77)	0.99 (0.60 to 1.64)
E + P intervention	1.30 (0.90 to 1.89)	1.50 (0.94 to 2.37)
E-alone control	1.13 (0.74 to 1.72)	1.26 (0.75 to 2.14)
E-alone intervention	1.24 (0.82 to 1.87)	1.14 (0.67 to 1.95)
CaD membership		
Not randomized	1.00 (Reference)	1.00 (Reference)
Control	0.99 (0.77 to 1.27)	1.03 (0.76 to 1.41)
Intervention	0.94 (0.73 to 1.21)	0.78 (0.56 to 1.09)
DM membership		
Not randomized	1.00 (Reference)	1.00 (Reference)
Control	0.88 (0.63 to 1.23)	0.98 (0.64 to 1.49)
Intervention	0.79 (0.56 to 1.14)	0.84 (0.53 to 1.31)
Age, years		
50-54	1.00 (Reference)	1.00 (Reference)
55-59	1.58 (1.13 to 2.20)*	1.59 (1.02 to 2.47)*
60-69	2.65 (1.96 to 3.60)*	2.65 (1.76 to 3.98)*
70-79	3.18 (2.29 to 4.42)*	3.80 (2.45 to 5.88)*
Education		
None to high school graduate	1.00 (Reference)	1.00 (Reference)
Some postsecondary	0.95 (0.83 to 1.10)	0.88 (0.73 to 1.06)
Smoking status		
Never	1.00 (Reference)	1.00 (Reference)
Current	2.26 (1.55 to 3.29)*	2.09 (1.28 to 3.39)*
Alcohol use		
Nondrinker	1.00 (Reference)	1.00 (Reference)
Past drinker	1.05 (0.77 to 1.43)	1.17 (0.76 to 1.77)
< 1 drink/month	0.91 (0.65 to 1.26)	0.89 (0.56 to 1.41)
< 1 drink/week	1.08 (0.80 to 1.48)	1.22 (0.80 to 1.86)
1-6 drinks/week	1.03 (0.76 to 1.40)	1.15 (0.76 to 1.75)
≥ 7 drinks/week	0.99 (0.72 to 1.37)	1.19 (0.77 to 1.83)
Postmenopausal HT		
Never used	1.00 (Reference)	1.00 (Reference)
Past hormone	1.01 (0.86 to 1.18)	0.94 (0.77 to 1.16)
Current hormone	1.07 (0.91 to 1.24)	1.05 (0.86 to 1.28)
Oral contraceptive use		
No	1.00 (Reference)	1.00 (Reference)
Yes	0.98 (0.85 to 1.12)	1.03 (0.86 to 1.23)
Family history of cancer		
No	1.00 (Reference)	1.00 (Reference)
Yes	1.15 (1.01 to 1.32)*	1.09 (0.92 to 1.29)
Calcium supplementation		
No	1.00 (Reference)	1.00 (Reference)
Yes	1.02 (0.83 to 1.24)	1.01 (0.78 to 1.30)
Vitamin D supplementation		
No	1.00 (Reference)	1.00 (Reference)
Yes	0.94 (0.77 to 1.14)	0.96 (0.75 to 1.24)
Baseline MET-h/week		
0	1.00 (Reference)	1.00 (Reference)
0-3	1.18 (0.96 to 1.45)	1.14 (0.88 to 1.48)
3-9	0.99 (0.82 to 1.20)	0.89 (0.70 to 1.13)
≥ 9	1.00 (0.83 to 1.20)	0.85 (0.68 to 1.07)
BMI, kg/m ²		
< 25	1.00 (Reference)	1.00 (Reference)
25-30	0.77 (0.66 to 0.89)*	0.71 (0.58 to 0.85)*
≥ 30	0.78 (0.66 to 0.92)*	0.74 (0.60 to 0.92)*
Age started smoking, years		
Nonsmoker	1.00 (Reference)	1.00 (Reference)
< 20	0.77 (0.36 to 1.64)	0.70 (0.24 to 2.07)
≥ 20	0.77 (0.36 to 1.63)	0.73 (0.25 to 2.17)

(continued in next column)

Table 5. Covariate ORs From Incidence and Mortality Logistic Regression Models (continued)

Characteristic	Incidence OR (95% CI)	Mortality OR (95% CI)
Fruit portions consumed	0.94 (0.88 to 0.99)*	0.96 (0.89 to 1.04)
Vegetable portions consumed	0.97 (0.92 to 1.02)	0.91 (0.84 to 0.98)*
Animal protein consumed	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)
Duration of smoking habit, years	1.03 (1.03 to 1.04)*	1.04 (1.02 to 1.05)*
Pack-year history		
Nonsmoker	1.00 (Reference)	1.00 (Reference)
Heavy smoker	2.52 (1.17 to 5.44)*	3.12 (1.04 to 9.38)*
Light smoker	0.93 (0.44 to 1.97)	1.16 (0.40 to 3.42)

NOTE. Data are from the Women's Health Initiative observational study and clinical trial cohorts.

Abbreviations: AIAN, American Indian/Alaskan Native; API, Asian/Pacific Islander; BMI, body mass index; CaD, calcium and vitamin D; DM, dietary modification; E, estrogen; HT, hormone therapy; MET, metabolic equivalent; OR, odds ratio; OS, observational study; P, progesterone.

*Significance of $P < .05$ and 95% CI does not cross or include 1.

also different from evaluations that demonstrate increased mortality among API women compared with NHW women.³⁹⁻⁴¹ Although we did not find decreased mortality for Hispanic women compared with NHW women after adjustment for other potential confounders, our study found that Hispanic women continued to have a decreased mortality risk after age and smoking adjustment; this finding is consistent with our previous findings reporting survival advantages for this patient population.³⁴ Similar to a previous study,¹⁸ we found an independent association of intensity of smoking and risk of lung cancer incidence and mortality, however, we found no interaction of intensity of smoking and race/ethnicity.

The various reasons for the differences noted in these studies compared with ours most likely reflect the importance of evaluating a wide variety of known risk factors cohesively in one data set. Failure to include key risk factors may result in mis-specified models that incorrectly attribute risk or advantage to members of specific racial/ethnic groups. Our study, unlike previous evaluations, comprehensively examined differences in lung cancer incidence and mortality by race/ethnicity in the WHI, a rich set of data that contains longitudinal and detailed information on smoking history and duration of smoking habits; other behavioral factors, such as diet, exercise, and vitamin and supplement intake; socioeconomic status; and demographic factors. In our fully adjusted multivariable models, mortality differences were no longer significant for any racial/ethnic group, nor were there differences when we stratified by histology. Similar to findings from WHI studies that evaluated disparities in other cancers,⁴² our results suggest that differences in risk and mortality can be explained, at least in part, by the effects of patient characteristics—mostly age and behavioral characteristics, including smoking-related factors, diet, and BMI—on lung cancer incidence and mortality.

The heterogeneity between results from other studies and those from our study may also be due to differences in study populations. The WHI study is comprised primarily of NHW women; however, the recruited study population is reflective of the racial/ethnic diversity in the United States at the time the study was initiated. Among all racial and ethnic groups represented in the WHI, women who self-select to participate in a longitudinal CT

and OS may represent a group with increased health status and education and with equal access to medical care. This level of access to and interest in care may also explain our findings, among other studies that examined cancer disparities in the WHI,⁴² which showed no differences in tumor characteristics, such as stage and histology at diagnosis, and which previous studies have demonstrated are differential among NHB women who have limited access to medical care.^{36,37} In addition, our low number of incident cases in some racial and ethnic groups may have contributed to wider CIs and decreased our ability to detect differences. However, lung cancer incidence and mortality cases in the WHI cohort reflect the general rates among the population of women at whole. The low rates of lung cancer in our study, therefore, are not a limitation of the sample but a direct reflection of the lower population incidence and mortality rates in particular racial/ethnic groups.^{1,8,33} The lack of additional information on women of Hispanic and API origin, including the country of origin and place of birth, limit our ability to evaluate whether the composition of these groups contribute to differences between our results and prior studies.^{43,44} Additionally, in our study, we were limited to baseline smoking status and could not account for changes in exposure during follow-up. This limitation may have caused misclassification and biased our results toward the null. However, in a cohort population of postmenopausal women in the WHI, 99% of women remained abstinent from smoking, and 60% of smokers continued to smoke at 9 years follow-up,⁴⁵ which suggests that the likely effect of changes in smoking status during follow-up may be minimal. Finally, we were unable to account for newer molecular and genetic factors that may play a role in incidence and mortality for particular racial/ethnic groups.⁴⁶⁻⁴⁸ The WHI Life and Longevity After Cancer study,²⁸ as well as recent cohort studies such as the United Kingdom Biobank⁴⁹ and European Prospective Investigations Into Cancer,⁵⁰ may provide some associations of lifestyle behaviors, molecular and genetic factors, and lung cancer incidence and mortality.

The strengths of our study include the prospective cohort design, large cohort size, pathologic confirmation of lung cancer

diagnoses, detailed information on demographic and environmental characteristics, and specificity of self-reported data. The validated rich WHI database allowed us to study multiple covariates that may influence lung cancer incidence and mortality among racial and ethnic groups and that have not previously been studied cohesively in one data set.

In conclusion, after adjustment for demographic, clinical, and behavioral factors, Hispanic women had decreased lung cancer incidence compared with NHW women; however, there were no racial/ethnic differences in mortality. There is considerable heterogeneity in the literature regarding these findings. However, this study is the first to evaluate sociodemographic and environmental covariates cohesively in one data set, and such data in a prospective cohort are rare. The findings of this study suggest that, although age is a significant risk factor, modifiable exposures, such as smoking, are a major focus for eliminating differences in the risk for and survival of lung cancer for women.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org

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GLOSSARY TERM

non-small-cell lung cancer (NSCLC): a type of lung cancer that includes squamous cell carcinoma, adenocarcinoma, and large-cell carcinoma.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Racial and Ethnic Variations in Lung Cancer Incidence and Mortality: Results From the Women's Health Initiative

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