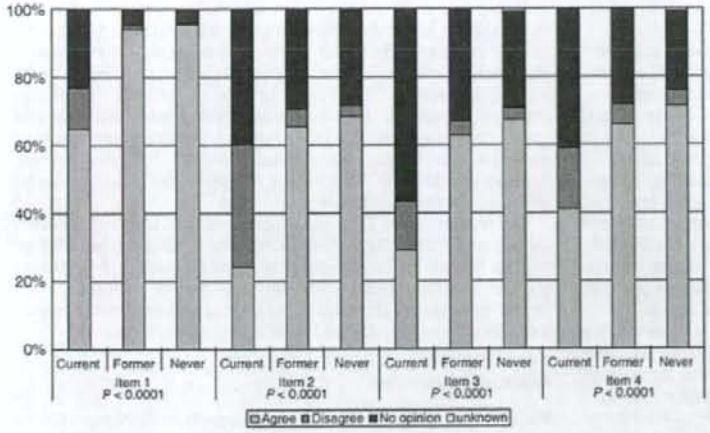

Fig. 1. Distribution of beliefs about smoking control according smoking status. Item 1 asked whether the respondents agree with no smoking in public spaces such as stations or hospitals. Item 2 asked whether the respondents agree with raising the price of tobacco. Item 3 asked whether the respondents agree with health warning labels describing the harmful effects of tobacco in large letters for easier reading. Item 4 asked whether the respondents agree with prevention of obtaining tobacco easily (regulation of tobacco vending machines).

Table 3. Distribution of views about the smoking habits of medical staff and patients

Question	Answer	Current smokers (%) (n = 83)	Former smokers (%) (n = 273)	Never smokers (%) (n = 564)	Total (%) (n = 920)	P-value
Do you agree medical staff should not be allowed to smoke?	Yes	32.5	67.8	72.3	67.4	<0.0001
	No	33.7	9.9	6.4	9.9	
	No opinion	14.5	8.1	3.9	6.1	
	Not a medical staff	15.7	12.1	15.2	14.3	
	Unknown	3.6	2.2	2.1	2.3	
How do you think about your patients' smoking?	Should not smoke	18.1	41.8	49.5	44.3	<0.0001
	Patients' choice	37.3	34.4	28.7	31.2	
	May smoke	38.6	15.4	12.6	15.8	
	No opinion	1.2	2.9	3.7	3.3	
	Unknown	4.8	5.5	5.5	5.4	
Do you lead your patients to stop smoking if they need to do so with medical reasons?	Yes	73.5	74.4	70.7	72.1	0.74
	No	0.0	1.1	0.7	0.8	
	No opinion	1.2	3.3	2.5	2.6	
	No clinical activity	19.3	16.8	20.9	19.6	
	Unknown	6.0%	4.4%	5.1%	5.0%	

health at school' and 'providing a favorable climate for avoidance by minors'.

Approximately two-thirds of the 920 responders believed that medical staff should not be allowed to smoke. Current smokers were significantly less likely than former or never smokers to believe that medical staff should not be allowed to smoke (Table 3). Responders tended to express more tolerate attitudes toward patients smoking than staff smoking, but more former and never smokers than current smokers thought that patients should not smoke in any case. However, when the patients had medical reasons to stop smoking, there was no significant difference in advice to stop smoking by the smoking status of the responders.

Frequently identified barriers to provide smoking-cessation treatment were 'taking a long time for treatment' (56.6%), 'lack of insurance coverage for medicine to stop smoking' (40.4%), 'patients refusal of treatment' (30.8%), and 'doctors themselves do not have an adequate education on smoking problems' (28.1%). A significant increment in perceived barriers was noted for current smokers compared with former and never smokers: 37.7, 61.6, and 56.9%, respectively, for 'taking a long time for treatment', 13.1, 27.6, and 30.6%, respectively, for 'doctors themselves do not have an adequate education on smoking problems', and 21.3, 27.1, and 34.1%, respectively, for 'patients refusal of treatment'. Approximately 44% of current smokers thought 'lack of insurance coverage for medicine to stop smoking' was the most important problem.

The smoking rate by 10-year age group in the JCA members ranged from approximately 2% (aged in their 60s) to approximately 17% (aged in their 20s), whereas that in the Japanese general population ranged from approximately 13% (aged 70 or over) to approximately 36% (aged in their 30s).[6] The JCA members in this survey were much less likely to be current smokers compared to the Japanese general population,[6] in all age groups, and also much more likely to be never smokers in all age groups except 60 years and over. Surveys on the smoking rates of medical staff in other countries have been done. These were found to be 1.3% of physicians in Minnesota, USA,[7] 9.6% of general practitioners in Germany,[8] and 4.3% of doctors in Hong Kong. In these countries, the smoking rate of medical staff was under 10% and lower than their general populations, as in our study. These findings suggest that most JCA members acting in the promotion of health and patient care develop a stronger sense of responsibility as leaders of health promotion. But this might also be because the response rate for general members was low both in 2004 and in 2006. It is usual with

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questionnaire surveys about smoking that there are more smokers among those who do not give responses.

The proportion of JCA members who recommend that their patients stop smoking if therapeutically needed was 72%, and this percentage was similar to or higher than that in other countries. In Minnesota 69% of physicians reported they always or almost always recommend smoking cessation to their patients,[7] and in Hong Kong 29.0 and 45.3% of doctors reported they advise all smokers and smokers with relevant medical conditions, respectively, to quit smoking.[9] Regretfully, approximately one-third of JCA members who are smokers think that medical staff and their patients should be allowed to smoke. To play a leading role as medical experts, and as JCA members, medical staff themselves should quit smoking and advise their patients and the smokers around them to quit for the sake of their health.

With regard to the barriers to smoking-cessation treatment for smokers, the responders felt that major barriers were the long period of time required for cessation programs and the lack of insurance coverage for smoking-cessation medication. In Germany, a lack of adequate reward, of training in the promotion of smoking cessation, and of demonstration materials were judged as barriers, and a lack of interest and the perception that smoking cessation is not their responsibility were rated as barriers by only a minority.[8] In Hong Kong, a lack of patient motivation and lack of doctor's time in consultation were likely to be judged as barriers.[9] In Japan, to provide effective smoking-cessation treatment, doctors should develop more effective and short-term programs. Health insurance coverage for smoking cessation medication, which many doctors felt was needed, became available in 2006, so the results of this change may be evaluated in the near future.

The present survey indicated that, despite their smoking behavior, most people hope to ban smoking while walking, to educate general people including children about tobacco and health, to provide an environment where children can not get tobacco, and to give information about tobacco and health. Based on the results, tobacco control should put feasible reforms into practice.

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Prevalence and Demographic Correlates of Meeting the Physical Activity Recommendation Among Japanese Adults

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Background: Although engaging in the recommended amount of physical activity provides disease-prevention benefits, few studies have examined the proportion and correlates of meeting the Japanese physical activity recommendation. This study investigated the prevalence and demographic correlates of attaining the recommended value on the Exercise and Physical Activity Reference for Health Promotion 2006. **Methods:** Data were analyzed for 5177 Japanese adults who took an Internet-based cross-sectional survey. The International Physical Activity Questionnaire and 6 possible demographic correlates were obtained. Respondents were divided into 3 groups—recommended, insufficient, and inactive—according to their estimated weekly physical activity level. A multivariate logistic regression analysis was used. **Results:** Overall, 26.6% of respondents were physically active according to the recommendation criterion. Gender, employment status, age, marital status, and educational level were statistically significant. In men, being employed and in women, being 30 to 39 years of age were negatively associated with the attainment of the recommendation. Being male, being a married woman, and having a college education or higher for women were positively correlated with the attainment of the recommendation. **Conclusions:** Different associations of demographic correlates with the physical activity recommendation for men and women were found, suggesting that gender-specific strategies for targeting the population or specific interventions might be more effective in promoting physical activity among Japanese adults.

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Keywords: guidelines and recommendations, exercise, Internet-based survey

Background

Physical activity promotion is now a national health priority for disease-prevention policy. The health benefits of physical activity are well established, and regular physical activity is associated with decreased incidence of cardiovascular diseases and stroke. In addition, it is associated with reduced coronary artery disease risk factors such as hypertension, diabetes mellitus, and obesity and improved mood states including depression and anxiety.[1,2]

In general, the recommended amount of physical activity is believed to confer general health promotion and disease-prevention benefits. The US Surgeon General's Report as well as the Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) recommend that individuals of all ages should accumulate "a minimum of 30 minutes of physical activity of moderate intensity (eg, brisk walking) on most, if not all, days of the week."[1,3] Previous studies found that the proportion of American adults who engaged in the recommended level of physical activity ranged from 26% to 45%.[4-7] In Japan, the guidelines on health promotion and recommendations for physical activity and exercise, the Exercise and Physical Activity Reference for Health Promotion 2006 (EPAR2006), were published in 2006.[8] The current guidelines are more focused on daily physical activity above 3 metabolic equivalents (METs), which includes both lifestyle physical activity and exercise as opposed to the former traditional exercise guidelines. In the current recommendation, every adult should accumulate 23 METs · h/wk of physical activity to prevent chronic diseases and to obtain numerous health benefits.[8] However, the proportion of Japanese adults meeting this new recommendation has not yet been determined.

To increase the proportion of individuals engaged in the recommended level of physical activity, it is essential to identify the correlates or determinants of participation in physical activity to target at-risk populations and develop tailored interventions. Previous studies have found that among sociodemographic variables, participating in physical activity was positively related with being male, younger, more educated, a nonsmoker, and earning a higher income.[9,10] These studies, however, have investigated the correlates of participation in physical activity. A limited number of studies in the United States and European countries have investigated the correlates of meeting the recommended level of physical activity in middle-age adults,[4,5,11,12] the elderly,[13] persons with a disability,[14] and ethnic minorities.[15–17] Although age and gender seemed to be consistent correlates of attaining the physical activity recommendation in adults, other correlates—such as marital status, educational level, employment status, and household income level—still produced mixed findings.[4,5,11–17] In addition, few studies have examined the demographic correlates of meeting the physical activity recommendation in the Japanese population. The purpose of the current study was to examine the prevalence of attaining the Japanese recommended level of physical activity and primarily to identify demographic correlates of meeting the physical activity recommendation among Japanese adults.

Methods

Participants

For the current study, the data sample consisted of 5253 male and female respondents to an Internet-based cross-sectional survey, which was conducted via the Japanese Internet research service organization. This Internet research service organization owned approximately 264,000 voluntary registered samples, had detailed sample sociodemographic attributes available, and was able to target specific attributes according to each survey requirement. The set sample size and attributes in the current study were as follows: approximately 5000 male and female adults age 20 to 79 years, with an equivalent number of men and women in each age bracket. Potential respondents were randomly and automatically selected in accordance with the set sample size and attributes from the registered samples and were invited to participate in an Internet-based survey from the Internet research service organization via e-mail. Internet-based questionnaires were placed in a protected area of a Web site, and the potential respondents received the specific URL of the Internet research service organization in an invitation e-mail. The potential respondents could log onto the protected area of a Web site using their own login ID and password. Reward points valued at 80 yen were provided as incentives for participation from the Internet research service organization. All respondents voluntarily completed and signed an online Institutional Review Board–approved letter of informed consent and demographic data information. In addition, the following measures were administered.

Measurements

Physical Activity. The short version of the International Physical Activity Questionnaire (IPAQ) was used to estimate the amount of physical activity the participants engaged in. The IPAQ has been used in several countries.[18] This self-administered questionnaire was designed to be used by adults age 18 to 65 years, and it identifies the frequency and duration of walking, moderate and vigorous physical activity, and sedentary activity during the past week.[18] The test–retest reliability of the short, self-administered, Japanese version of the IPAQ is good (Spearman $r = .72–.93$). The criterion validity for the Japanese version of the IPAQ against an accelerometer is acceptable (Spearman $r = .39$).[19]

The short-form data were used to estimate the total weekly physical activity level (METs · h/wk) by weighting the reported hours per week within each of 3 activity categories—walking, moderate, and vigorous activity—by MET energy expenditure estimates assigned to each category of activity. MET values for each activity category were obtained from the study of Craig et al.[18] Current national guidelines for exercise in Japan recommend 23 METs · h/wk of physical activity.[8] Based on their estimated total weekly physical activity level, respondents were assigned to 1 of 3 (mutually exclusive and exhaustive) groups. Those who engaged in no physical activity, indicating none reported, were assigned to the inactive group. Those who engaged in physical activity that was less than the recommended level but greater than none were assigned to the insufficient group. Finally, persons who engaged in 23 METs · h/wk of physical activity or more were assigned to the recommended group.

Possible Demographic Correlates. Possible demographic correlates of participation in the recommended level of physical activity included gender, age, marital status, educational level, household income level, and employment status. Age was classified in years as 20 to 29, 30 to 39, 40 to 49, and 50 or older. Marital status was categorized as currently married or not currently married. Educational level was classified as less than high school graduate, junior college graduate or equivalent, and college graduate or higher. Household income level was classified into 5 categories ranging from less than 3,000,000 yen to 15,000,000 yen or more annually. The current study used the existing classification of household income level set by the Internet research service organization with reference to the National Survey of Family Income and Expenditure by the Statistics Bureau Ministry of Public Management Home Affairs Japan. Employment status was categorized as employed or unemployed.

Statistical Analyses

For the analysis, data were analyzed for 5177 persons who provided complete information for the study variables (n = 122). All the analyses were stratified by gender. Descriptive statistics were reported by physical activity levels (recommended, insufficient, and inactive). Chi-square tests were used to determine the differences in the proportions of individuals who were assigned to either the recommended, insufficient, or inactive group within the demographic variables. A multivariate logistic regression analysis was conducted to examine whether potential demographic correlates related to physical activity levels even after controlling for all other demographic variables. The adjusted odds ratios and 95% confidence intervals were calculated for the potential demographic variables. Independent variables included age, marital status, educational status, employment status, and household income level. Statistical significance was considered to be $P < .05$. The Statistical Package for Social Science (SPSS) for Windows 14.0 was used to compute the statistics.[20]

Results

Basic Characteristics of Respondents

In the current study, 2587 men and 2590 women were classified into 3 groups according to their physical activity level. Table 1 presents the distribution of age, marital status, educational level, household income level, and employment status for men and women. Overall, 65% of the respondents were married (59% of men and 71% of women). Twenty-four percent of the samples (21% of men and 29% of women) had less than a high school diploma, whereas 51% had graduated from a college or graduate school (67% of men and 35% of women). Eighty-three percent of men and 31% of women were employed. Overall, 15% of the respondents had a household income of less than 3,000,000 yen, whereas 3% earned more than 15,000,000 yen per year. The distributions of age and household income level were similar for men and women. Responders were more likely to be younger and have a higher educational status and household income level compared with the general Japanese population.[21–24] Similar trends were observed in gender, marital status, and employment status.[21–23] Table 1 presents the distribution of age, marital status, educational level, employment status, and household income level for the study participants and the general Japanese adults.[21–24]

Prevalence of Meeting the Physical Activity Recommendation

Table 2 presents the prevalence of physical activity levels by gender. Overall, 26.6% of the respondents were physically active at the recommended level. Men (30.3%) surpassed women (22.9%) in attaining the recommended level. Furthermore, women (52.4%) were more likely to engage in insufficient levels of physical activity than were men (44.6%). The prevalence of those who were inactive was similar for both men and women (25.0% of men and 24.7% of women).

For men, the prevalence of meeting the recommended level of physical activity decreased with advancing age until the 40-year age group and increased in the 50-year age group. The prevalence of meeting the recommended level of physical activity was the highest in the younger (20–29 years) age group and lowest in the 40-year age group (29.6%). For women, the prevalence of attaining the recommended level of physical activity decreased in the 30-year age group and then successively increased with advancing age. Meeting the recommended level of physical activity was the highest in the older age group (>50 years: 28.0%) and the lowest in the 30-year age group (19.0%). For both men and women, the proportion of those attaining the recommended level of physical activity was lower in the middle-age (30–49 years) groups than in the other 2 groups. Although men surpassed women in meeting the physical activity recommendation in all the age groups, the gender difference in the 50-year age group (3.4%) was less than that in the other age groups (9.2% of the 20-year, 10.6% of the 30-year, and 6.8% of the 40-year age groups).

With regard to marital status, for men, those who were married were less physically active at the recommended level (29.6% vs 31.4%); whereas, the married women were more active (24.3% vs 19.5%) at the recommended level. Meeting the physical activity recommendation was successively lower for men but slightly higher for women with greater educational attainment. As for employment status, the unemployed men (36.5%) were more physically active at the recommended level than the employed men (25.0%). For women, the prevalence of meeting the recommended level of physical activity was similar for both the employed (22.9%) and the unemployed (23.1%). With regard to income level, for both men and women, those with a household income of 5,000,000 yen to 7,000,000 yen had the lowest prevalence of meeting the recommended level of physical activity.

Demographic Correlates of Meeting the Physical Activity Recommendation

Odds ratios for physical activity levels are presented in Table 3 by age, marital status, educational level, employment status, and household income level. Gender and employment status for men, and age, marital status, and educational level for women were the demographic correlates that had a statistical significance for meeting the recommended level of physical activity. Women were less likely to attain the recommended level of physical activity than were men (OR = 0.71, 95% CI = 0.59 to 0.86). For men, employment status was inversely correlated with meeting the physical activity recommenda-

Table 1 Basic Characteristics for Male and Female Respondents and General Japanese Adults

	Participants						General Japanese[a,b]
	Men		Women		Total		
	n	%	n	%	n	%	%
Total	2587	50.0	2590	50.0	5177	100.0	—
Age							
20–29	643	24.9	651	25.1	1294	25.0	15.9
30–39	646	25.1	646	24.9	1295	25.0	19.0
40–49	651	25.2	651	25.1	1302	25.1	16.3
≥50	644	24.9	642	24.8	1286	24.9	48.8
Marital status							
married	1529	59.1	1845	71.2	3374	65.2	64.5
unmarried	1058	40.9	745	28.8	1803	34.8	35.5
Educational status							
≤high school graduate	538	20.8	739	28.5	1277	24.7	67.7
2 years college or equivalent	322	12.4	955	36.9	1277	24.7	12.6
≥college graduate	1727	66.8	896	34.6	2623	50.7	15.5
Employment status							
employed	2138	82.6	811	31.3	2949	57.0	56.0
unemployed	449	17.4	1779	68.7	2228	43.0	44.0
Household income level							
<3,000,000 yen	372	14.4	424	16.4	796	15.4	30.6
3,000,000 yen	704	27.2	739	28.5	1443	27.9	23.2
5,000,000 yen	628	24.3	575	22.2	1203	23.2	13.5
7,000,000 yen	516	19.9	531	20.5	1047	20.2	17.2
10,000,000 yen	268	10.4	258	10.0	526	10.2	7.6
15,000,000 yen	99	3.8	63	2.4	162	3.1	3.7

[a] Reference age, marital status, and employed status: 2005 Population Census of Japan; educational status: 2000 Population Census of Japan; household income levels: 2006 National Livelihood Survey.
[b] All data of those age 19 and below were excluded.

tion (OR = 0.64, 95% CI = 0.46 to 0.87). For women, marital status was positively associated with meeting the recommended physical activity level (OR = 1.41, 95% CI = 1.02 to 1.94). Moreover, those with college degrees or higher were approximately twice as likely to meet the recommended level of physical activity compared with those with less than a high school education (OR = 1.86, 95% CI = 1.37 to 2.52). However, women in the 30-year age group were less likely to be physically active at the recommended level than were the other age groups (OR = 0.65, 95% CI = 0.46 to 0.91).

As for the associations between insufficient level of physical activity and demographic correlates, marital status was positively related to engagement in an insufficient level of physical activity for men (OR = 1.28, 95% CI = 1.01 to 1.63). In addition, those with a college degree or higher (OR = 1.32, 95% CI = 1.03 to 1.70) as well as those with a household income of 7,000,000 yen or more (OR = 1.51, 1.85, 1.97; 95% CI = 1.04 to 2.18, 1.19 to 2.87, 1.05 to 3.69) were more likely to participate in an insufficient level of physical activity than were the other corresponding groups. Women age 50 years or older (OR = 0.90, 95% CI = 1.02 to 1.94) as well as those with a college degree or higher (OR = 1.88, 95% CI = 1.46 to 2.43) were more likely to engage in insufficient physical activity than were the corresponding groups.

Discussion

The current investigation was designed to examine the prevalence of meeting the Japanese physical activity recommendation and primarily to identify the demographic correlates of engagement in physical activity at the recommended level among Japanese adults. Although the participants who responded to the present survey were more likely to be younger and have a higher educational status and household income level compared with the corresponding demographic parameters reported by population-based surveys of Japanese adults, overall, 26.6% of the surveyed Japanese adults met the recommendation for physical activity.[21–24]

Table 2 Prevalence of Physical Activity Status by Gender

	Men								Women							
	Recommended		Insufficient		Inactive				Recommended		Insufficient		Inactive			
	n	%	n	%	n	%	χ^2	(df, n)	n	%	n	%	n	%	χ^2	(df, n)
Total	785	30.3	1154	44.6	648	25.0			593	22.9	1356	52.4	641	24.7		
Age							6.98	6, 2587							31.22[a]	6, 2590
20–29	207	32.2	266	41.4	170	26.4			150	23.0	350	53.8	151	23.2		
30–39	192	29.6	287	44.2	170	26.2			123	19.0	331	51.2	192	29.7		
40–49	184	28.3	304	46.7	163	25.0			140	21.5	333	51.2	178	27.3		
≥50	202	31.4	297	46.1	145	22.5			180	28.0	342	53.3	120	18.7		
Marital status							10.45[b]	2, 2587							7.13[c]	2, 2590
married	453	29.6	720	47.1	356	23.3			448	24.3	945	51.2	452	24.5		
unmarried	332	31.4	434	41.0	292	27.6			145	19.5	411	55.2	189	25.4		
Educational status							21.78[a]	4, 2587							27.99[a]	4, 2590
≤high school graduate	196	36.4	199	37.0	143	26.6			163	22.1	357	48.3	219	29.6		
2 years college or equivalent	94	29.2	136	42.2	92	28.6			212	22.2	490	51.3	253	26.5		
≥college graduate	495	28.7	819	47.4	413	23.9			218	24.3	509	56.8	169	18.9		
Employment status							9.83[b]	2, 2587							0.68	2, 2590
employed	621	29.0	971	45.4	546	25.5			182	22.4	420	51.8	209	25.8		
unemployed	164	36.5	183	40.8	102	22.7			411	23.1	936	52.6	432	24.3		
Household income level							29.52[b]	10, 2587							23.41[b]	10, 2590
<3,000,000 yen	125	33.6	144	38.7	103	27.7			93	21.9	217	51.2	114	26.9		
3,000,000 yen	220	31.3	291	41.3	193	27.4			175	23.7	386	52.2	178	24.1		
5,000,000 yen	166	26.4	286	45.5	176	28.0			113	19.7	295	51.3	167	29.0		
7,000,000 yen	162	31.4	244	47.3	110	21.3			120	22.6	282	53.1	129	24.3		
10,000,000 yen	80	29.9	139	51.9	49	18.3			75	29.1	138	53.5	45	17.4		
15,000,000 yen	32	32.3	50	50.5	17	17.2			17	27.0	38	60.3	8	12.7		

[a] $P < .000$. [b] $P < .001$. [c] $P < .05$.

Moreover, approximately one-third of the men and one-fourth of the women engaged in physical activity at the recommended level in the current study.

The current study is, perhaps, the first to examine the prevalence of meeting the Japanese recommendation for physical activity. A similar tendency to that found in the current study was acquired in the objectives of a national interim report of Healthy Japan 21.[25] The prevalence of engaging in habitual leisure-time physical activity was found in 30.9% of men and 25.8% of women in Japan. However, in the current study, the percentages were much lower than those of the previous studies in other countries even though those studies used the physical activity level specified by the CDC/ACSM guidelines as the recommended level.[3] According to the 2003 Behavioral Risk Factor Surveillance System (BRFSS), overall, 45.9% of American adults engaged in physical activity at the recommended level.[7] In Australia, a similar prevalence was reported in the study by Cerin et al,[12] using data from the 2000 National Physical Activity Survey (NPAS). In addition, in the Supplementation en Vitamines et Mineraux Antioxydants (SUVIMAX) study,[11] Bertrains et al estimated that approxi-

Table 3 Adjusted Odds Ratios for Meeting Recommended and Insufficient Levels of Physical Activity Among Men and Women

	Recommended		Insufficient	
	Men	Women	Men	Women
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age				
20–29	1 (ref)	1 (ref)	1 (ref)	1 (ref)
30–39	1.02 (0.74–1.41)	0.65 (0.46–0.91) [c]	1.05 (0.78–1.42)	0.84 (0.64–1.11)
40–49	0.92 (0.65–1.29)	0.76 (0.54–1.09)	1.01 (0.74–1.39)	0.90 (0.67–1.21)
≥50	0.97 (0.68–1.39)	1.44 (0.99–2.08)	1.03 (0.74–1.44)	1.41 (1.02–1.94) [c]
Marital status				
unmarried	1 (ref)	1 (ref)	1 (ref)	1 (ref)
married	1.19 (0.92–1.54)	1.41 (1.02–1.94) [c]	1.28 (1.01–1.63) [c]	0.93 (0.71–1.21)
Educational status				
≤high school graduate	1 (ref)	1 (ref)	1 (ref)	1 (ref)
2 years college or equivalent	0.76 (0.53–1.10)	1.23 (0.93–1.62)	1.07 (0.76–1.51)	1.25 (0.99–1.57)
≥college graduate	0.83 (0.64–1.07)	1.86 (1.37–2.52) [a]	1.32 (1.03–1.70) [c]	1.88 (1.46–2.43) [a]
Employment status				
unemployed	1 (ref)	1 (ref)	1 (ref)	1 (ref)
employed	0.64 (0.47–0.88) [b]	0.97 (0.74–1.27)	0.79 (0.58–1.07)	0.85 (0.68–1.06)
Household income level				
<3,000,000 yen	1 (ref)	1 (ref)	1 (ref)	1 (ref)
3,000,000 yen	1.05 (0.75–1.50)	1.17 (0.82–1.68)	1.10 (0.79–1.53)	1.23 (0.91–1.67)
5,000,000 yen	0.88 (0.61–1.27)	0.77 (0.53–1.14)	1.13 (0.80–1.59)	0.99 (0.72–1.35)
7,000,000 yen	1.41 (0.95–2.08)	0.98 (0.66–1.46)	1.51 (1.04–2.18) [c]	1.15 (0.83–1.61)
10,000,000 yen	1.58 (0.98–2.53)	1.55 (0.95–2.51)	1.85 (1.19–2.87) [b]	1.44 (0.94–2.20)
15,000,000 yen	1.88 (0.97–3.67)	1.82 (0.73–4.50)	1.97 (1.05–3.69) [c]	2.07 (0.92–4.67)

Abbreviation: ref, referent group.
[a] $P < .000$.
[b] $P < .001$.
[c] $P < .05$.

mately 61.7% of the men and 51.7% of the women in France achieved the recommended level of physical activity.

The current study found that physical activity participation at the recommended level was higher in men than in women. As for gender-specific correlates, for men, being employed and for women, being between 30 and 39 years of age emerged as negative correlates with regard to meeting the physical activity recommendation. On the other hand, being married and having higher education were found to be positive correlates for attaining the recommended level of physical activity only for women. No association was found with household income level for either gender.

Previously, numerous studies have examined the demographic correlates of participation in physical activity.[9,10] All variables listed in the current study, excluding marital and employment status, were well documented as the consistent correlates of physical activity behavior.[9,10] Nevertheless, few studies have examined the association between the physical activity recommendation and demographic variables, especially in a large population with a wide range of age groups.[4,5,11,12] Therefore, the relationship of these correlates with the physical activity recommendation is still less clear. The results of the current study clearly replicate and strengthen the findings of the previous research with respect to gender.[4,5,9–12] In addition, educational level in the current study emerged as having a positive association with meeting the physical activity recommendation only for women, which was a similar result to the SUVIMAX study.[11] Moreover, former population-based cross-sectional investigations, using data of the 2001 BRFSS and 2000 NPAS, found that a higher level of education was a positive correlate for both genders. This finding suggests that individuals with higher education might be more aware of the benefits of regular

physical activity at the recommended level with regard to disease prevention and health promotion.[5,12]

With regard to age, a strong inverse association between age and meeting the physical activity recommendation was found in the 2001 BRFSS, the 2000 NPAS, and the cross-sectional study (which included both age diversity and gender) in the United States.[4,5,12] The current study, however, failed to reveal an association of age with attaining the physical activity recommendation, with the exception of a specific age bracket—30 to 39 years—for women. This might imply that women in this age group are unable to engage in physical activity at a sufficient level because of the overlapping roles as a mother and as an employee. The social situation for Japanese women, which is characterized by a higher employment rate and the trend to marry at a later stage in life, might influence this finding.[26]

The notable finding of the current study is the relatively strong association of employment status with attaining the physical activity recommendation in men. Even though some previous studies investigated occupational situation,[5,9] few of them examined whether employment status (employed versus unemployed) was correlated with physical activity participation. Thus, this finding highlights the significance of identifying the association between employment status and physical activity recommendation in a large Japanese population. Additional studies are clearly required to examine such a relationship. A second noteworthy point was the examination of the association between marital status and meeting the physical activity recommendation, which has not been studied before. Previous studies examined the demographic correlates of participating in physical activity; the results were controversial.[27–31] Some studies reported a positive association,[27,30] whereas others reported a negative[31] or no association.[28,29] However, most of these studies examined only women, minorities, or samples with narrow age ranges.[27–30]

The results of the current study found different associations for men and women with regard to meeting the physical activity recommendation. In addition, more demographic correlates were explained for women than for men. This suggests that there might be other significant correlates associated with meeting the physical activity recommendation for men that were not obtained in the current study. Previous reviews of physical activity correlates in adults mentioned that physical activity was a multifactorial behavior influenced by demographic, biological, psychological, behavioral, social and/or cultural, and physical environmental factors.[9,10] In addition, the findings on gender-specific associations with meeting the physical activity recommendation imply that subgroups based on elements such as gender, age, and location of residence might be likely to differ in the factors that influence their physical activity behaviors. The current investigation has implications for developing interventions to promote physical activity among a large population of Japanese adults. The difference in correlates between men and women might indicate that gender-specific interventions or approaches might be needed. For example, being employed was significantly related to meeting physical activity recommendations among men, suggesting that developing a program promoting physical activity at worksites might be more effective. Furthermore, a unique contribution in the current study was that it examined the demographic correlates of engaging in physical activity at an insufficient level, something that has not been extensively studied before. These correlates should also be taken into account when targeting specific program participants.

The current investigation had a number of limitations. First, the analysis was cross-sectional, thereby making determinations of cause and effect impossible. Next, level of physical activity was assessed using only the self-reported questionnaire. Ishikawa-Takata et al[32] found that only 36% of 150 healthy free-living Japanese adults were classified into the same level of physical activity groups (insufficiently active, sufficiently active, and highly active) by both the total METs assessed by IPAQ and physical activity level measured by the doubly labeled water method. Thus, inaccurate estimation of physical activity level and recall bias are unavoidable. In addition, the detail listed examples of physical activities, especially lifestyle physical activity, were limited in the IPAQ. However, additional examples of yard work, house work, and occupation with moderate intensity are included in the EPAR2006,[8] which might lead to a lower estimation of physical activity level among the participants. Moreover, the current study was conducted in an Internet setting. Eysenbach et al[33] indicated that issues of generalizability, mainly because of selection bias, were important considerations because of the nonrepresentative nature of the Internet population and the self-selection of participants to survey. Rhodes et al[34] mentioned that younger, more educated, and higher income individuals have greater access to the Internet. In addition, people are more likely to respond to a survey if they are interested in its contents or are attracted by the incentives offered for participation.[33–35] Therefore, the basic characteristics of the respondents might possibly be biased, implying that the findings under such a setting might not be sufficiently applicable to the general population.

Conclusions

In summary, gender, marital status, and educational level in women were the demographic correlates that were positively associated with meeting the recommended physical activity level; whereas, a negative association was found with employment status in men and with the age bracket in women. To specify the target population and develop effective interventions and policies, further investigation on Japanese populations is needed. Such investigation is necessary to determine the extended associations of meeting the physical activity

recommendation with other possible variables or among subgroups, especially in the potentially inactive population. In addition, more effective interventions for physical activity promotion that match the needs and expectations of the target population should be developed to increase engagement in regular physical activity and exercise, and consequently, improve their overall health status.

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Lung Cancer Occurrence in Never-Smokers: An Analysis of 13 Cohorts and 22 Cancer Registry Studies

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Abbreviations: BWHS, Black Women's Health Study; CI, confidence interval; CPS-I, Cancer Prevention Study; CPS-II, Cancer Prevention Study II; CPS-II Nutrition, Cancer Prevention Study II Nutrition Cohort; HPFS, Health Professionals' Follow-up Study; HR, hazard ratio; KCPS, Korean Cancer Prevention Study; MEC, Multiethnic Cohort; NHS, Nurses' Health Study; RR, rate ratio; SEER, Surveillance Epidemiology and End Results; WHS, Women's Health Study

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ABSTRACT

Background

Better information on lung cancer occurrence in lifelong nonsmokers is needed to understand gender and racial disparities and to examine how factors other than active smoking influence risk in different time periods and geographic regions.

Methods and Findings

We pooled information on lung cancer incidence and/or death rates among self-reported never-smokers from 13 large cohort studies, representing over 630,000 and 1.8 million persons for incidence and mortality, respectively. We also abstracted population-based data for women from 22 cancer registries and ten countries in time periods and geographic regions where few women smoked. Our main findings were: (1) Men had higher death rates from lung cancer than women in all age and racial groups studied; (2) male and female incidence rates were similar when standardized across all ages 40+ y, albeit with some variation by age; (3) African Americans and Asians living in Korea and Japan (but not in the US) had higher death rates from lung cancer than individuals of European descent; (4) no temporal trends were seen when comparing incidence and death rates among US women age 40–69 y during the 1930s to contemporary populations where few women smoke, or in temporal comparisons of never-smokers in two large American Cancer Society cohorts from 1959 to 2004; and (5) lung cancer incidence rates were higher and more variable among women in East Asia than in other geographic areas with low female smoking.

Conclusions

These comprehensive analyses support claims that the death rate from lung cancer among never-smokers is higher in men than in women, and in African Americans and Asians residing in Asia than in individuals of European descent, but contradict assertions that risk is increasing or that women have a higher incidence rate than men. Further research is needed on the high and variable lung cancer rates among women in Pacific Rim countries.

The Editors' Summary of this article follows the references.

Introduction

Most of the more than 1.4 million lung cancer deaths that occur annually worldwide are caused by tobacco smoking [1]. The rest comprise only a small fraction of the total, yet they account for a substantial disease burden. For example, in the United States (US), factors other than cigarette smoking are estimated to account for 10%–15% of all lung cancer deaths [2] on the basis of surveys of smoking in the general population and relative risk estimates from a large American Cancer Society cohort study [2]. This percent range corresponds to between 16,000 and 24,000 of the more than 161,000 lung cancer deaths projected to occur in the US in 2008 [3]. If these deaths were considered as a separate category, they would rank among the seven to nine most common fatal cancers in the US [4].

Not all lung cancers caused by factors other than active smoking occur in people who have never smoked; the background risk resulting from other exposures and their interactions with genetic and epigenetic processes also affects current and former smokers. However, lung cancer occurrence among never-smokers is of special interest for several reasons. First, geographic and temporal variations in risk caused by other environmental exposures and/or differences in biological susceptibility should, in principle, be more easily detected in populations that have never smoked. Second, never-smokers comprise a growing proportion of adults in economically developed countries. Whereas only 44% of US adults (age $\geq$18 y) reported never having smoked 100 or more cigarettes in 1965 [5], this proportion increased to 59% in 2006 [6]. Third, clinical studies have shown that lung tumors in never-smokers have a different molecular profile and better response to targeted therapy than cancers in smokers, and in some respects represent a different type of cancer [7,8]. Finally, some researchers have hypothesized on the basis of limited data that, among never-smokers, women may have higher risk of developing lung cancer than men but lower risk of dying from it [9,10], that age may influence the gender relationship [11], that African Americans [4] or Asians [7] may be at greater risk than individuals of European descent, and that factors other than cigarette smoking may be contributing to temporal changes in lung cancer risk [12–14].

To examine these issues, we pooled data on lung cancer incidence and death rates among self-reported never-smokers from 13 large cohort studies representing over 630,000 and 1.8 million participants for the incidence and mortality analyses, respectively. The studies spanned the time period 1960 to 2004 and were based in North America, Europe, and Asia. We supplemented the cohort analyses with population-based incidence and death rates from lung cancer for women in 22 cancer registries and ten countries or geographic regions during time periods when the prevalence of female smoking was reportedly low. All of these data are provided in extensive supplemental tables as a resource for other researchers (Tables S1–S23).

Methods

General Population Rates

We abstracted data on lung cancer incidence among women from ten countries (21 cancer registries) [15] reported to have a low prevalence of female smoking [16]. The registries were located in India, China, and selected areas in Asia, Africa, Europe, and the Middle East (Table 1). We selected registries in countries where the prevalence of female smoking was known to be low nationally or regionally in the year 2000 [16], or where cultural or religious prohibitions discourage smoking among women. We chose the time period 1983–1987 [15] rather than more contemporary data to circumvent uncertainties about recent increases in female smoking. The exact time period differed slightly in certain countries. For example, the incidence data for Algeria pertain to the years 1986–1989; Mali to 1987–1989; Thailand-Khon Kaen to 1988–1989; and the Basque region of Spain to 1986–1987 [15].

We also abstracted incidence and death rates among women in the US for the years 1935–1940 using the Connecticut Tumor Registry for incidence [17] and US vital statistics for mortality (Table 2) [18]. The time interval of 6 y (1935–1940) rather than 5 y was chosen for comparability with published data from the Connecticut Tumor Registry [17]. The lung cancer incidence rates in Connecticut and death rates in the US in 1935–1940 were compared to each other and to international rates during the 1980s in other countries where few women were known to smoke. In making temporal and geographic comparisons we focused on the age range 40–69 y, where the diagnosis of primary lung cancer was thought to be less affected by changing diagnostic technologies and more reliable than at older ages [19]. However, Tables 1 and 2 present the data over a broad range of age as a potential resource for future studies. All age-standardized rates were based on the IARC 2000 world population standard.

Cohort Studies

We contacted the principal investigators of large cohorts that included a minimum of approximately 20,000 participants who reported no history of regular tobacco smoking. Never-smokers or lifelong nonsmokers were those who reported never having smoked 100 cigarettes or more in their lifetime or never having smoked any tobacco product regularly. We excluded cohorts that were defined by exposure to specific occupational or environmental toxicants. Researchers were asked to provide age-, sex-, and race-specific data on lung cancer cases and/or deaths and person years at risk among the lifelong nonsmokers. Mortality data were provided for 11 studies (Table S1); incidence data for eight (Table S2). Among the mortality studies, seven were located in North America and Europe (the Black Women's Health Study [BWHS] [20], Cancer Prevention Study I [CPS-I] and II [CPS-II] [4], the Health Professionals' Follow-up Study [HPFS] [21], the Multiethnic Cohort [MEC] [22], the Nurses' Health Study [NHS] [21], and the Women's Health Study [WHS] [23]) and four in Asia (Hirayama or Six Prefecture Study in Japan [24], the Japanese Collaborative Cohort Study [JACC] [25], the Japanese Three Prefectures Study [26], and the Korean Cancer Prevention Study [KCPS] [27]). All of the eight studies that provided incidence data were located in North America or Europe (Table S2). These included BWHS, Cancer Prevention Study II Nutrition Cohort (CPS-II Nutrition) [28], the European Prospective Investigation into Cancer and Nutrition (EPIC) [29], HPFS, MEC, NHS, the Swedish Construction Worker cohort (SCW) [30], and WHS. Only two of these cohorts [24,30] have previously published age-specific rates in never-smokers for the length of follow-up considered here.

We tabulated the number of events, person years at risk,

and age-specific and age-standardized rates among never-smokers in each contributing cohort for mortality (Tables S3–S8) and incidence (Tables S9–S12). Most of the studies included both men and women. The two studies of health professionals (HPFS and NHS) were considered a paired analysis of men and women, respectively. Two mortality studies (WHS and BWHS) were included only in the analyses of women. The total number of incident cases and deaths is shown in Table 3 by gender and race.

Before pooling the data from these cohorts, we tested for heterogeneity of the rates among the cohorts within strata of gender and race. We first used the likelihood ratio test in generalized linear models (SAS GENMOD) [31] to determine whether controlling for "study" improved the fit of the model, within each sex and race combination. Heterogeneity across studies was defined as a $p < 0.05$. Heterogeneity within gender was observed in the mortality data for women of European descent ($p < 0.0001$), Asian women ($p = 0.0007$), and Asian men ($p < 0.0001$) and in the incidence data for women of European descent ($p = 0.0015$), and reached borderline statistical significance for men of European descent ($p = 0.066$). The two smallest studies (WHS and MEC) accounted for the heterogeneity of the mortality rates among individuals of European descent (both WHS and MEC) and Asians (MEC). Their exclusion did not appreciably change the rates, since they contributed less than 4% of deaths to any analysis. We could not account for the higher incidence rates among women of European descent in the CPS-II Nutrition Survey than in the NHS.

To examine whether the age pattern for men and women differed, we again used generalized linear models to assess whether the age-specific rate difference changed with age. The statistical significance of the trend in the rate difference (treated as linear) was tested using two-way interaction terms between gender and age and the likelihood ratio test. Three-way interaction terms between age, gender, and cohort were also tested and were not significant.

Lastly, we evaluated potential effects associated with heterogeneity by conducting sensitivity analyses that compared the rates and rate ratios from the pooled data with the results from random effects models within strata of gender and race where heterogeneity was detected. The results of these two approaches were similar.

Despite some evidence of heterogeneity in both the incidence and death rates among cohorts, we present both pooled and cohort specific results. The pooled mortality data are presented in Tables S13–S16 for individuals of European descent, Asians, and African Americans, respectively; the pooled incidence data are presented in Tables S17–S20. In both the pooled and cohort specific analyses, the age-standardized rates were calculated using direct standardization to the IARC 2000 world population weights. The rates were standardized to four different age ranges (40–69, 40–79, 40–84, and 40+ y) to facilitate comparisons with cancer registry and national vital statistics data and with other published results. We calculated age-specific ratios of the male to female rates only in age strata where both sexes had at least five events.

Two other analyses were conducted to provide additional perspective on these risks. To compare the lung cancer risk in never-smokers to that in smokers, we contrasted the age-specific death rates from lung cancer among never-smokers in the pooled data with those of current smokers in CPS-II for individuals of European descent and KCPS for Asians (Figure 1 and Table S21). These two studies were the only contemporary cohorts for which we had the relevant information on smokers. For validity, we restricted the follow-up of the current smokers to first 6 y after enrollment in order to minimize the effect of cessation, since neither CPS-II nor KCPS collected information on changes in smoking status during follow-up. We also calculated the cumulative probability of dying from lung cancer before age 85 y among male and female smokers and never-smokers. The age category 80–84 y was used as the upper limit in calculating cumulative probability because the category age 85+ was open-ended and undefined. The other analysis compared lung cancer occurrence among lifelong nonsmokers in the pooled data with the incidence and death rates for other cancers in the general population. Population-based incidence rates were based on the Surveillance Epidemiology and End Results (SEER) Cancer Statistics Review for the years 2000–2004 [32]; mortality rates were derived from US vital statistics from the same years and source. Only the data for individuals of European descent are presented here.

Results

International Comparisons Based on Cancer Registry Data

Table 1 presents the age-specific and age-standardized lung cancer incidence rates among women in the 21 cancer registries covering populations where female smoking was thought to be uncommon. The age-standardized rates varied by more than 30-fold even when restricted to the age range 40–69 y where the data were considered most reliable. The lowest recorded incidence rates were among women in Africa (Algeria and Mali) and India (Ahmedabad, Bangalore, Madras, Mumbai). Women in the Basque region of Spain were also in the lowest tertile ($\leq$ 9 cases per 100,000) when the comparison was restricted to the age range 40–69 y. Incidence rates (per 100,000) in the middle tertile ranged from 11.2 in Kuwait to 27.4 in Qidong City, China and included women in all of the registries in Japan, the Malay population of Singapore, the Khon Kaen registry in Thailand, and the Qidong City registry in China. Rates in the highest tertile ranged from 30.9 per 100,000 among women in the Rizal Province in the Philippines to 87.8 per 100,000 in Chiang Mai, Thailand. The variability of the rates within individual countries was greatest in China and Thailand.

Table 1 also presents lung cancer incidence rates among women from the Connecticut tumor registry during the years 1935–1940, a time period when few American women smoked. The lung cancer incidence rate among Connecticut women, ages 40–69 y was 8.5 per 100,000 in the late 1930s, similar to that among women of the same age in the Basque region of Spain (8.6 per 100,000) and Kuwait (11.2 per 100,000) 50 y later. The Connecticut rates reach a plateau at age 70 y and then decrease in the oldest age groups, consistent with underdiagnosis of lung cancer in the elderly. The problem of underdiagnosis in older age groups exists wherever minimally invasive diagnostic technologies are unavailable, as would also have been true in the US during the 1930s.

Table 2 compares the lung cancer incidence rates among women in selected registries with national or regional mortality rates during the same time period. With the

Table 1. Age-Specific and Age-Standardized Lung Cancer Incidence Rates (Per 100,000) among Women in Selected Populations with Low Female Smoking [15]

Country/Region	Region/City	Years	Age Group (y)													Age Standardized Rates[a]
			20–24	25–29	30–34	35–39	40–44[b]	45–49[b]	50–54[b]	55–59[b]	60–64[b]	65–69[b]	70–74	75–79	80–84	85+	
India	Ahmedabad	1983–1987	0.1	0.1	1.0	0.5	1.8	2.1	5.3	7.8	8.2	12.8	15.1	11.3	7.8	—	5.4
	Bangalore	1983–1987	0.1	0.1	—	0.6	2.1	1.7	4.9	5.1	10.2	12.3	6.2	12.0	—	—	5.2
	Mumbai	1983–1987	0.2	0.3	0.3	1.3	1.9	3.3	5.1	10.0	10.2	22.1	21.7	18.1	—	—	7.3
	Madras	1983–1987	—	0.1	0.3	1.3	2.0	2.7	5.0	5.6	3.3	7.4	4.3	3.5	—	—	4.0
Africa	Algeria	1986–1989	—	—	—	2.1	—	2.5	3.5	2.1	8.9	—	—	—	—	—	2.7
	Mali	1987–1989	—	2.3	4.7	—	2.7	3.7	9.4	7.0	8.0	—	—	65.2	—	—	5.2
China	Qidong city	1983–1987	—	0.7	1.7	3.0	6.5	11.1	18.0	33.4	52.9	75.2	74.9	93.6	86.6	66.8	27.4
	Shanghai	1983–1987	0.4	0.5	2.4	4.1	9.2	13.4	26.1	44.4	76.0	125.8	162.6	167.7	157.6	129.8	40.2
	Tianjin	1983–1987	0.5	1.5	1.8	4.4	13.3	29.9	62.7	102.6	179.6	230.2	263.2	200.8	213.7	72.2	85.4
	Hong Kong	1983–1987	1.0	2.4	2.7	6.6	14.2	24.4	43.8	80.8	139.6	195.9	280.5	314.3	344.7	390.2	68.6
Japan	Osaka	1983–1987	—	0.6	0.5	1.6	4.3	7.1	14.8	25.8	39.4	73.4	108.8	154.5	157.7	150.3	22.3
	Saga	1984–1986	—	—	3.0	1.0	7.1	7.1	8.6	22.2	31.4	55.2	82.1	88.0	121.2	137.7	18.2
	Yamagata	1983–1986	—	—	2.7	3.3	7.6	5.7	11.4	22.8	30.9	42.8	73.2	106.5	120.6	86.5	17.1
Philippines	Manila	1983–1987	0.2	1.2	1.6	7.8	8.8	17.6	21.0	40.1	81.5	88.0	129.3	133.1	—	—	36.2
	Rizal Province	1983–1987	0.3	1.3	1.7	2.8	6.3	17.8	23.5	44.4	61.7	59.8	91.8	119.0	—	—	30.9
Singapore	Chinese	1983–1987	0.2	0.6	1.1	4.7	5.0	14.8	29.7	52.8	90.3	138.5	204.4	247.5	227.4	—	44.8
	Malay	1983–1987	—	1.1	2.7	3.9	4.3	11.8	25.4	15.0	50.3	92.7	137.0	128.2	—	—	27.2
Thailand	Chiang Mai	1983–1987	—	2.1	2.6	4.7	23.9	37.2	101.3	140.9	153.2	135.9	93.7	118.4	—	—	87.8
	Khon Kaen	1988–1989	—	3.2	—	1.1	2.6	8.0	9.2	18.1	15.1	34.0	19.2	37.7	—	—	12.3
Other	Spain, Basque	1986–1987	—	0.6	0.7	2.0	2.9	9.6	8.1	7.1	9.2	20.2	25.0	39.4	36.8	24.5	8.6
	Kuwait	1983–1987	—	1.5	—	—	—	2.1	13.5	19.4	18.4	27.1	28.4	37.3	79.1	35.1	11.2
	US, CT	1935–1940	0.2	0.7	1.3	1.0	4.5	4.7	7.6	9.7	13.3	17.5	23.6	23.2	17.5	11.3	8.5

[a]Lung cancer rates at ages 40–69 y standardized to the world population, 2000.
[b]Rates at ages 40–69 y considered most reliable.
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Table 2. Comparison of Incidence and Death Rates (Per 100,000) from Lung Cancer among Women in Five Countries and Two Time Periods

Country/ Region	Variable	Region/ City	Years	Age Group (y)													Age Standardized Rate[a]
				20–24	25–29[b]	30–34[b]	35–39	40–44	45–49[b]	50–54[b]	55–59	60–64	65–69[b]	70–74[b]	75–79	80–84	85+	
United States	Mortality [18]	US	1935–1940	0.2	0.5	0.8	1.3	2.5	4.1	6.5	9.1	11.7	14.7	16.4	15.6	13.6	10.4	7.1
	Incidence [17]	CT	1935–1940	0.2	0.7	1.3	1.0	4.5	4.7	7.6	9.7	13.3	17.5	23.6	23.2	17.5	11.3	8.5
India	Mortality [33]	Mumbai	1984–1987	0.0	0.2	0.2	0.5	1.0	1.6	4.9	6.4	7.2	14.8	20.4	20.7	—	—	5.0
	Incidence [15]	Ahmedabad	1983–1987	0.1	0.1	1.0	0.5	1.8	2.1	5.3	7.8	8.2	12.8	15.1	11.3	7.8	—	5.4
		Bangalore	1983–1987	0.1	0.1	—	0.6	2.1	1.7	4.9	5.1	10.2	12.3	6.2	12.0	—	—	5.2
		Mumbai	1983–1987	0.2	0.3	0.3	1.3	1.9	3.3	5.1	10.0	10.2	22.1	21.7	18.1	—	—	7.3
		Madras	1983–1987	—	0.1	0.3	1.3	2.0	2.7	5.0	5.6	3.3	7.4	4.3	3.5	—	—	4.0
Hong Kong	Mortality [33]	All	1983–1987	—	0.9	—	5.1	—	22.2	—	76.3	—	185.6	—	259.4	—	—	48.4
	Incidence [15]	All	1983–1987	1.0	2.4	2.7	6.6	14.2	24.4	43.8	80.8	139.6	195.9	280.5	314.3	344.7	390.2	68.6
Thailand	Mortality [33]	All	1983–1987	—	0.3	—	1.0	—	3.7	—	6.8	—	13.6	—	16.4	—	—	5.5
	Incidence [15]	Chiang Mai	1983–1987	—	2.1	2.6	4.7	23.9	37.2	101.3	140.9	153.2	135.9	93.7	118.4	—	—	87.8
		Khon Kaen	1988–1989	—	3.2	—	1.1	2.6	8.0	9.2	18.1	15.1	34.0	19.2	37.7	—	—	12.3
Japan	Mortality [33]	All	1983–1987	—	0.6	—	2.6	—	7.5	—	20.8	—	55.2	—	105.0	—	—	14.4
	Incidence [15]	Osaka	1983–1987	—	0.6	0.5	1.6	4.3	7.1	14.8	25.8	39.4	73.4	108.8	154.5	157.7	150.3	22.3
		Saga	1984–1986	—	—	3.0	1.0	7.1	7.1	8.6	22.2	31.4	55.2	82.1	88.0	121.2	137.7	18.2
		Yamagata	1983–1986	—	—	2.7	3.3	7.6	5.7	11.4	22.8	30.9	42.8	73.2	106.5	120.6	86.5	17.1

[a]Standardized to IARC World Population, 2000; ages 40–69 y.

[b]Mortality rates for women in Hong Kong, Thailand, and Japan were reported in 10-y intervals. Two of the age categories (35–44 y and 65–74 y) overlapped with the age range of 40–69 y. We therefore estimated the rates for ages 40–44 y and 65–69 y in the three populations using a weighted average of the 10-y intervals, using the ratio of the incidence rates to distribute the mortality rate into 5-y intervals.

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Table 3. Total Number of Lung Cancer Cases and Deaths among Lifelong Nonsmokers Included in the Pooled Analyses of Cohort Studies

Race/Ethnicity	Deaths			Incident Cases		
	Men	Women	Total	Men	Women	Total
European Descent	899	2,229	3,128	899	2,229	3,128
African American	39	146	185	39	146	185
Asian	486	996	1,482	486	996	1,482
Total	1,424	3,371	4,795	1,424	3,371	4,795

doi:10.1371/journal.pmed.0050185.t003

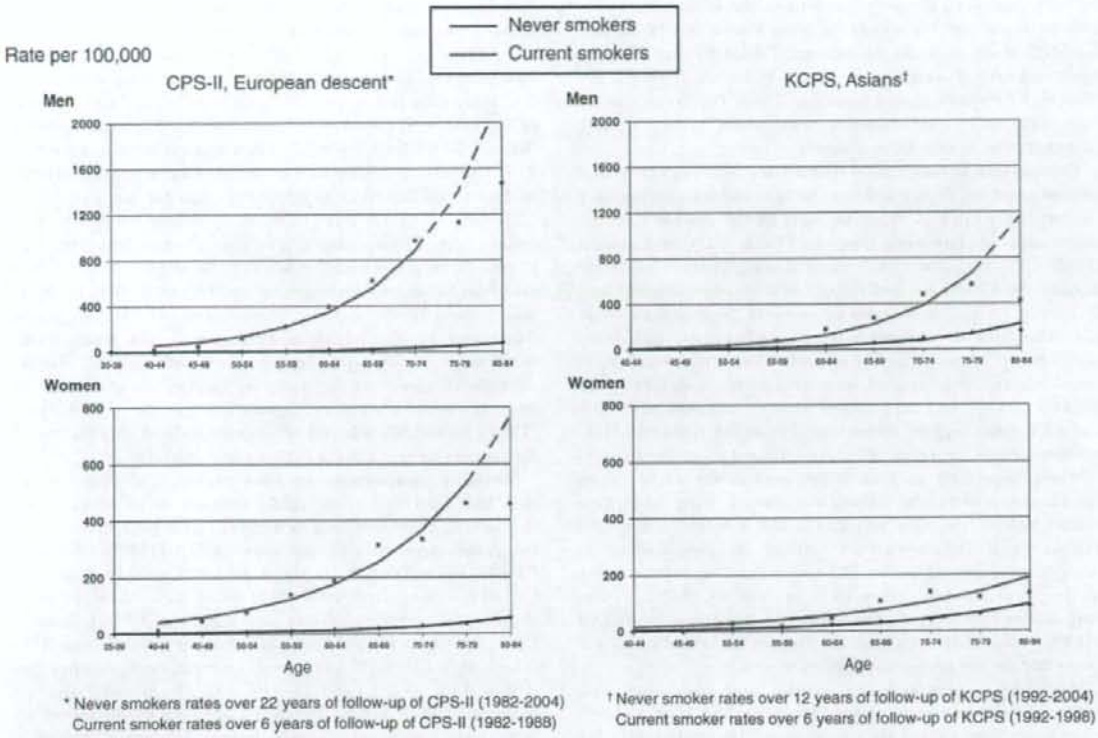

Figure 1. Age-Specific Lung Cancer Mortality Rates Comparing Current Smokers with Never-Smokers in Two Large Cohorts

Blue line indicates never-smokers; red line indicates current smokers.

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exception of Hong Kong and India, the death rates shown [33] pertain to wider geographic areas than the incidence rates and are substantially lower, due to a combination of regional variations in incidence and under-diagnosis of lung cancer in areas outside of the incidence registries. The discrepancy between the regional incidence rate and national mortality rate is especially large in Thailand, where the incidence among women in Chiang Mai is almost 16 times greater than the national death rate, and even the incidence in Khon Kaen is more than twice the national death rate. The issue of regional variability in countries such as Thailand and China is discussed below. Among Japanese women, the regional incidence rates correspond well with the national mortality data, and suggest that lung cancer risk among women in Japan during the 1980s was in fact two to three times higher than that of women in Kuwait or the Basque region of Spain at that time or the incidence rate among US women during the 1930s.

Cohort Studies of Lung Cancer Incidence and Mortality in Never-Smokers

Study populations. As shown in Tables S1 and S2, the cohort studies varied in size, length of follow-up, time period covered, composition (by age, gender, and race), and nature of the cancer endpoint (incidence and/or mortality). The 11 mortality studies are listed first (Table S1), because they are larger and more informative than the incidence studies. Collectively they include 1.4 million women and nearly 440,000 men who reported never having smoked regularly. The eight incidence studies, listed in Table S2, represent more than 630,000 never-smokers (376,600 women and 253,600 men). The total number of lung cancer deaths among lifelong nonsmokers is 4,795, about five times more than the number of incident cases (958) (Table 3). This total is smaller for Asians (1,482) and African Americans (185) than for individuals of European descent (3,128). Most of the incident cases are among women of European descent (511) or men of European descent (284). Fewer than 100 incident cases have been observed to date among Asian (69) or African American (63) women in these cohorts, and even fewer among Asian (22) or African American (9) men (Table 3).

The two American Cancer Society cohorts, CPS-I and CPS-II, contributed over 90% of the mortality data for individuals of European descent (Tables S3 and S4). The age-standardized lung cancer death rate (per 100,000 persons per year) among women of European descent was similar in CPS-I (9.3), CPS-II (10.6), and the NHS (10.3), but lower in the WHS (4.0) when standardized across all ages 40 y and above (Table S3). The death rate (per 100,000) among men of European descent was higher in CPS-I (15.3), CPS-II (13.4), and HPFS (12.6) than in MEC (6.4) when standardized within comparable age ranges. CPS-I represents a time period 20–30 y earlier than

the other cohorts. Larger variations in the death rates were seen between the Asian cohorts from Korea and Japan and the MEC study of Asian Americans (Tables S5 and S6). The age-standardized rates were about twice as high in the massive KCPS cohort and Japanese Three Prefectures study as in MEC. KCPS contributed approximately 90% of all lung cancer deaths in the Asian cohorts.

Comparison of lung cancer death rates between never- and current smokers. Figure 1 shows the age- and sex-specific lung cancer death rates in never-smokers in the pooled data for individuals of European descent (Table S13) and Asians (Table S15) with the death rates among current cigarette smokers in CPS-II for individuals of European descent and KCPS for Asians (death rates in smokers presented in Table S21). The rates for current smokers were based on the first 6 y of follow-up to minimize the effects of smoking cessation, as noted above. Men and women of European descent who smoked actively had lung cancer death rates that were 21.9 and 13.7 times higher, respectively, than the rates of never-smokers, when the rates were standardized to all ages 40+ y.

When expressed as cumulative probability rather than annual death rates, the cumulative risk of dying from lung cancer before age 85 y was 22.1% for a male smoker and 11.9% for a female current smoker, in the absence of competing causes of death. The corresponding estimates for lifelong nonsmokers were a 1.1% probability of dying from lung cancer before age 85 for a man of European descent, and a 0.8% probability for a woman. The actual probabilities are lower because of competing causes of death.

Mortality comparisons by gender and age. Men who reported no history of regular smoking had higher death rates from lung cancer than women in the pooled data for individuals of European descent, Asians, and African Americans (Tables S13, S15, S16, respectively). The rate ratios comparing the male and female death rates reflected significantly higher death rates in men of European descent (rate ratio [RR] = 1.32, 95% confidence interval [CI] = 1.2–1.5) and Asian men (RR = 1.96, 95% CI = 1.4–2.7) than women, at all ages 40+ (Tables S13 and S15, respectively). Age-specific comparisons could not be made among African Americans because of the small number of deaths in men (Table S16). However, the age-standardized death rates were 20%–33% higher in African American men than in African American women, depending on the age range being considered. The gender gap increased with age among individuals of European descent and Asians. Figure 2 illustrates the divergence of the male and female death rates among never-smokers with increasing age in the three largest cohort mortality studies. The gender difference was largest in KCPS for the years 1992–2004, intermediate in CPS-I from 1959 to 1970, and smallest in CPS-II from 1982–2004. When the pooled data were examined by Poisson regression analyses that controlled for study, age significantly modified the association with gender in individuals of European descent ($p = 0.01$) and Asians ($p = 0.0004$) but not African Americans ($p = 0.79$) (Tables S13, S15, S16, respectively). The age-related increase in the rate ratio estimates comparing the male and female lung cancer death rate remained statistically significant in analyses restricted to cohorts or pairs of cohorts that provided data on both men and women (p-trend = 0.002, Table S14).

Mortality comparisons by race. The lung cancer death rates in the pooled analyses were highest in Asians, intermediate in African Americans, and lowest in individuals of European descent who reported no history of regular smoking (Figure 3 and Table 4). The rate ratio estimates compared to individuals of European descent were statistically significant for Asian men (RR = 1.96, 95% CI = 1.7–2.3), Asian women (RR = 1.69, 95% CI = 1.5–1.8), and African American women (RR = 1.34, 95% CI = 1.1–1.7) when standardized to ages 40–84 y. The rate ratio comparing African American men to men of European descent was similar to that for women (RR = 1.33, 95% CI = 0.9–2.1) (Table 4). It should be noted that among the Asian cohorts (Tables S5 and S6), the age standardized lung cancer death rates were two- to five times lower for Japanese Americans in the MEC study than for men and women in the cohorts from Korea (KCPS) and Japan (Hirayama, JACC, and Three Prefectures). The lung cancer death rates among Japanese living in California and Hawaii were much closer to the rates of individuals of European descent than to the rates of Asians living in Korea and Japan (Tables S5 and S6). Age did not significantly modify the racial differences in risk among lifelong nonsmokers.

Mortality comparisons by time period. The only cohort data that provided meaningful comparisons of lung cancer risk among never-smokers in different time periods were the two American Cancer Society cohorts CPS-I (1959–1972) and CPS-II (1982–2004) [4,34–37]. A previous analysis based on CPS-II follow-up from 1982–2000 found that the lung cancer death rate in never-smokers was higher in CPS-II than in CPS-I among women of European descent (hazard ratio [HR] = 1.25, 95% CI = 1.12–1.41) but not men of European descent (HR = 0.89, 95% CI = 0.74–1.08) [4]. The present analysis extended CPS-II follow-up for 4 additional y and found no statistically significant evidence that the death rate was higher in CPS-II than in CPS-I for women of European descent (RR = 1.11, 95% CI = 0.98–1.25), African American women (RR = 1.15, 95% CI = 0.62–2.13), or men of European descent (RR = 0.83, 95% CI = 0.66–1.05). In other analyses, we divided the CPS-II follow-up into two segments of equal duration and found essentially the same age-standardized death rates among never-smokers during both periods (analyses not shown).

Incidence rates in cohort studies. The lung cancer incidence rates in the cohort studies were based on fewer cases than the mortality studies and were less precise, especially for Asians and African Americans. However, the incidence rate among women of European descent age 40–69 y in the pooled cohort data (Table S17) was very similar to the general population rates among individuals of European descent in populations with a low prevalence of female smoking (Table 1). For example, the age-standardized incidence rate among women of European descent age 40–69 y in the cohort studies was 9.7 per 100,000 (Table S17) compared to 8.5 per 100,000 among US women in the 1930s and 8.6 in the Basque region of Spain during the 1980s (Table 1). At older ages, the female death rates increased more rapidly with age in the pooled cohort data than among women in Connecticut in the 1930s or in the Basque region of Spain during the 1980s. No similar comparisons could be made between incidence rates among Asian women in the cohort studies and women in Asian countries; the only incidence data on Asian never-smokers came from the MEC cohort in North America.

Incidence comparisons by gender and age. The age-specific and age-standardized rate estimates in the cohort studies

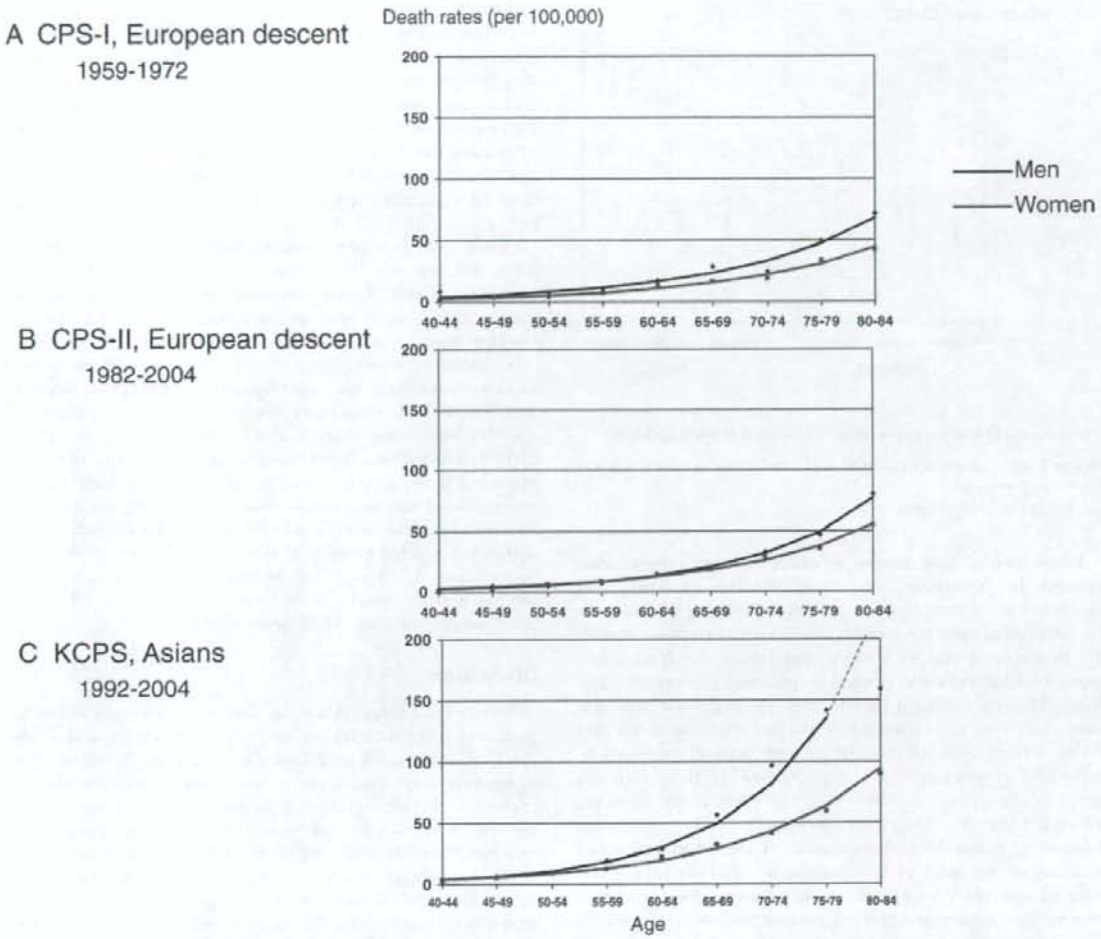
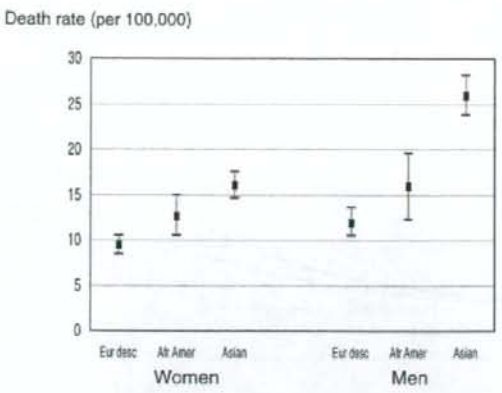


Figure 2. Sex- and Age-Specific Lung Cancer Death Rates in Three Large Cohorts
(A–C) Blue line indicates men; red line indicates women.
doi:10.1371/journal.pmed.0050185.g002

were much less precise for incidence (Tables S9–S12) than for mortality (Tables S3–S8), even among individuals of European descent. Age-specific comparisons could be made only in this latter group. No meaningful difference was observed between the lung cancer incidence rate in men of European descent (14.0 per 100,000) and women (13.8 per 100,000) who had never smoked, when the rates were standardized to all ages 40 y and above (Table S17). However, the gender relationship observed in the incidence data for individuals of European descent appeared to change qualitatively with increasing age (Figure 4). In the pooled data, women who never smoked had higher incidence rates than men in the age range 40–59 y; similar incidence rates between ages 60 y and 79 y; and lower incidence rates beginning at approximately age 80 y. In only two 5-y age groups (50–54 y and 55–59 y) did the ratio of the male to female rate achieve borderline statistical significance (Table S17). Furthermore, the absolute difference between the male and female death rates was small, even in these two age groups (absolute difference = 3.9 and 4.4 cases per 100,000 at ages 50–54 y and 55–59 y, respectively). The trend in the rate difference with age was not statistically significant ($p = 0.06$) when all cohorts were included in the pooled analysis. The evidence of a trend was further weakened by restricting the analysis to cohorts or pairs of cohorts that provide incidence data on both sexes ($p = 0.21$) (Table S18).

Incidence comparisons by race and ethnicity. African American women had significantly higher incidence rates from lung cancer than women of European descent who had never smoked (RR = 1.56, 95% CI = 1.1– 2.1). The incidence data available for African American men and Asian men and women were too sparse to make meaningful comparisons. As noted above, incidence data for Asian never-smokers derived entirely from the MEC study in the US (Tables S11 and S12).



*Rates are age-standardized to the 2000 IARC World population, ages 40-84

Figure 3. Age-Standardized Lung Cancer Death Rates by Race and Sex in the Pooled Analyses
doi:10.1371/journal.pmed.0050185.g003

Frequency of lung cancer in never-smokers versus other cancers in population. We compared the mortality and incidence rates from lung cancer among lifelong nonsmokers in the pooled data for individuals of European descent with US death rates and with SEER incidence rates from other types of cancer in the general population (Tables S22 and S23). The lung cancer death rate in never-smokers was comparable to, and in some cases higher than, the death rate from other types of cancer in the general population, especially at older ages. For example, the death rate among men of European descent who reported never smoking exceeded the general population death rate for melanoma beginning at age 50 y, from cancer of the brain and other nervous system at ages 65+ y, from cancers of the kidney and liver at ages 70+ y, and from cancer of the esophagus at ages 80+ y. The same was observed among women of European descent for cancers of the uterine corpus and liver beginning at age 35 y, for melanoma and cancer of the esophagus at ages 40+ y, for all leukemia at ages 45+ y, for uterine cervix at ages 50+ y, and for cancers of the brain and other nervous system at ages 60+ y.

Using the lung cancer death rates in the pooled data, we estimated the number of lung cancer deaths that would have occurred among individuals of European descent and African Americans in the US in 2004, if the entire population in these two groups, age 40+ y had experienced the death rates of lifelong nonsmokers. We limited the analysis to individuals of European descent and African Americans, because of the lack of reliable death rates or populations at risk for other racial and ethnic groups. The estimated number of deaths (15,943) comprises slightly more than one-tenth the number of lung cancer deaths (154,202) that actually occurred among individuals of European descent and African Americans in 2004. This exceeds the number of deaths reported in 2004 from five of the 12 most common fatal cancers in the US: cancer of the ovary, liver and intrahepatic bile duct, urinary bladder, esophagus, and kidney or renal pelvis.

A similar approach, using the lung cancer incidence rates in the pooled data for never-smokers of European descent and African American never-smokers and the populations, age 40 y and above living in the 17 SEER areas of the US in 2004, estimated that 5,064 incident lung cancers would have occurred if no one smoked. By this estimate, lung cancer among never-smokers would rank 11th among the 12 most common incident cancers in SEER areas of the US in 2004. By comparison, 6,432 cases of leukemia, 4,737 cases of stomach cancer, and 4,516 cases of thyroid cancer were diagnosed among African American residents and residents of European descent of these SEER areas in 2004.

Discussion

To our knowledge, this is the first comprehensive effort to pool and compare data on lung cancer incidence and death rates in lifelong nonsmokers from multiple sources. The combination of data from cohort studies and population registries provides a more coherent picture of how background lung cancer risk varies by age, sex, geographic location, race/ethnicity, and time period than can be obtained from any single study. All of the available data have limitations and unknowns regarding the accuracy of the diagnostic information, the validity and comparability of the exposure information on active smoking or its absence, and the lack of measurements of other exposures that affect lung cancer risk. In the interest of clarity, however, we first discuss the series of questions raised in the introduction and later consider how these data limitations could affect our conclusions.

Table 4. Comparing Pooled Lung Cancer Rates (Per 100,000) among Lifelong Nonsmokers by Race

Variable	Category	Men		Women	
		Age-Standardized Rate[a]	Rate Ratio[b]	Age-Standardized Rate[a]	Rate Ratio[b]
Mortality	European Descent	12.0 (10.5, 13.6)	1.00 (referent)	9.5 (8.5, 10.5)	1.00 (referent)
	African American	16.0 (12.3, 19.6)	1.33 (0.9, 2.1)	12.7 (10.5, 15.0)	1.34 (1.1, 1.7)
	Asian	26.0 (23.8, 28.1)	1.96 (1.7, 2.3)	16.1 (14.6, 17.5)	1.69 (1.5, 1.8)
Incidence	European Descent	11.2 (9.8, 12.6)	1.00 (referent)	12.4 (11.3, 13.5)	1.00 (referent)
	African American	12.3 (3.2, 21.4)	1.10 (0.5, 2.3)	19.4 (14.2, 24.6)	1.56 (1.2, 2.1)
	Asian	12.9 (6.7, 19.1)	1.15 (0.7, 1.9)	15.0 (10.4, 19.7)	1.14 (0.8, 1.6)

[a]Standardized to the IARC World Standard Population for 2000, ages 40–84 y (95% confidence intervals).
[b]Rate ratio in comparison to individuals of European descent.
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