

Epidemiology of Non-small Cell Lung Cancer in Asian Americans

Incidence Patterns Among Six Subgroups by Nativity

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Background: Differences in the epidemiology of lung cancer between Asians and non-Hispanic whites have brought to light the relative influences of genetic and environmental factors on lung cancer risk. We set out to describe the epidemiology of non-small cell lung cancer (NSCLC) among Asians living in California, and to explore the effects of acculturation on lung cancer risk by comparing lung cancer rates between U.S.-born and foreign-born Asians.

Methods: Age-adjusted incidence rates of NSCLC were calculated for Chinese, Filipino, Japanese, Korean, Vietnamese, and South Asians in California between 1988 and 2003 using data from the California Cancer Registry. Incidence rates were calculated and stratified by sex and nativity. We analyzed population-based tobacco smoking prevalence data to determine whether differences in rates were associated with prevalence of tobacco smoking.

Results: Asians have overall lower incidence rates of NSCLC compared with whites (29.8 and 57.7 per 100,000, respectively). South Asians have markedly low rates of NSCLC (12.0 per 100,000). Foreign-born Asian men and women have an approximately 35% higher rate of NSCLC than U.S.-born Asian men and women. The incidence pattern by nativity is consistent with the population prevalence of smoking among Asian men; however, among women, the prevalence of smoking is higher among U.S.-born, which is counter to their incidence patterns.

Conclusions: Foreign-born Asians have a higher rate of NSCLC than U.S.-born Asians, which may be due to environmental tobacco

smoke or nontobacco exposures among women. South Asians have a remarkably low rate of NSCLC that approaches white levels among the U.S.-born. More studies with individual-level survey data are needed to identify the specific environmental factors associated with differential lung cancer risk occurring with acculturation among Asians.

Key Words: Lung cancer, Epidemiology, Asian, Nativity, Smoking, Exposures.

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Lung cancer is the most common cause of cancer death in the United States and worldwide.^{1,2} Other than tobacco exposure, factors associated with increased lung cancer risk, such as environmental exposures and genetic susceptibility, are not well understood.³ Differences in the epidemiology of lung cancer among ethnic groups may shed light on possible genetic and environmental influences on lung cancer development. Studies in Asian populations, in particular, have drawn attention to possible links between lung cancer and environmental exposures, other than tobacco smoke.⁴ Relative to other racial/ethnic groups, Asians in general have been reported to have a lower incidence rate of lung cancer,^{4,5} a predisposition to adenocarcinoma and bronchioloalveolar carcinoma (BAC),^{6,7} and a high prevalence of epidermal growth factor receptor mutations.⁸ It is unclear the extent to which genetic factors or environmental exposures account for differences in lung cancer rates among Asians and non-Hispanic whites. The identification of relevant environmental risk factors that explain the lower rates in Asian populations may be useful targets for primary prevention of lung cancer, particularly in nonsmokers. Identification of lung cancer susceptibility genes may help to define high-risk groups for secondary prevention. A detailed examination of rates among detailed Asian subgroups by nativity will lend some clues to the relative contributions of genetic and environmental factors.

With a diverse catchment population encompassing all 4.1 million Asians, including large populations of Chinese, Filipino, South Asian (Asian-Indian and Pakistani), Korean, Japanese, and Vietnamese, the California Cancer Registry

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(CCR) offers a unique population to study the effect of race/ethnicity on the epidemiology of lung cancer.⁹ We set out to describe the epidemiology of non-small cell lung cancer (NSCLC) among Asians living in California, and to explore the effects of acculturation on lung cancer risk by comparing NSCLC rates between U.S.-born and foreign-born Asians. Differences in lung cancer incidence between U.S.-born and foreign-born Asian populations may be explained by environmental exposures, whereas differences in lung cancer incidence between Asians and non-Hispanic whites (hereafter referred to as whites) that are maintained among both U.S.-born and foreign-born Asians may be explained by genetic factors. We hypothesized that both U.S.-born and foreign-born East Asians are at disproportionately high risk for adenocarcinoma and BAC compared with whites. We also posited that the risk of NSCLC among U.S.-born and foreign-born Asians would closely mirror the prevalence of cigarette smoking in these groups.

METHODS

Data were obtained on cases of NSCLC in the CCR diagnosed between 1988 and 2003. Case reporting to the CCR is estimated to be 99% complete (<http://www.ccrca.org/questions.html#how%20complete%20is%20ccr%20data>). NSCLC cases were identified using primary site and histology codes for large cell carcinoma, squamous cell carcinoma, adenocarcinoma, BAC, and nonspecified NSCLC as previously described.¹⁰ This study was reviewed and approved by the institutional review boards at the Northern California Cancer Center and at the University of California San Francisco. No human subjects were contacted for this study.

Race/ethnicity and country of birth were obtained routinely by the CCR from hospital medical records. Patients of Chinese, Filipino, Japanese, Vietnamese, Korean, or South Asian descent were included; these six ethnic groups comprised 91% of all Asian patients in the CCR between 1988 and 2003. Of 14,569 Asians with NSCLC in this study, 4889 cases (34%) were Chinese, 4542 (31%) were Filipino, 2060 (14%) were Japanese, 1618 (11%) were Vietnamese, 1149 (11%) were Korean, and 311 (2%) were South Asian. By comparison, in 2000, the statewide distribution of these six Asian ethnic groups (which comprised 90% of the total Asian population in California) was 29% Chinese, 28% Filipino, 9% Japanese, 13% Vietnamese, 10% Korean, and 10% South Asian. At that time, 36% of all Asians in the United States resided in California.

There was information on country of birth in the CCR for 13,398 (92%) cases. For 1170 cases (8%) with unknown country of birth, the first five digits of the social security number (SSN), which correlates with its year of issuance, and date of birth were used to impute nativity. We had previously found that, compared with self-reported nativity, the sensitivity and positive predictive value of imputing nativity based on SSN and age of issue exceeded 80%. Thus, cases who had received their SSN before age 19 was imputed as being U.S.-born, and those who had received their SSN on or after age 19 was imputed as foreign-born.^{11,12}

Population estimates by sex, race/ethnicity, nativity, and 5-year age group were obtained from the 1990 and 2000 SF-3 census files for the state of California and extracensal estimates were produced by the Greater Bay Area Cancer Registry and the CCR. Population counts for the detailed Asian subgroups for the year 2000 were based on an average of the minimum (single race alone) and maximum (multiple race Asians) estimate for each subgroup. Using the 1990 and 2000 estimates as benchmarks, a linear interpolation and extrapolation method was used to estimate the 1988–1989 and 2001–2003 population data. Linear interpolation and extrapolation assumes a fixed amount of population growth each year. Detailed explanation of this methodology is available elsewhere.¹³ To apply nativity to these estimates, we used the 5% public use microdata sample from the 1990 and 2000 censuses¹⁴; this allowed us to estimate the percent foreign-born by Asian subgroup, sex, and 5-year age group for California. Using linear interpolation, we estimated the percent foreign-born for all intercensal years. Extrapolations beyond the most recent census year were fixed at their last known values. Application of these percentages to the population estimates yielded our estimates of the foreign-born and native-born population.

Incidence rates were age-standardized to the 2000 U.S. standard million population. Incidence rate ratios (IRRs) were used to compare incidence rates between two groups, such as foreign-born and U.S.-born. Incidence rates were examined by year of diagnosis, and an age-adjusted annual percentage change (APC) statistic was calculated to evaluate secular trends in incidence rates. Rates based on fewer than 15 cases or a population less than 25,000 persons were considered unstable and not reported. Statistics were calculated using SEER*STAT software (Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 6.3.5).

Tobacco consumption data on individual cases are not available in cancer registry data. Nevertheless, population prevalence data on cigarette smoking status among all Asians, Chinese, Filipinos, and Koreans in California were obtained from the California Health Interview Survey (CHIS) using *AskCHIS* Pro (<http://www.chis.ucla.edu>) combining data from the 2001 and 2003 CHIS. Information on smoking status among South Asians was obtained from the California Department of Health Services Tobacco Use Survey.¹⁵ Data were not available on the Japanese population through *AskCHIS*, and smoking estimates among Vietnamese were unstable and are not presented.

RESULTS

The incidence rate of NSCLC for California Asians between 1998 and 2003 was approximately half that of whites (Table 1). Among Asian subgroups, South Asians had the lowest (12.0 per 100,000 person-years), Vietnamese had the highest (39.2 per 100,000 person-years), and Japanese and Koreans had intermediate rates of NSCLC. The incidence rates of histologic subtypes of NSCLC among Asian subgroups followed similar patterns to the rates of all NSCLC. Six percent of NSCLC cases among Asians were BAC

TABLE 1. Age-Adjusted Annual Incidence Rates of NSCLC, California 1988–2003^a

	All NSCLC	Adenocarcinoma	Squamous	BAC	Other NSCLC
Whites (<i>n</i> = 177,181)	57.7	20.7	14	2.3	20.7
Male	72.8	23.7	20.6	2.2	26.3
Female	46.7	18.5	8.9	2.4	16.8
All Asians (<i>n</i> = 14,569)	29.8	12.1	6	1.7	10.1
Male	42.4	14.9	10.8	1.7	15.1
Female	20	9.8	2.3	1.7	6.2
Chinese (<i>n</i> = 4889)	31.8	13.1	5.3	2	11.4
Male	41.4	14.9	9.1	1.7	16
Female	23.9	11.9	2.1	2.2	7.8
Filipino (<i>n</i> = 4542)	32	13.1	6.9	1.7	10.3
Male	51.2	18.2	13.9	2	17.1
Female	17.8	9.5	1.7	1.5	5.1
Japanese (<i>n</i> = 2060)	24.9	9.8	5.6	1.4	8.2
Male	34.9	12.3	9.3	1.1	12.1
Female	18.3	8.1	3.1	1.5	5.6
Korean (<i>n</i> = 1149)	26	8.8	7.4	1.2	8.6
Male	41.8	11.9	14.2	1.4	14.3
Female	16	6.8	3	1.1	5.2
Vietnamese (<i>n</i> = 1618)	39.2	17.1	7	2	13.1
Male	54.1	21.1	11.9	2	19
Female	26.5	13.6	2.8	1.9	8.2
South Asian (<i>n</i> = 311)	12	4.8	2.5	0.8	4
Male	14.9	4.5	3.9	^b	5.7
Female	9.2	4.9	1.2	^b	2.4

^a Rates are per 100,000 person-years, adjusted to 2000 U.S. Census population.

^b Statistic not calculated, based on less than 15 cases.

NSCLC, non-small cell lung cancer; BAC, bronchioloalveolar carcinoma.

compared with 4% among whites ($p < 0.0001$); however, the incidence rate of BAC was slightly higher in whites (2.3 compared with 1.7 per 100,000 person-years among Asians).

Age-adjusted incidence rates of NSCLC were higher among Asian men than women resulting in an IRR of 2.13 (95% confidence interval [CI]: 2.05–2.21); the IRR of white men relative to women was 1.56 (95% CI: 1.55–1.58). The IRRs comparing Asian men with women was 1.52 (95% CI: 1.45–1.60) for adenocarcinoma, 4.78 (95% CI: 4.33–5.28) for squamous cell carcinoma, and 1.00 (95% CI: 0.86–1.16) for BAC.

Incidence rates were stratified by nativity (Table 2). Foreign-born Asians had a higher rate of NSCLC compared with U.S.-born Asians, with men 40% higher and women 34% higher overall (IRR 1.40, 95% CI: 1.31–1.50 among men; IRR 1.34, 95% CI: 1.23–1.46 among women), with IRRs varying among the Asian subgroups. In contrast to most other groups, foreign-born South Asians were much less likely than U.S.-born South Asians to develop NSCLC. Foreign born Vietnamese also seemed to be less likely to develop NSCLC than their U.S.-born counterparts, although the estimate was unstable because of the relatively small number of U.S.-born Vietnamese. IRRs were also calculated for histologic subgroup of NSCLC, although analysis among U.S.-born Koreans, Vietnamese, and South Asians was limited by small numbers. Although rates were higher among men than women, as seen in Table 1, IRRs of NSCLC

comparing foreign-born with U.S.-born Asians were similar between men and women (Table 2). Foreign-born men and women both had higher incidence rates of NSCLC and each of the histologic subgroups, compared with U.S.-born men and women. The same held true among Chinese and Japanese, the two largest ethnic subgroups studied.

The APC in the incidence rate was calculated among U.S.-born and foreign-born Asian men and women between 1988 and 2003. The APC for U.S.-born Asian men was –9.9% (95% CI: –17.1 to –2.1), reflecting an average of 10 percentage points decline per year in the incidence rate, whereas the APC for all other groups was small and not statistically significant (data not shown). This means that there was no significant change in NSCLC rates among women and foreign-born men.

Differences in incidence rates of NSCLC were compared with differences in the prevalence of cigarette smoking across groups by race/ethnicity, nativity, and sex (Table 3). Figure 1 shows the proportion of ever-smokers plotted against NSCLC incidence rates within population subgroups. Although rates of smoking vary considerably among Asian groups, in general, smoking is less common among U.S.-born Asian men compared with foreign-born Asian men consistent with the higher rates of NSCLC among foreign-born men. Although the opposite smoking pattern by nativity is true of Asian women, we find that NSCLC incidence rates

TABLE 2. Incidence Rates of Lung Cancer among Asian Americans, Stratified by Nativity^a

	All NSCLC	Adenocarcinoma	Squamous	BAC	Other NSCLC
Incidence rates of lung cancer among Asian American men					
All Asians (95% CI)					
Foreign-born	45 (43.5–46.6)	15.6 (14.7–16.5)	11.6 (11.0–12.2)	1.8 (1.6–2.0)	16.0 (15.1–16.9)
U.S.-born	32.1 (28.1–36.2)	12.0 (9.6–14.5)	7.8 (6.5–9.1)	1.1 (0.7–1.5)	11.2 (9.7–13.9)
IRR	1.40 (1.31–1.50)	1.30 (1.17–1.45)	1.48 (1.31–1.70)	1.63 (1.18–2.31)	1.43 (1.28–1.61)
Chinese (95% CI)					
Foreign-born	41.9 (40.1–43.7)	14.4 (13.4–15.4)	9.6 (8.8–10.5)	1.7 (1.4–2.1)	16.2 (15.1–17.4)
U.S.-born	38.2 (33.5–43.2)	16.1 (13.2–19.3)	5.3 (3.8–7.2)	<i>b</i>	15.2 (12.1–18.8)
IRR	1.10 (0.96–1.26)	0.89 (0.73–1.10)	1.81 (1.32–2.57)	<i>b</i>	1.06 (0.85–1.36)
Filipino (95% CI)					
Foreign-born	52.3 (50.3–54.4)	18.6 (17.4–19.9)	14.2 (13.2–15.4)	2.1 (1.7–2.5)	17.4 (6.0–55.2)
U.S.-born	31.1 (24.7–38.5)	11.4 (7.9–15.9)	6.2 (3.6–9.7)	<i>b</i>	11.7 (7.6–16.8)
IRR	1.68 (1.36–2.13)	1.63 (1.17–2.38)	2.31 (1.46–3.96)	<i>b</i>	1.49 (1.03–2.30)
Japanese (95% CI)					
Foreign-born	62.2 (54.2–71.1)	20.4 (15.9–25.5)	17 (12.7–22.0)	<i>b</i>	22.0 (17.4–27.4)
U.S.-born	31.1 (28.1–32.8)	11.2 (9.8–12.7)	8.4 (7.2–9.6)	0.8 (0.5–1.3)	10.0 (8.7–11.5)
IRR	2.05 (1.75–2.39)	1.82 (1.38–2.37)	2.03 (1.47–2.75)	<i>b</i>	2.19 (1.67–2.85)
Korean (95% CI)					
Foreign-born	42.5 (13.4–65.5)	12.4 (10.5–14.5)	14.8 (12.7–17.2)	1.3 (0.8–2.2)	14.0 (11.7–16.4)
U.S.-born	33.7 (38.8–46.5)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	1.26 (0.64–3.19)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
Vietnamese (95% CI)					
Foreign-born	54 (50.0–58.3)	21.3 (18.9–24.0)	11.8 (10.0–13.8)	2.0 (1.4–2.9)	18.9 (16.5–21.6)
U.S.-born	75.4 (40.8–123.9)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	0.72 (0.43–1.33)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
South Asian (95% CI)					
Foreign-born	14.5 (11.9–17.5)	4.2 (3.0–5.7)	3.7 (2.5–5.3)	<i>b</i>	5.8 (4.1–8.0)
U.S.-born	35.2 (16.1–63.4)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	0.41 (0.22–0.93)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
Incidence rates of lung cancer among Asian American women					
All Asians (95% CI)					
Foreign-born	20.9 (20.1–21.7)	10.3 (9.6–11.0)	2.3 (2.2–2.6)	1.7 (1.4–2.0)	6.5 (5.9–7.1)
U.S.-born	15.6 (13.5–18.7)	7.6 (6.3–8.9)	1.9 (1.2–2.3)	1.4 (0.8–2.1)	4.8 (3.4–6.2)
IRR	1.34 (1.23–1.46)	1.36 (1.20–1.54)	1.25 (0.98–1.63)	1.23 (0.93–1.66)	1.37 (1.17–1.61)
Chinese (95% CI)					
Foreign-born	24.4 (23.2–25.6)	12.1 (11.2–13.0)	2.1 (1.8–2.6)	2.2 (1.8–2.6)	8.0 (7.3–8.7)
U.S.-born	20.9 (18.1–24.1)	10.4 (8.5–12.6)	1.7 (1.0–2.8)	2.0 (1.2–3.1)	6.8 (5.2–8.7)
IRR	1.16 (1.00–1.36)	1.16 (0.95–1.45)	1.26 (0.75–2.30)	1.07 (0.67–1.83)	1.17 (0.89–1.56)
Filipino (95% CI)					
Foreign-born	17.8 (16.8–18.9)	9.5 (8.8–10.3)	1.7 (0.7–3.6)	1.6 (1.3–1.9)	5.1 (4.5–5.7)
U.S.-born	18.2 (13.1–24.3)	9.0 (5.4–13.7)	<i>b</i>	<i>b</i>	6.3 (3.4–10.2)
IRR	0.98 (0.73–1.37)	1.06 (0.69–1.80)	<i>b</i>	<i>b</i>	0.81 (0.49–1.50)
Japanese (95% CI)					
Foreign-born	26.4 (23.8–29.2)	10.6 (9.0–21.4)	5.3 (4.2–6.7)	1.8 (1.2–2.6)	8.7 (7.2–10.5)
U.S.-born	13.3 (11.9–14.9)	6.4 (9.0–12.4)	1.7 (1.2–2.4)	1.3 (0.9–1.8)	3.9 (3.1–4.8)
IRR	1.98 (1.69–2.32)	1.65 (1.30–2.10)	3.04 (2.04–4.62)	1.43 (0.83–2.51)	2.23 (1.67–2.99)
Korean (95% CI)					
Foreign-born	16.2 (14.4–18.1)	6.8 (5.7–8.1)	3.1 (2.4–4.0)	1.1 (0.7–1.7)	5.1 (4.1–6.4)
U.S.-born	16.9 (9.2–28.0)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	0.96 (0.57–1.78)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
Vietnamese (95% CI)					
Foreign-born	26.7 (24.2–29.4)	13.7 (12.0–15.6)	2.7 (2.0–3.7)	1.9 (1.3–2.7)	8.4 (6.9–10.1)
U.S.-born	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
South Asian (95% CI)					
Foreign-born	9.0 (6.9–11.5)	4.9 (3.3–6.8)	<i>b</i>	<i>b</i>	2.5 (1.5–3.9)
U.S.-born	31.2 (15.9–54.2)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
IRR	0.29 (0.16–0.59)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>

^a Rates are per 100,000 person-years, adjusted to 2000 U.S. Census population.^b Statistic not calculated, based on less than 15 cases.

CI, confidence interval; IRR, incidence rate ratio comparing Foreign-born with U.S.-born; NSCLC, non-small cell lung cancer; BAC, bronchioloalveolar carcinoma.

TABLE 3. Smoking History of Asian American Adults, California

	Smoking Status, Men (%)				Smoking Status, Women (%)			
	Current	Former	Never	Ever	Current	Former	Never	Ever
Whites	19	34	47	53	16	28	56	44
Asian								
U.S.-born	17	19	65	35	11	11	78	22
Foreign-born	19	27	54	46	5	6	89	11
Chinese								
U.S.-born	9	14	77	24	9	7	84	16
Foreign-born	16	24	59	41	3	3	94	6
Filipino								
U.S.-born	25	9	66	34	13	11	76	24
Foreign-born	25	29	46	54	7	9	85	15
Korean								
U.S.-born	30	11	59	41	24	16	59	41
Foreign-born	38	33	29	71	8	7	85	15
South Asian ^a								
U.S.-born	9	11	80	20	5	4	91	9
Foreign-born	9	17	75	25	1	2	97	3

Source: California Health Interview Survey 2001 and 2003, all groups except South Asians.

^a Source: California Asian Indian Tobacco Use Survey 2004.

Ever smoker defined as having smoked at least 100 cigarettes over lifetime.

are higher among foreign-born women, compared with U.S.-born women.

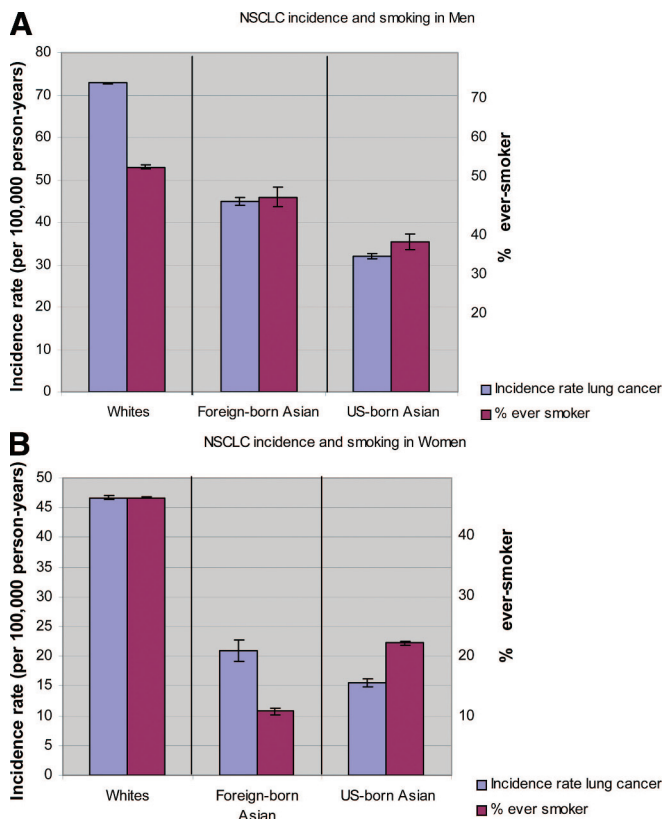


FIGURE 1. Non-small cell lung cancer rates and percentage of ever-smokers among whites, foreign-born Asian, and U.S.-born Asian men (A) and women (B).

DISCUSSION

In this study, we have identified several surprising findings with implications for differences in lung cancer susceptibility or environmental exposures between Asians and whites living in California. Although we did not have individual-level smoking data, our findings support further research into the genetic and environmental exposures that lead to the varying rates of NSCLC among the populations studied. Specifically, foreign-born Asian men and women together had a 35% higher rate of NSCLC on average than U.S.-born Asian men and women. There is substantial heterogeneity in the rates of NSCLC among the Asian subgroups, with South Asians having a strikingly low rate. Consistent with previous reports, we found that the rate of NSCLC among U.S. Asians is lower than that of whites.^{4,5} For the most part, the rates of histologic subtypes of NSCLC were proportional to the overall rate of NSCLC in each subgroup analyzed. Of note, a larger proportion of Asians with NSCLC had BAC than whites, a finding that seems to be consistent with the notion that BAC is more common among Asians.^{7,16} Nevertheless, the incidence rate of BAC is actually higher in whites. The IRR of BAC among foreign-born compared with U.S.-born Asians was similar to that for the other NSCLC subtypes studied.

Using population-based prevalence data from two California surveys, we found that foreign-born Asian men were more likely to smoke than their U.S.-born counterparts (46% versus 35%), whereas foreign-born Asian women were less likely to be smokers than U.S.-born Asians (11% versus 22%). Unfortunately, data on tobacco use among Japanese

Americans were not available for this study. A recent study describing the effects of acculturation on smoking among Asian-subgroups in California reported that, unlike other Asian subgroups, smoking rates among foreign-born Japanese women were higher compared with U.S.-born Japanese women. This may, in part, explain why the effect of foreign-birth on lung cancer is highest among Japanese women.¹⁷ With the exception of Japanese women, the inverse relationship between smoking and acculturation among Asian men and women has been reported elsewhere.¹⁸ Yet foreign-born Asian women have substantially higher rates of NSCLC than U.S.-born women, suggesting that the increased rate of NSCLC among foreign-born Asian women is likely not completely attributable to personal history of cigarette smoking. Specifically, foreign-born Asian women have a higher rate of adenocarcinoma and squamous cell carcinoma, the two dominant histologies of NSCLC. Although both adenocarcinoma and squamous cell carcinoma are tobacco associated, squamous cell carcinoma is less common among never-smokers. These findings suggest that the increased rate of lung cancers among foreign-born Asian women may be related to environmental tobacco exposure, given that smoking prevalence is higher among foreign-born Asian men compared with U.S.-born Asian men. Other exposures that have been previously associated with a moderately increased risk of lung cancer among Chinese female nonsmokers in Asia include cooking oil vapors, indoor coal burning, fungal infection, and tuberculosis.^{3,4} Investigation of the specific exposures responsible for the relatively high rates of lung cancer among U.S. Asian women, particularly notable given their low smoking rates, is needed.

Exposures other than tobacco smoke may also play a role in the low rate of lung cancer among South Asians. Although the prevalence of cigarette smoking in South Asians is about half that of other Asian subgroups, rates of NSCLC are still lower than those in subgroups with comparable cigarette smoking prevalences.¹⁹ Meanwhile, the incidence rate of NSCLC among U.S.-born South Asian men is more than double the rate among foreign-born South Asian men, whereas that among U.S.-born South Asian women is more than triple the rate seen among foreign-born South Asian women, despite similar tobacco exposure. There are several potential explanations for this finding. First, foreign-born South Asians are more likely to use Indian tobacco products, such as gutka (chewable flavored tobacco), bidis (shredded tobacco wrapped in tendu leaves which are smoked), and snuff. These products may not increase the risk of lung cancer to the same degree as cigarettes do, and their use may also lead to the consumption of fewer Western cigarettes daily.^{15,20} In addition, other environmental exposures such as dietary habits that are specific to South Asian cultures may be protective for lung cancer and warrant further study. Genetic factors that are protective against NSCLC are also possible, but seem less likely to play a protective role in this population given the much higher rate of NSCLC with acculturation. Epidemiologic studies with detailed individual-level exposure information may be useful to identify exposures associated with lung cancer risk modification among

U.S.-born and foreign-born South Asians given the large difference in NSCLC rates seen with acculturation in this population.

Despite similar smoking prevalences, incidence rates of NSCLC are still lower among Asian men compared with white men; this finding is suggestive of differences in lung cancer susceptibility, racial/ethnic differences in tobacco metabolism, or differences in tobacco use among smokers. A recent study in the prospective, population-based multiethnic cohort revealed that Japanese Americans had lower tobacco-adjusted incidence rates of lung cancer compared with whites, suggesting that genetic and/or environmental factors are protective for lung cancer among Japanese.²¹ Genetic polymorphisms and mutations modifying susceptibility to lung cancer may, in part, account for the lower incidence rate of lung cancer of Asians compared with whites. Several investigators have reported increased odds of lung cancer among Asians with polymorphisms in genes responsible for enzymatic inactivation of carcinogens.²²⁻²⁶ The relative importance of specific polymorphisms in lung cancer development and the prevalence and roles of these polymorphisms among the Asian ethnic groups is not known and deserves further study.

This is the largest study of the descriptive epidemiology of NSCLC in U.S. Asians reported to date. Nevertheless, certain limitations are worthy of mention. The CCR lacks information on smoking status among cancer cases; therefore, we were unable to calculate NSCLC incidence rates directly stratified by or adjusted for smoking status. The lack of individual-level smoking data limits our conclusions of the relative effects of cigarette smoking relative to other exposures on NSCLC risk. Moreover, the prevalence of current or ever smoking may not accurately reflect the number of cigarettes smoked over a lifetime, which may vary among ethnic subgroups.¹⁸

Despite these limitations, population-based cancer surveillance data, used in conjunction with population risk factor survey data, is a powerful way to generate clues about cancer etiology. In this case, we found several notable patterns of lung cancer by nativity among U.S. Asian subgroups. The most interesting pattern is the paradoxical relationship between foreign birthplace (which was associated with a lower prevalence of cigarette smoking) and a higher rate of NSCLC among Asian women. Epplein et al.²⁷ computed smoking-adjusted lung cancer incidence rates among Asians in two urban California Surveillance Epidemiology and End Results (SEER) regions and the Seattle-Puget Sound region using smoking prevalence data for the state of California reported through a 1991-1992 California Department of Health Services survey on tobacco use. Similar to our correlational analyses, their analysis showed a large discrepancy between smoking prevalence and lung cancer rates among Chinese women; we were able to show that this relationship was particularly notable among foreign-born Asian women.

This study is the first to our knowledge to incorporate nativity information in the population-based analysis of the descriptive epidemiology of lung cancer among Asians. This analysis was made possible through use of the CCR data, for

which there are relatively large numbers of Asians, and relatively complete birthplace data. Because previous research suggests that registry birthplace incompleteness is not random,²⁸ we used a novel imputation method based on SSNs to fill-in nativity for patients missing the information. Although based on the largest numbers of lung cancer cases available in any published work to-date, our study was still limited by small numbers of cases among less populous Asian subgroups. Specifically, there were relatively few U.S.-born Korean, Vietnamese, and South Asians with lung cancer, resulting in unstable estimates of incidence rates in subgroups defined by sex-nativity and histologic subtype. Although larger population-based registries such as the 18 combined SEER registries contain more Asian patients with lung cancer than the CCR alone, information on nativity is absent in approximately 28% of Asians in SEER, and SSNs are not readily available for imputation. Furthermore, most other registries lack intra- and extracensal population estimates by Asian subgroup, sex, and nativity, precluding estimation of rates and examination of trends, stratified by these characteristics.

In conclusion, Asians living in the United States are a diverse population with different environmental exposures that may in turn be responsible for differences in NSCLC incidence rates. More studies with individual-level survey data are needed to identify the specific environmental agents associated with differential lung cancer risk occurring with acculturation among Asians, especially among Chinese women and South Asians. Identification of such risk factors may lead to more successful primary prevention of lung cancer. Moreover, additional studies of lung cancer in a diverse populations, including bio-specimen collection are crucial to understanding the interactions between genetic susceptibility, environmental exposures, and tumor genetics on lung cancer development, treatment, and outcomes.

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