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# Lymphoid Malignancies in U.S. Asians: Incidence Rate Differences by Birthplace and Acculturation

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## Abstract

**Background:** Malignancies of the lymphoid cells, including non-Hodgkin lymphomas (NHL), HL, and multiple myeloma, occur at much lower rates in Asians than other racial/ethnic groups in the United States. It remains unclear whether these deficits are explained by genetic or environmental factors. To better understand environmental contributions, we examined incidence patterns of lymphoid malignancies among populations characterized by ethnicity, birthplace, and residential neighborhood socioeconomic status (SES) and ethnic enclave status.

**Methods:** We obtained data about all Asian patients diagnosed with lymphoid malignancies between 1988 and 2004 from the California Cancer Registry and neighborhood characteristics from U.S. Census data.

**Results:** Although incidence rates of most lymphoid malignancies were lower among Asian than white populations, only follicular lymphoma (FL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and nodular sclerosis (NS) HL rates were statistically significantly lower among foreign-born than U.S.-born Asians with incidence rate ratios ranging from 0.34 to 0.87. Rates of CLL/SLL and NS HL were also lower among Asian women living in ethnic enclaves or lower SES neighborhoods than those living elsewhere.

**Conclusions:** These observations support strong roles of environmental factors in the causation of FL, CLL/SLL, and NS HL.

**Impact:** Studying specific lymphoid malignancies in U.S. Asians may provide valuable insight toward understanding their environmental causes. *Cancer Epidemiol Biomarkers Prev; 20(6); 1064–77. ©2011 AACR.*

## Introduction

Malignancies of the lymphoid cells, including non-Hodgkin lymphomas (NHL), HL, and multiple myeloma (MM), are highly heterogeneous with respect to clinical features and patterns of occurrence (1). Despite this variation, U.S. populations of Asian origin consistently have much lower incidence rates of lymphoid malignancies than populations of Caucasian or African origin (2). In our recent assessment of lymphoid malignancies in the United States, overall incidence rates were substantially lower among Filipinos (67% of non-Hispanic white rate), South Asians (64%), Vietnamese (62%), Japanese (53%), Chinese (47%), and Koreans (33%) than among non-Hispanic whites (2). These striking differences may contain important clues about genetic or environmental risk factors for these diseases, especially whether incidence rates change with migration from low-risk (e.g., Asia) to higher risk areas (e.g., United States).

Unfortunately, cancer incidence rates according to measures of migration or acculturation cannot be readily calculated. Although patient's birthplace is collected by cancer registries, it is missing in a biased manner for a substantial proportion of patients (3–6), and the birthplace-specific annual population counts needed for rate denominators are not readily available from governmental agencies. Measures of immigrant acculturation (e.g., years since migration, language used at home) are not collected at all by cancer registries. To surmount these challenges, we have developed a resource (7) incorporating cancer registry data from California and population data needed to calculate cancer incidence rates among U.S. Asians by birthplace and 2 residential neighborhood measures of acculturation: socioeconomic status (SES) and ethnic enclave status. By using this resource, we examined variation in incidence rates of lymphoid malignancies among U.S. Asians by these factors.

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## Materials and Methods

### Cancer data for rate numerators

From the California Cancer Registry (CCR), which comprises 3 of the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program registries (8), we obtained information on all California residents diagnosed with a primary invasive lymphoid malignancy [International Classification of Disease for Oncology, 3rd Edition, (ICD-O-3) morphology codes 9590–9591, 9650–9655, 9661–9734, 9761, 9764, 9823, 9827–9837, 9940, 9948, and 9970] during the period 1 January 1988 to 31 December 2004. By using InterLymph Consortium guidelines (9, 10), we further classified lymphoid malignancies by histologic subtype into diffuse large B-cell lymphoma (DLBCL; ICD-O-3 morphology codes 9680 and 9684, excluding those with code 9684 and a T-cell, NK-cell, or null-cell immunophenotype); follicular lymphoma (FL; codes 9690, 9691, 9695, and 9698); chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; codes 9823 and 9670); MM (codes 9731–9734); classical HL (codes 9650–9655 and 9661–9667) and its 2 most common subtypes, nodular sclerosis (NS) HL (codes 9663–9665 and 9667) and mixed cellularity (MC) HL (code 9652); and T- or NK-cell NHL (TCL; codes 9700–9719, 9729, 9827, 9831, 9834, 9837, and 9948 plus codes 9590, 9591, 9675, 9684, 9727, 9820, 9832, 9835, or 9970 and a T-cell or NK cell immunophenotype). Overall NHL was categorized as including codes 9590–9591, 9670–9729, 9761, 9764, 9820, 9823, 9827, 9831–9837, 9940, 9948, and 9970.

### Incidence rates by birthplace

We included in these analyses 8,638 lymphoid malignancies (6,712 NHL, 526 NHL, and 1,410 MM) occurring in patients from the 6 Asian ethnic populations that together comprised 92% of all Asian and Pacific Islander patients with lymphoid malignancies in the CCR in the study period. Of these, 2,385 (28%) cases were Chinese, 1,246 (14%) Japanese, 2,913 (34%) Filipino, 506 (6%) Korean, 701 (8%) South Asian (including Asian Indians, Pakistanis, Sri Lankans, and Bangladeshis), and 887 (10%) Vietnamese. Approximately 5% of patients were originally coded in the registry data as "Asian, not otherwise specified;" for 55% of these patients, we could determine a more specific Asian ethnic designation on the basis of birthplace and names (first, maiden, and last) by applying the North American Association of Central Cancer Registries Asian/Pacific Islander Identification Algorithm (11). We also included as a reference group 110,789 non-Hispanic white patients diagnosed with lymphoid malignancies (85,465 NHL, 8,967 HL, and 16,357 MM) during the same period.

Because patients in the cancer registry with unknown birthplace data are more likely to be U.S. born than those with available data (3–6), we developed a method on the basis of patients' social security numbers (SSN) to more accurately classify patient immigrant status, as described previously (7). Briefly, we used: (i) registry-based birthplace data available for 81% of cases (73% from hospital medical records and 8% from death certificates) and (ii) for the 19% of cases with unknown birthplace, statistical imputation of immigrant status by using the patient's SSN. By comparing the age of SSN issue with self-reported birthplace in previously interviewed cancer patients ($n = 1{,}836$) and based on maximization of the area under the receiver operating characteristic curve and confirmation with logistic regression modeling, we considered cases who received an SSN before age 25 years U.S. born, and those who had received an SSN at or after age 25 years as foreign born. This age cut point resulted in 84% sensitivity and 80% specificity for assigning foreign-born status across the Asian populations. Fewer than 3% of cases with missing or invalid SSNs were assigned an immigrant status on the basis of the ethnicity–sex–age birthplace distribution of the overall sample.

### Incidence rates by neighborhood socioeconomic and ethnic enclave status

By using patient residential address and small-area (census tract) information from the U.S. Census, we classified neighborhood SES and ethnic enclave status for all Asian patients diagnosed between 1 January 1998 and 31 December 2002. We considered all Asians together as a single group because detailed ethnicity-specific population estimates are not available for census tracts and chose the time period in question (i.e., within 2 years of the 2000 U.S. Census) because census tract estimates are only available for decennial census years. Census tracts were geocoded from patient residential address at time of diagnosis. A total of 3% of eligible cases whose address could not be precisely geocoded to a census tract were randomly assigned to a census tract within their county of residence. We assigned neighborhood SES by using a previously described index (12) that incorporates 2,000 census data on education, income, occupation, and housing costs. We categorized this measure by quintiles on the basis of the distribution of the composite SES index across the state of California, then recategorized into 2 groups because of small sample sizes in the quintiles: lower SES (quintiles 1–3) or higher SES (quintiles 4 and 5). Because the CCR does not collect any individual-level information on patient SES, we could not assess neighborhood-level effects separately from those at the individual level.

We defined a neighborhood ethnic enclave as a geographical unit that is relatively more concentrated in terms of its population and language (in this study specific to Asians) than other geographical units in California. To characterize residence in an ethnic enclave, we applied principal components analysis (13) to selected census variables at the block group level, which was, in turn, averaged to the census tract level. The census variables included in the ethnic enclave index were: percent of Asian language speaking households that are linguistically isolated, percent of all Asian language speakers

who speak limited English, percent of recent immigrants, and percent of Asian. This index explained 63% of the variability in the data. Neighborhood ethnic enclave was classified into quintiles on the basis of the distribution of the composite ethnic enclave index across the state of California, then recategorized into 2 groups because of small sample sizes in the quintiles: lower (quintiles 1–3) or higher (quintiles 4 and 5) enclave status.

### Population data for cancer rate denominators

From the 1990 and 2000 Census Summary File 3, we obtained population counts by sex, race/ethnicity, immigrant status, and 5-year age group for the state of California. We also used data from the 20% integrated public use microdata sample of the census to estimate age- and birthplace-specific population counts for the 6 Asian groups (14–17) by smoothing with a spline-based function (18). For intercensal years, we estimated the percent of foreign born by using cohort component interpolation and extrapolation methods (19), adjusting estimates to the populations by age and year provided by the California Department of Finance for years 1988 to 1989 and the U.S. Census for years 1990 to 2004 due to data availability.

### Statistical analysis

We used SEER*Stat Software (20) to compute age-adjusted incidence rates (standardized to the 2,000 U.S. standard million population) and 95% CIs. To comply with CCR regulations, we do not present case counts or rates based on fewer than 15 cases. For HL, we also calculated age-adjusted rates for persons ages 15 to 44 ($n = 159$ men and 153 women) and 45 and above ($n = 110$ men and 70 women) at diagnosis because of strong previous evidence of etiologic differences between these groups (21). We calculated incidence rate ratios (IRR) to compare incidence rates. Because of small case numbers, Asian ethnic groups were combined for analyses of NHL subtypes, MM, and HL, and analyses of HL rates jointly by SES and enclave could not be undertaken by age group. We could not carry out joint analyses by birthplace and neighborhood SES or ethnic enclave status due to the lack of census-tract-level population data by birthplace. All analyses had the approval of the Institutional Review Board of the Cancer Prevention Institute of California, Fremont, CA.

## Results

Among the 8,638 Asians diagnosed with a lymphoid malignancy in California in the years 1988 to 2004, the majority (75%) were foreign born, although this proportion was much lower for Japanese (32%; Table 1). Among histologic subtypes of NHL, the most common among Asians was DLBCL ($n = 2,345$, 35% of all NHL), followed by TCL ($n = 721$, 11%), FL ($n = 661$, 10%), and CLL/SLL ($n = 560$, 8%); by comparison, non-Hispanic whites had higher proportions of FL, CLL/SLL, and a lower proportion of TCL. A total of 1,410 Asians were diagnosed with MM and 516 with HL, including 322 (62%) with NS HL and 96 (19%) with MC HL.

### Lymphoid malignancy incidence among Asians as compared with whites

For NHL overall, age-adjusted incidence rates for most Asian ethnic groups were substantially lower than those for non-Hispanic whites (Table 2). For example, the IRR among foreign-born Filipino men versus white men was 0.70 (95% CI: 0.65–0.75) and the corresponding IRR for women was 0.76 (95% CI: 0.70–0.83); the IRR among foreign-born Chinese men versus white men was 0.49 (95% CI: 0.44–0.54); and the corresponding IRR among women was 0.50 (95% CI: 0.45–0.55). The only groups for which rates were not significantly different from those of non-Hispanic whites were the relatively small populations of foreign-born Japanese men and U.S.-born South Asian and Vietnamese men and women.

For most specific lymphoid malignancy subtypes, incidence rates for both U.S.- and foreign-born Asians were lower than those for non-Hispanic whites. The most marked deficits were observed for CLL/SLL (among men, IRR for foreign-born Asians versus whites = 0.22, 95% CI: 0.18–0.25; among women, IRR = 0.24, 95% CI: 0.18–0.30) and NS HL (among men, IRR for foreign-born Asians versus whites = 0.25, 95% CI: 0.13–0.37; among men, IRR = 0.19, 95% CI: 0.13–0.26). However, for TCL and DLBCL (in most ethnic groups), rates were comparable to those for non-Hispanic whites.

### Lymphoid malignancy incidence among Asians by birthplace

For overall NHL, foreign-born Chinese, South Asian, and Vietnamese men and women had consistently lower incidence rates than their U.S.-born counterparts (Table 2). By contrast, foreign-born Japanese men had incidence rates 71% higher than their U.S.-born counterparts, whereas no birthplace difference was observed among Japanese women or Korean men or women.

For specific subtypes, Table 3 shows that FL incidence was consistently lower among foreign-born than U.S.-born Asian men and women. For DLBCL, for which numbers of cases were adequate for examining rates for Chinese and Japanese, patterns were similar to those observed for overall NHL, with lower incidence rates for foreign-born versus U.S.-born Chinese men and women, in contrast to higher rates among foreign-born versus U.S.-born Japanese men. Among Japanese and other Asian (Filipina, South Asian, and Vietnamese) women, there were no significant differences in the incidence rate of DLBCL by birthplace. Incidence rates of TCL did not vary by birthplace among Asian men or women. For MM, rates were marginally higher (37%) among foreign-born than U.S.-born Asian women, but comparable by birthplace in men.

For overall HL, rates among foreign-born Asians were approximately half those among U.S.-born Asians. IRR

**Table 1.** Demographic and disease characteristics of Asian and non-Hispanic white patients diagnosed with lymphoid malignancies, California, 1988–2004

| Characteristic | Chinese | | Japanese | | Filipino | | Korean | | South Asian | | Vietnamese | | All Asian | | Non-Hispanic white | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age at diagnosis, y | | | | | | | | | | | | | | | | |
| 0–29 | 272 | 11% | 58 | 5% | 285 | 10% | 79 | 16% | 131 | 19% | 165 | 19% | 990 | 11% | 7,455 | 7% |
| 30–49 | 381 | 16% | 141 | 11% | 467 | 16% | 97 | 19% | 147 | 21% | 195 | 22% | 1,428 | 17% | 17,158 | 15% |
| 50–69 | 801 | 34% | 433 | 35% | 1,009 | 35% | 173 | 34% | 264 | 38% | 299 | 34% | 2,979 | 34% | 36,730 | 33% |
| 70+ | 931 | 39% | 614 | 49% | 1,152 | 40% | 157 | 31% | 159 | 23% | 228 | 26% | 3,241 | 38% | 49,446 | 45% |
| Sex | | | | | | | | | | | | | | | | |
| Men | 1,359 | 57% | 642 | 52% | 1,572 | 54% | 278 | 55% | 419 | 60% | 485 | 55% | 4,755 | 55% | 62,674 | 57% |
| Women | 1,026 | *43%* | 604 | 48% | 1,341 | 46% | 228 | 45% | 282 | 40% | 402 | 45% | 3,883 | 45% | 48,115 | 43% |
| Nativity | | | | | | | | | | | | | | | | |
| U.S. born | 620 | 26% | 850 | 68% | 355 | 12% | 72 | 14% | 134 | 19% | 112 | 13% | 2,143 | 25% | — | — |
| Foreign born | 1,765 | 74% | 396 | 32% | 2,558 | 88% | 434 | 86% | 567 | 81% | 775 | 87% | 6,495 | 75% | — | — |
| Tumor histology | | | | | | | | | | | | | | | | |
| DLBCL | 621 | 26% | 366 | 29% | 845 | 29% | 131 | 26% | 118 | 17% | 264 | 30% | 2,345 | 27% | 21,920 | 20% |
| FL | 225 | 9% | 142 | 11% | 147 | 5% | 29 | 6% | 51 | 7% | 67 | 8% | 661 | 8% | 12,027 | 11% |
| CLL/SLL | 183 | 8% | 82 | 7% | 156 | 5% | 23 | 5% | 69 | 10% | 47 | 5% | 560 | 6% | 18,973 | 17% |
| T-cell lymphoma | 207 | 9% | 88 | 7% | 212 | 7% | 58 | 11% | 65 | 9% | 91 | 10% | 721 | 8% | 5,454 | 5% |
| Other NHL | 682 | 29% | 352 | 28% | 789 | 27% | 159 | 31% | 192 | 27% | 251 | 28% | 2,425 | 28% | 27,091 | 24% |
| MM | 342 | 14% | 170 | 14% | 575 | 20% | 85 | 17% | 123 | 18% | 115 | 13% | 1,410 | 16% | 16,357 | 15% |
| Overall HL | 125 | 5% | 46 | 4% | 189 | 6% | 21 | 4% | 83 | 12% | 52 | 6% | 516 | 6% | 8,967 | 8% |
| NS HL | 76 | 3% | 27 | 2% | 122 | 4% | 13 | 3% | 51 | 7% | 33 | 4% | 322 | 4% | 5,808 | 5% |
| MC HL | 28 | 1% | 8 | 1% | 31 | 1% | 2 | 0% | 16 | 2% | 11 | 1% | 96 | 1% | 1,532 | 1% |
| Other classical HL | 21 | 1% | 11 | 1% | 36 | 1% | 6 | 1% | 16 | 2% | 8 | 1% | 98 | 1% | 1,627 | 1% |
| Total | 2,385 | | 1,246 | | 2,913 | | 506 | | 701 | | 887 | | 8,638 | | 110,789 | |

**Table 2.** Age-adjusted incidence rates (per 100,000 person-years) of overall NHL and incidence rate ratios (IRRs) by nativity among Asians and non-Hispanic whites, California, 1988–2004

| Ethnic group | Nativity | Men | | | | |
|---|---|---|---|---|---|---|
| | | Cases (*n*) | Incidence rate | 95% CI | IRR | 95% CI |
| Chinese | U.S. born | 320 | 30.6 | (26.7–34.8) | 1.00 | reference |
| | Foreign born | 775 | 16.9 | (15.2–18.7) | **0.55** | **(0.47–0.65)** |
| Japanese | U.S. born | 396 | 18.1 | (16.3–20.1) | 1.00 | reference |
| | Foreign born | 130 | 30.9 | (25.1–37.6) | **1.71** | **(1.35–2.14)** |
| Filipino | U.S. born | 156 | 23.3 | (18.0–29.6) | 1.00 | reference |
| | Foreign born | 1,026 | 24.1 | (22.3–26.0) | 1.03 | (0.8–1.36) |
| Korean | U.S. born | 36 | 16.8 | (7.0–32.4) | 1.00 | reference |
| | Foreign born | 188 | 12.7 | (10.7–15.1) | 0.76 | (0.38–1.84) |
| South Asian | U.S. born | 58 | 46.9 | (27.7–73.1) | 1.00 | reference |
| | Foreign born | 244 | 20.1 | (17.1–23.4) | **0.43** | **(0.27–0.74)** |
| Vietnamese | U.S. born | 50 | 66.3 | (36.1–109.5) | 1.00 | reference |
| | Foreign born | 350 | 19.3 | (16.9–22.0) | **0.29** | **(0.17–0.54)** |
| Non-Hispanic white | | 48,816 | 34.5 | (34.2–34.8) | — | — |
| | | **Women** | | | | |
| **Asian ethnic group** | **Nativity** | **Cases (*n*)** | **Incidence rate** | **95% CI** | **IRR** | **95% CI** |
| Chinese | U.S. born | 195 | 15.5 | (13.1–18.1) | 1.00 | reference |
| | Foreign born | 628 | 10.4 | (9.5–11.4) | **0.67** | **(0.56–0.81)** |
| Japanese | U.S. born | 298 | 13 | (11.5–14.7) | 1.00 | reference |
| | Foreign born | 206 | 14 | (12–16.4) | 1.08 | (0.88–1.32) |
| Filipino | U.S. born | 106 | 13.5 | (9.8–18.1) | 1.00 | reference |
| | Foreign born | 861 | 15.8 | (14.3–17.3) | 1.17 | (0.86–1.62) |
| Korean | U.S. born | 25 | 6.3 | (2.5–13.1) | 1.00 | reference |
| | Foreign born | 151 | 7.2 | (5.9–8.6) | 1.14 | (0.53–2.98) |
| South Asian | U.S. born | 37 | 35 | (18.6–58.4) | 1.00 | reference |
| | Foreign born | 156 | 14.3 | (11.8–17.2) | **0.41** | **(0.24–0.79)** |
| Vietnamese | U.S. born | 39 | 34.9 | (17.3–62.7) | 1.00 | reference |
| | Foreign born | 281 | 14.8 | (13–16.9) | **0.42** | **(0.23–0.87)** |
| Non-Hispanic white | | 36,649 | 20.7 | (20.5–20.9) | — | — |

patterns were similar for NS HL, but no nativity differences occurred in rates of MC HL. In data stratified by age, the protective effect of foreign birthplace was limited to young adults of both genders for HL overall; for NS HL, it was apparent for both younger and older women [IRRs of 0.34 (95% CI: 0.23–0.50) for ages 15 to 44 and 0.32 (95% CI: 0.14–0.80) for ages 45 and above].

Although we had limited statistical power to assess rate changes over time stratified by birthplace, rates did not vary significantly between the periods 1988 to 1996 and 1997 to 2004 (data not shown). For overall NHL, rates increased significantly among U.S.-born Chinese and Filipino men and foreign-born Korean men, but not among women of the same groups. IRRs comparing foreign-born versus U.S.-born Asians were generally similar between 1988 to 1996 and 1997 to 2004, although for overall HL and NS HL, they were statistically significant only in the latter period (data not shown).

### Lymphoid malignancies by neighborhood ethnic enclave and SES

Among Asian men, ethnic enclave status did not impact the incidence rates of overall NHL, DLBCL, FL, CLL/SLL, TCL, MM, overall HL, NS HL, or MC HL (Table 4). By contrast, among Asian women, overall NHL, CLL/SLL, overall HL, and MC HL were significantly less common in neighborhoods with higher ethnic enclave status. For HL, these patterns did not differ by age group for either gender. Asian men living in higher SES neighborhoods had significantly elevated incidence rates of FL and NS HL (an effect limited to young adult men), but not of other lymphoma subtypes. Asian women in higher SES neighborhoods had significantly higher incidence rates of FL, TCL, and overall HL (apparent only for women older than 45 at diagnosis); marginally higher rates of NS HL and MC HL; but lower rates of CLL/SLL.

**Table 3.** Age-adjusted incidence rates (per 100,000 person-years) of NHL histologic subtypes, MM, HL subtypes, and IRRs by nativity among Asians and non-Hispanic whites, California, 1988–2004

| | | | Men | | | | |
|---|---|---|---|---|---|---|---|
| **Lymphoid malignancy** | **Ethnic group** | **Nativity** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| DLBCL | All Asians | U.S. born | 314 | 8.5 | (7.5–9.5) | 1.00 | reference |
| | | Foreign born | 961 | 6.5 | (6.1–7.0) | **0.77** | **(0.67–0.88)** |
| | Chinese | U.S. born | 96 | 10.9 | (8.6–13.6) | 1.00 | reference |
| | | Foreign born | 257 | 4.7 | (4.1–5.4) | **0.43** | **(0.33–0.57)** |
| | Japanese | U.S. born | 149 | 6.7 | (5.6–8.0) | 1.00 | reference |
| | | Foreign born | 49 | 11.5 | (8.0–15.7) | **1.71** | **(1.14–2.46)** |
| | Other Asian | U.S. born | 69 | 8.8 | (6.3–11.8) | 1.00 | reference |
| | | Foreign born | 655 | 7.4 | (6.8–8.1) | 0.85 | (0.62–1.20) |
| | Non-Hispanic white | | 12,636 | 8.8 | (8.7–9.0) | — | — |
| FL | All Asians | U.S. born | 96 | 2.7 | (2.1–3.3) | 1.00 | reference |
| | | Foreign born | 244 | 1.5 | (1.3–1.7) | **0.57** | **(0.44–0.73)** |
| | Non-Hispanic white | | 5,981 | 4.1 | (4.0–4.2) | **—** | **—** |
| CLL/SLL | All Asians | U.S. born | 81 | 2.4 | (1.9–2.9) | 1.00 | reference |
| | | Foreign born | 249 | 1.7 | (1.5–1.9) | **0.72** | **(0.56–0.95)** |
| | Non-Hispanic white | | 11,094 | 7.9 | (7.8–8.1) | **—** | **—** |
| T-cell lymphoma | All Asians | U.S. born | 122 | 2.2 | (1.8–2.7) | 1.00 | reference |
| | | Foreign born | 305 | 2.0 | (1.8–2.3) | 0.91 | (0.71–1.18) |
| | Non-Hispanic white | | 3,348 | 2.4 | (2.3–2.5) | — | — |
| MM | All Asians | U.S. born | 128 | 3.8 | (3.2–4.5) | 1.00 | reference |
| | | Foreign born | 614 | 4.3 | (4.0–4.7) | 1.14 | (0.94–1.41) |
| | Non-Hispanic white | | 8,929 | 6.4 | (6.2–6.5) | — | — |
| Overall HL | All Asians | U.S. born | 105 | 1.8 | (1.4–2.2) | 1.00 | Reference |
| | | Foreign born | 179 | 1.1 | (0.9–1.2) | **0.60** | **(0.46–0.80)** |
| | Non-Hispanic white | | 4,929 | 3.4 | (3.3–3.5) | — | — |
| HL, age <45 y | All Asians | U.S. born | 82 | 1.7 | (1.3–2.2) | 1.00 | Reference |
| | | Foreign born | 92 | 0.7 | (0.6–1.0) | **0.43** | **(0.30–0.63)** |
| | Non-Hispanic white | | 3,010 | 3.2 | (3.1–3.3) | — | — |
| HL, age 45+ y | All Asians | U.S. born | 23 | 1.8 | (1.1–2.7) | 1.00 | Reference |
| | | Foreign born | 87 | 1.6 | (1.3–2.0) | 0.90 | (0.55–1.51) |
| | Non-Hispanic white | | 1,919 | 3.8 | (3.7–4.0) | — | — |
| HL, NS | All Asians | U.S. born | 64 | 1.0 | (0.8–1.4) | 1.00 | reference |
| | | Foreign born | 92 | 0.5 | (0.4–0.7) | **0.53** | **(0.36–0.79)** |
| | Non-Hispanic white | | 2,900 | 2.0 | (1.9–2.1) | **—** | **—** |
| HL, MC | All Asians | U.S. born | 15 | 0.3 | (0.2–0.5) | 1.00 | reference |
| | | Foreign born | 47 | 0.3 | (0.2–0.4) | 0.90 | (0.48–1.86) |
| | Non-Hispanic white | | 1,001 | 0.7 | (0.7–0.7) | — | — |
| | | | **Women** | | | | |
| **Lymphoid malignancy** | **Asian ethnic group** | **Nativity** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| DLBCL | All Asians | U.S. born | 198 | 4.6 | (4.0–5.4) | 1.00 | reference |
| | | Foreign born | 872 | 4.7 | (4.4–5.0) | 1.01 | (0.86–1.19) |
| | Chinese | U.S. born | 49 | 4.5 | (3.3–6.0) | 1.00 | reference |
| | | Foreign born | 219 | 3.6 | (3.1–4.1) | 0.80 | (0.58–1.14) |
| | Japanese | U.S. born | 107 | 4.4 | (3.5–5.3) | 1.00 | reference |
| | | Foreign born | 61 | 4.1 | (3.0–5.4) | 0.94 | (0.65–1.34) |
| | Other Asian | U.S. born | 42 | 5.1 | (3.3–7.4) | 1.00 | reference |
| | | Foreign born | 592 | 5.5 | (5.0–5.9) | 1.07 | (0.73–1.66) |
| | Non-Hispanic white | | 9,284 | 5.2 | (5.1–5.3) | — | — |

*(Continued on the following page)*

**Table 3.** Age-adjusted incidence rates (per 100,000 person-years) of NHL histologic subtypes, MM, HL subtypes, and IRRs by nativity among Asians and non-Hispanic whites, California, 1988–2004 (Cont'd)

| | | | Women | | | | |
|---|---|---|---|---|---|---|---|
| **Lymphoid malignancy** | **Asian ethnic group** | **Nativity** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| FL | All Asians | U.S. born | 77 | 2.0 | (1.5–2.5) | 1.00 | reference |
| | | Foreign born | 244 | 1.2 | (1.0–1.4) | **0.61** | **(0.47–0.81)** |
| | Non-Hispanic white | | 6,046 | 3.5 | (3.4–3.6) | — | — |
| CLL/SLL | All Asians | U.S. born | 44 | 1.2 | (0.8–1.6) | 1.00 | reference |
| | | Foreign born | 186 | 1.0 | (0.9–1.2) | **0.87** | **(0.56–0.95)** |
| | Non-Hispanic white | | 7,879 | 4.2 | (4.1–4.3) | — | — |
| T-cell lymphoma | All Asians | U.S. born | 77 | 1.5 | (1.1–1.9) | 1.00 | reference |
| | | Foreign born | 217 | 1.1 | (1.0–1.3) | 0.75 | (0.56–1.03) |
| | Non-Hispanic white | | 2,106 | 1.3 | (1.2–1.3) | — | — |
| MM | All Asians | U.S. born | 87 | 2.3 | (1.8–2.9) | 1.00 | reference |
| | | Foreign born | 581 | 3.2 | (2.9–3.5) | **1.37** | **(1.09–1.75)** |
| | Non-Hispanic white | | 7,428 | 4.0 | (3.9–4.1) | — | — |
| Overall HL | All Asians | U.S. born | 107 | 1.6 | (1.2–1.9) | 1.00 | Reference |
| | | Foreign born | 125 | 0.6 | (0.5–0.7) | **0.38** | **(0.28–0.52)** |
| | Non-Hispanic white | | 4,038 | 2.8 | (2.7–2.8) | — | — |
| HL, age <45 y | All Asians | U.S. born | 91 | 1.7 | (1.3–2.1) | 1.00 | Reference |
| | | Foreign born | 71 | 0.5 | (0.4–0.7) | **0.29** | **(0.20–0.43)** |
| | Non-Hispanic white | | 2,600 | 2.9 | (2.8–3.1) | — | — |
| HL, age 45+ y | All Asians | U.S. born | 16 | 1.3 | (0.7–2.1) | 1.00 | Reference |
| | | Foreign born | 54 | 0.8 | (0.6–1.0) | 0.60 | (0.34–1.14) |
| | Non-Hispanic white | | 1,438 | 2.4 | (2.3–2.5) | — | — |
| HL, NS | All Asians | U.S. born | 83 | 1.1 | (0.9–1.4) | 1.00 | reference |
| | | Foreign born | 83 | 0.4 | (0.3–0.5) | **0.34** | **(0.24–0.48)** |
| | Non-Hispanic white | | 2,908 | 2.1 | (2.0–2.1) | — | — |
| HL, MC | All Asians | U.S. born | 11 | — | — | 1.00 | reference |
| | | Foreign born | 23 | 0.1 | (0.1–0.2) | 0.64 | (0.28–1.67) |
| | Non-Hispanic white | | 531 | 0.3 | (0.3–0.4) | — | — |

[a]Standardized to the 2,000 U.S. population age standard. Incidence rates with numerator less than 15 are not computed.

When we analyzed rates by neighborhood ethnic enclave status and SES jointly, we found that Asian men living in areas with both lower ethnic enclave status and higher SES had significantly higher incidence rates of overall NHL and FL, and a marginally higher incidence rate of DLBCL, than Asian men living in areas with both higher enclave status and lower SES (Table 4). For overall HL and NS HL, rates were marginally higher for Asian men living in neighborhoods of higher than lower SES irrespective of their ethnic enclave status. Compared with Asian women living in neighborhoods with both higher ethnic enclave status and lower SES, Asian women living in neighborhoods with lower ethnic enclave status and higher SES also had significantly elevated incidence rates of overall NHL, FL, overall HL, and NS HL; elevations were particularly marked for the latter 2 (IRR = 4.1, 95% CI: 2.15–7.74, and 2.5, 95% CI: 1.17–5.14, respectively). In addition, Asian women who resided in neighborhoods with both higher ethnic enclave status and higher SES had elevated incidence rates of FL, TCL, and overall HL but a lower rate of CLL/SLL. MM incidence rates did not vary by neighborhood enclave status and SES among Asian men or women.

## Discussion

A role for environmental exposures in cancer etiology can be inferred from changes in cancer incidence after migration from low- to high-risk areas. In a large population–based series of U.S. Asians with lymphoid malignancies, we found that rates were substantially lower in foreign-born than U.S.-born patients for certain lymphoma subtypes, specifically CLL/SLL, FL, and NS HL. Rates of CLL/SLL and NS HL were also significantly lower among Asian women living in ethnic enclaves or lower SES neighborhoods than rates of Asian women living in lower enclave or higher SES neighborhoods, respectively. For HL, the risks associated with higher

**Table 4.** Age-adjusted incidence rates (per 100,000 person-years) of NHL and histologic subtypes, MM, and HL and histologic subtypes, and incidence rate ratios (IRRs) by neighborhood immigrant enclave status and SES among Asians, California, 1998–2002

| | | Men | | | | |
|---|---|---|---|---|---|---|
| **Lymphoid malignancy** | **Neighborhood characteristic** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| Overall NHL | Low enclave status | 343 | 22.6 | (20.2–25.2) | 1.00 | reference |
| | High enclave status | 1,139 | 20.6 | (19.4–21.9) | 0.91 | (0.80–1.04) |
| | Low SES | 715 | 20.2 | (18.7–21.7) | 1.00 | reference |
| | High SES | 767 | 22.1 | (20.4–23.8) | 1.09 | (0.98–1.22) |
| | High enclave status/low SES | 546 | 19.9 | (18.2–21.7) | 1.00 | reference |
| | Low enclave status/low SES | 169 | 20.7 | (17.6–24.2) | 1.04 | (0.87–1.24) |
| | High enclave status/high SES | 593 | 21.4 | (19.5–23.3) | 1.07 | (0.95–1.21) |
| | Low enclave status/high SES | 174 | 24.8 | (21.0–29.0) | **1.24** | **(1.03–1.49)** |
| DLBCL | Low enclave status | 112 | 7.6 | (6.2–9.2) | 1.00 | reference |
| | High enclave status | 374 | 7.0 | (6.2–7.7) | 0.92 | (0.74–1.16) |
| | Low SES | 235 | 6.7 | (5.9–7.7) | 1.00 | reference |
| | High SES | 251 | 7.6 | (6.6–8.6) | 1.12 | (0.93–1.36) |
| | High enclave status/low SES | 184 | 6.8 | (5.9–7.9) | 1.00 | reference |
| | Low enclave status/low SES | 51 | 6.4 | (4.7–8.5) | 0.94 | (0.67–1.29) |
| | High enclave status/high SES | 190 | 7.2 | (6.1–8.4) | 1.05 | (0.85–1.31) |
| | Low enclave status/high SES | 61 | 9.0 | (6.8–11.7) | 1.32 | (0.95–1.79) |
| FL | Low enclave status | 36 | 2.3 | (1.6–3.2) | 1.00 | reference |
| | High enclave status | 106 | 1.8 | (1.5–2.2) | 0.81 | (0.55–1.24) |
| | Low SES | 57 | 1.5 | (1.2–2.0) | 1.00 | reference |
| | High SES | 85 | 2.4 | (1.9–2.9) | **1.52** | **(1.06–2.19)** |
| | High enclave status/low SES | 48 | 1.7 | (1.2–2.2) | 1.00 | reference |
| | Low enclave status/low SES | 9 | — | | 0.62 | (0.27–1.29) |
| | High enclave status/high SES | 58 | 2.0 | (1.5–2.6) | 1.19 | (0.79–1.81) |
| | Low enclave status/high SES | 27 | 3.7 | (2.4–5.5) | **2.19** | **(1.29–3.64)** |
| CLL/SLL | | | | | | |
| | Low enclave status | 32 | 2.1 | (1.4–3.1) | 1.00 | reference |
| | High enclave status | 102 | 1.9 | (1.6–2.4) | 0.91 | (0.60–1.42) |
| | Low SES | 64 | 1.8 | (1.4–2.3) | 1.00 | reference |
| | High SES | 70 | 2.2 | (1.7–2.8) | 1.20 | (0.83–1.73) |
| | High enclave status/low SES | 46 | 1.7 | (1.2–2.3) | 1.00 | reference |
| | Low enclave status/low SES | 18 | 2.2 | (1.3–3.5) | 1.30 | (0.70–2.29) |
| | High enclave status/high SES | 56 | 2.2 | (1.6–2.9) | 1.30 | (0.85–1.99) |
| | Low enclave status/high SES | 14 | — | | 1.20 | (0.58–2.27) |
| T-cell lymphoma | Low enclave status | 37 | 2.2 | (1.5–3.1) | 1.00 | reference |
| | High enclave status | 148 | 2.5 | (2.1–2.9) | 1.13 | (0.77–1.71) |
| | Low SES | 87 | 2.3 | (1.8–2.8) | 1.00 | reference |
| | High SES | 98 | 2.6 | (2.1–3.2) | 1.13 | (0.82–1.54) |
| | High enclave status/low SES | 72 | 2.4 | (1.9–3.1) | 1.00 | reference |
| | Low enclave status/low SES | 15 | 1.7 | (0.9–2.8) | 0.69 | (0.36–1.23) |
| | High enclave status/high SES | 76 | 2.5 | (2.0–3.2) | 1.03 | (0.73–1.47) |
| | Low enclave status/high SES | 22 | 2.8 | (1.7–4.4) | 1.14 | (0.65, 1.92) |
| MM | Low enclave status | 62 | 4.4 | (3.3–5.7) | 1.00 | reference |
| | High enclave status | 202 | 3.8 | (3.3–4.4) | 0.87 | (0.65–1.19) |
| | Low SES | 137 | 4.0 | (3.3–4.7) | 1.00 | reference |
| | High SES | 127 | 3.9 | (3.2–4.6) | 0.97 | (0.75–1.25) |
| | High enclave status/low SES | 101 | 3.8 | (3.1–4.6) | 1.00 | reference |
| | Low enclave status/low SES | 36 | 4.8 | (3.3–6.6) | 1.26 | (0.83–1.86) |

*(Continued on the following page)*

**Table 4.** Age-adjusted incidence rates (per 100,000 person-years) of NHL and histologic subtypes, MM, and HL and histologic subtypes, and incidence rate ratios (IRRs) by neighborhood immigrant enclave status and SES among Asians, California, 1998–2002 (Cont'd)

| | | Men | | | | |
|---|---|---|---|---|---|---|
| **Lymphoid malignancy** | **Neighborhood characteristic** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| | High enclave status/high SES | 101 | 3.9 | (3.1–4.7) | 1.02 | (0.76–1.37) |
| | Low enclave status/high SES | 26 | 3.9 | (2.5–5.8) | 1.04 | (0.64–1.63) |
| Overall HL | Low enclave status | 27 | 1.5 | (1.0–2.2) | 1.00 | reference |
| | High enclave status | 84 | 1.2 | (0.9–1.5) | 0.79 | (0.50–1.28) |
| | Low SES | 42 | 1.0 | (0.7–1.4) | 1.00 | reference |
| | High SES | 69 | 1.5 | (1.1–1.9) | 1.46 | (0.98–2.23) |
| HL, age <45 y | Low enclave status | 12 | — | — | 1.00 | reference |
| | High enclave status | 56 | 1.1 | (0.8–1.4) | 1.19 | (0.63–2.45) |
| | Low SES | 21 | 0.7 | (0.4–1.0)) | 1.00 | reference |
| | High SES | 47 | 1.4 | (1.0–1.9) | **2.12** | **(1.24–3.75)** |
| HL, age 45+ y | Low enclave status | 15 | 2.6 | (1.4–4.3) | 1.00 | reference |
| | High enclave status | 28 | 1.4 | (0.9–2.0) | 0.53 | (0.27–1.09) |
| | Low SES | 21 | 1.6 | (1.0–2.5) | 1.00 | reference |
| | High SES | 22 | 1.6 | (1.0–2.5) | 0.96 | (0.50–1.89) |
| HL, NS | Low enclave status | 14 | — | — | 1.00 | reference |
| | High enclave status | 49 | 0.7 | (0.5–0.9) | 0.92 | (0.49–1.83) |
| | Low SES | 20 | 0.4 | (0.3–0.7) | 1.00 | reference |
| | High SES | 43 | 0.9 | (0.6–1.2) | **2.01** | **(1.14–3.66)** |
| HL, MC | Low enclave status | 6 | — | — | 1.00 | reference |
| | High enclave status | 16 | 0.2 | (0.1–0.4) | 0.67 | (0.24–2.13) |
| | Low SES | 12 | — | — | 1.00 | reference |
| | | **Women** | | | | |
| **Lymphoid malignancy** | **Neighborhood characteristic** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| Overall NHL | Low enclave status | 307 | 16.0 | (14.2–17.9) | 1.00 | reference |
| | High enclave status | 921 | 13.7 | (12.8–14.7) | **0.86** | **(0.75–0.98)** |
| | Low SES | 604 | 13.8 | (12.7–14.9) | 1.00 | reference |
| | High SES | 624 | 14.7 | (13.5–15.9) | 1.06 | (0.95–1.20) |
| | High enclave status/low SES | 442 | 13.2 | (12.0–14.5) | 1.00 | reference |
| | Low enclave status/low SES | 162 | 15.7 | (13.3–18.3) | 1.18 | (0.98–1.43) |
| | High enclave status/high SES | 479 | 14.2 | (12.9–15.6) | 1.08 | (0.94–1.23) |
| | Low enclave status/high SES | 145 | 16.5 | (13.8–19.5) | **1.24** | **(1.02–1.51)** |
| DLBCL | Low enclave status | 108 | 5.7 | (4.7–6.9) | 1.00 | reference |
| | High enclave status | 343 | 5.2 | (4.7–5.8) | 0.91 | (0.73–1.15) |
| | Low SES | 235 | 5.3 | (4.7–6.1) | 1.00 | reference |
| | High SES | 216 | 5.3 | (4.6–6.1) | 1.00 | (0.82–1.21) |
| | High enclave status/low SES | 169 | 5.0 | (4.3–5.8) | 1.00 | reference |
| | Low enclave status/low SES | 66 | 6.4 | (4.9–8.2) | 1.28 | (0.94–1.71) |
| | High enclave status/high SES | 174 | 5.5 | (4.7–6.4) | 1.09 | (0.87–1.36) |
| | Low enclave status/high SES | 42 | 4.9 | (3.5–6.7) | 0.98 | (0.67–1.39) |
| FL | Low enclave status | 32 | 1.6 | (1.1–2.2) | 1.00 | reference |
| | High enclave status | 88 | 1.2 | (1.0–1.5) | 0.80 | (0.53–1.25) |
| | Low SES | 44 | 1.0 | (0.7–1.3) | 1.00 | reference |
| | High SES | 76 | 1.7 | (1.3–2.1) | **1.71** | **(1.16–2.55)** |
| | High enclave status/low SES | 31 | 0.9 | (0.6–1.3) | 1.00 | reference |

*(Continued on the following page)*

**Table 4.** Age-adjusted incidence rates (per 100,000 person-years) of NHL and histologic subtypes, MM, and HL and histologic subtypes, and incidence rate ratios (IRRs) by neighborhood immigrant enclave status and SES among Asians, California, 1998–2002 (Cont'd)

| | | Women | | | | |
|---|---|---|---|---|---|---|
| **Lymphoid malignancy** | **Neighborhood characteristic** | **Cases (*n*)** | **Incidence rate[a]** | **95% CI** | **IRR** | **95% CI** |
| | Low enclave status/low SES | 13 | — | | 1.26 | (0.60-2.50) |
| | High enclave status/high SES | 57 | 1.6 | (1.2–2.0) | **1.71** | **(1.08–2.76)** |
| | Low enclave status/high SES | 19 | 2.1 | (1.2–3.3) | **2.25** | **(1.17–4.18)** |
| CLL/SLL | Low enclave status | 29 | 1.7 | (1.1–2.4) | 1.00 | reference |
| | High enclave status | 60 | 1.0 | (0.7–1.2) | **0.58** | **(0.36–0.95)** |
| | Low SES | 59 | 1.4 | (1.1–1.8) | 1.00 | reference |
| | High SES | 30 | 0.8 | (0.5–1.1) | **0.53** | **(0.33–0.85)** |
| | High enclave status/low SES | 39 | 1.2 | (0.9–1.7) | 1.00 | reference |
| | Low enclave status/low SES | 20 | 2.1 | (1.3–3.3) | 1.76 | (0.95–3.11) |
| | High enclave status/high SES | 21 | 0.7 | (0.4–1.0) | **0.55** | **(0.30–0.96)** |
| | Low enclave status/high SES | 9 | — | | 0.91 | (0.37–1.94) |
| T-cell lymphoma | Low enclave status | 25 | 1.2 | (0.8–1.8) | 1.00 | reference |
| | High enclave status | 104 | 1.4 | (1.2–1.8) | 1.22 | (0.77–2.00) |
| | Low SES | 52 | 1.1 | (0.8–1.5) | 1.00 | reference |
| | High SES | 77 | 1.7 | (1.3–2.1) | **1.45** | **(1.00–2.12)** |
| | High enclave status/low SES | 40 | 1.2 | (0.8–1.6) | 1.00 | reference |
| | Low enclave status/low SES | 12 | 1.1 | (0.6–1.9) | 0.95 | (0.44–1.87) |
| | High enclave status/high SES | 64 | 1.7 | (1.3–2.2) | 1.50 | (0.99–2.30) |
| | Low enclave status/high SES | **13** | — | | 1.18 | (0.56–2.29) |
| MM | Low enclave status | 63 | 3.2 | (2.5–4.1) | 1.00 | reference |
| | High enclave status | 211 | 3.3 | (2.9–3.8) | 1.03 | (0.77–1.40) |
| | Low SES | 150 | 3.5 | (2.9–4.1) | 1.00 | reference |
| | High SES | 125 | 3.2 | (2.6–3.8) | 0.92 | (0.72–1.18) |
| | High enclave status/low SES | 112 | 3.4 | (2.8–4.1) | 1.00 | reference |
| | Low enclave status/low SES | 38 | 3.6 | (2.5–5.0) | 1.06 | (0.71–1.56) |
| | High enclave status/high SES | 99 | 3.3 | (2.6–4.0) | 0.95 | (0.72–1.26) |
| | Low enclave status/high SES | 25 | 2.7 | (1.7–4.1) | 0.80 | (0.49–1.26) |
| Overall HL | Low enclave status | 41 | 2.0 | (1.4–2.7) | 1.00 | reference |
| | High enclave status | 68 | 0.9 | (0.7–1.1) | **0.44** | **(0.29–0.67)** |
| | Low SES | 40 | 0.8 | (0.6–1.1) | 1.00 | reference |
| | High SES | 69 | 1.4 | (1.1–1.8) | **1.71** | **(1.13–2.62)** |
| HL, age <45 y | Low enclave status | 28 | 1.9 | (1.2–2.7) | 1.00 | reference |
| | High enclave status | 50 | 0.9 | (0.7–1.2) | **0.50** | **(0.30–0.82)** |
| | Low SES | 32 | 1.0 | (0.7–1.4) | 1.00 | reference |
| | High SES | 46 | 1.3 | (1.0–1.8)) | 1.37 | (0.84–2.23) |
| HL, age 45+ y | Low enclave status | 13 | — | — | 1.00 | reference |
| | High enclave status | 18 | 0.8 | (0.4–1.2) | **0.35** | **(0.12–0.79)** |
| | Low SES | 8 | — | — | 1.00 | reference |
| | High SES | 23 | 1.6 | (1.0–2.4)) | **2.83** | **(1.20–7.46)** |
| HL, NS | Low enclave status | 24 | 1.1 | (0.7–1.7) | 1.00 | reference |
| | High enclave status | 56 | 0.7 | (0.5–0.9) | 0.63 | (0.38–1.08) |
| | Low SES | 31 | 0.6 | (0.4–0.9) | 1.00 | reference |
| | High SES | 49 | 0.9 | (0.7–1.3) | 1.51 | (0.93–2.48) |
| HL, MC | Low enclave status | 9 | — | — | 1.00 | reference |
| | High enclave status | 5 | — | — | **0.16** | **(0.04–0.55)** |
| | Low SES | <5 | — | — | 1.00 | reference |
| | High SES | 11 | — | — | 3.76 | (0.98–21.08) |

[a]Standardized to the 2,000 U.S. population age standard. Incidence rates with numerator less than 15 are not computed.

SES and lower enclave neighborhoods were stronger in women than in men. For MM, incidence rates did not differ according to birthplace, ethnic enclave status, or neighborhood SES. We also confirmed that the incidence rates of most subtypes were substantially lower than rates in non-Hispanic white populations; for TCL and DLBCL—the 2 subtypes for which absolute incidence rates were most similar between Asians and non-Hispanic whites—we did not observe consistent differences in incidence according to birthplace or neighborhood characteristics.

There is little published information about the incidence patterns of lymphoid malignancy subtypes among Asians according to detailed ethnicity and birthplace. Our recent analysis based on SEER data documented lower incidence of lymphoid malignancies among 6 Asian ethnic groups than whites (2), but lacked the data to consider differences by birthplace. In SEER data, an assessment of NHL cases diagnosed in the period 1973 to 1986 and classified according to the working formulation scheme also found reduced risk of FL in foreign-born compared with U.S.-born Chinese and Japanese (but not Filipinos), with incidence rates 60% to 80% lower than rates in their U.S.-born counterparts (22). However, in that analysis, the authors assumed that the SEER cases without birthplace information had randomly missing data. As we have shown that those with missing data are more likely to be U.S.-born (5), this earlier analysis may have underestimated rate differences by birthplace, which may explain the difference in findings for CLL/SLL and HL. To our knowledge, ours is the first study to address lymphoid malignancy incidence patterns among U.S. Asians according to neighborhood characteristics, although we did report previously that rates of young–adult HL were lower among Asian women (but not men) living in the lowest terciles of neighborhood SES in California (23). Our findings of lowered rates of CLL/SLL and NS HL among Asian women living in impoverished or ethnic enclave communities as compared with more affluent and presumably more acculturated communities further support the notion that the causation of these particular lymphoid malignancy subtypes involves environmental exposures more common in Westernized environments.

Differences in cancer incidence rates between Asians who immigrate to the United States (and their descendents) and those who remain in Asia have long been considered strong evidence of environmental influences on carcinogenesis, although it is possible that there are also genetic differences among persons who are healthy enough to emigrate. For breast cancer, incidence rates among Chinese and Filipina women born in the United States are nearly twice those of women living in Asia, and these differences are increasingly thought to relate to reproductive and dietary changes associated with Westernized lifestyle (7, 24). For NS HL, exposures of interest include correlates of the childhood social environment (ref. 25; e.g., family size and household crowding) and measures of microbial burden or other immunological relevant environmental exposures (e.g., age at diagnosis with mononucleosis; ref. 26), particularly in early life (21, 25, 27–33). Childhood environment has not been consistently associated with the risk of FL or CLL/SLL (34–36), although a recent pooled analysis including more than 13,500 NHL cases did report for FL significantly positive associations with both birth order and sibship size (36). However, risk of both FL and CLL/SLL has inversely been associated with atopic disease (37), which could be associated, in turn, with early-life microbial exposures. It is uncertain whether chronic infection with hepatitis viruses, linked to doubled risks of NHL (38, 39) and endemic in Asia (40, 41), are relevant to the observed rate patterns. Although U.S.-born Asians have lower rates of chronic infection with hepatitis B and C viruses than their foreign-born counterparts in the United States and Asia (40, 42), the associations of viral hepatitis with the risk of specific NHL subtypes (e.g., DLBCL) do not correspond the observed incidence rate differences by birthplace in our study (43).

The stronger effects of birthplace and neighborhood characteristics for CLL/SLL and HL observed in women than men could, in part, reflect socially determined differences in exposure opportunities (such as those involving children) and biologically determined differences in immunoresponse to exposures (23). For HL, the gender difference in the effect of nativity may result from protection in low-acculturation women afforded by both early exposure to infection and higher parity or lactation, as hormonal exposures through pregnancy and breast feeding may interact with childhood exposures to affect the risk of HL (44).

For HL, the varying impact of birthplace by age group is consistent with prior evidence of differing pathogenesis of HL by age (21). It is also relevant to the differential effect of birthplace on incidence of the NS and MC subtypes, given that young adult HL is predominant of the NS subtype. Furthermore, subtype differences in birthplace associations may reflect etiologic differences in immunocontrol and age at infection of Epstein-Barr virus (EBV), as EBV is more commonly found in tumors of the MC than NS type (45, 46) and Asians than whites (47).

Dietary patterns and energy balance/obesity, which also vary by birthplace among U.S. Asians (48), may also be associated with the risk of developing certain lymphoid malignancies (49–52), and therefore represent important areas for future study in Asian immigrant populations. For MM, our observation of substantially lowered rates among Asians as compared with non-Hispanic whites, but no difference according to birthplace or neighborhood characteristics, suggests a more important role for genetic susceptibility and less of an influence of environmental exposures that change with acculturation. In support of this hypothesis, MM risk has been associated with polymorphisms in genes thought to influence innate immunity and immunoregulatory processes (53, 54).

By using more than 16 years of SEER data from California, we could capitalize on the relatively large size of the Asian population in this state and draw conclusions on the basis of the representativeness of these high-quality population–based data. We consider the ethnic and birthplace classifications used here to have low probabilities of misclassification or bias. Specific Asian ethnic group was classified directly from registry records or, for those without specific registry information on ethnicity, from applying a validated ethnicity classification algorithm. With this approach, a small proportion (<3%) of patients was excluded from these analyses because of missing ethnic classification. Furthermore, cancer registry classification of specific Asian ethnicity shows good agreement with self-reported information (55). For cases for whom birthplace information was reported to the registry (the vast majority), we have also shown that this classification shows excellent agreement in comparison with self-reported birthplace (4, 5); for the remaining cases, we applied a validated birthplace classification algorithm with good sensitivity and specificity.

Despite these important strengths, our results may also be subjected to some limitations. First, we had limited statistical power to analyze certain subgroups, such as specific Asian ethnic groups and uncommon lymphoid malignancies. Second, the heterogeneity in the complex pathologic methods required to diagnose and classify lymphoma cases may have resulted in misclassification of some cases by subtype. Our prior comparisons of cancer registry ICD-O-3 classifications to those obtained from uniform rereview of pathologic specimens suggest a high degree of reliability for the diagnosis of overall NHL and HL (56) and for particular subtype classifications including FL (89%), SLL (79%), DLBCL (90%), and NS HL (95%), but more moderate reliability for rarer subtypes (57, 58). In addition, cancer registry data lack detail about certain histopathologic characterizations (e.g., t(14;18) translocations for FL, and EBV tumor-cell status for HL), and information about parental race/ethnicity, individual-level education, and other measures of SES, medical history, age at immigration, duration of immigration, and other risk factors that could be relevant to our observed incidence rate differentials. Finally, these data cannot speak to the independent or joint influence of genetic factors in modifying risk of FL and CLL/SLL across populations. Recent genome-wide association studies found genetic variants that influence the risk for FL (59) and SLL/CLL (60) and the absolute difference between rates in U.S.-born Asians and whites does not rule out a role for genetic predisposition to FL and CLL/SLL. Regardless, our results suggest that environmental exposures have greater influence than genes on the variation in incidence rates by ethnicity and nativity.

The markedly lowered rates of lymphoid malignancies among Asians relative to other racial/ethnic groups in the United States and among foreign-born Asians relative to U.S.-born Asians have suggested some kind of protection from lymphomagenic processes, but it has been unclear whether this protection relates to genetic or environmental differences. Our data suggest a clear pattern of increased risk of FL, CLL/SLL, and HL in Asians according to U.S. birthplace and neighborhood acculturation indicators, and thereby point to a strong influence of environmental factors that change with immigration and acculturation to a Westernized lifestyle. Future studies of FL, CLL/SLL, and HL designed to collect a wide array of environmental exposure information (and implicated genetic variants of risk) are warranted among Asian immigrant populations in the United States and other Westernized countries, as they may identify heretofore unrecognized and modifiable causes of these malignancies.

## Disclosure of Potential Conflicts of Interest

The ideas and opinions expressed herein are those of the authors and endorsement by the State of California, Department of Public Health, National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors are not intended nor should be inferred. No authors report any financial conflict of interest.

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