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# The role of nativity in heterogeneous dementia incidence in a large cohort of three Asian American groups and white older adults in California

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#### **Abstract**

**INTRODUCTION:** Literature shows lower dementia incidence in Asian American groups versus whites, varying by Asian ethnicity. One hypothesized driver is nativity differences (e.g., healthy immigrant effect).

**METHODS:** We followed a cohort of 6243 Chinese, 4879 Filipino, 3256 Japanese, and 141,158 white Kaiser Permanente Northern California members for incident dementia (2002 to 2020), estimating age-adjusted dementia incidence rates by ethnicity and nativity, and hazard ratios (HR) for nativity on dementia incidence using ethnicity-stratified age- and sex-adjusted Cox proportional hazards models.

**RESULTS:** Dementia incidence appeared higher in foreign- versus US-born Filipinos (HR=1.39, 95% confidence interval 1.02–1.89); differences were small in Japanese (HR=1.07, 0.88–1.30) and Chinese (HR=1.07, 0.92–1.24). No nativity differences were observed among whites (HR=1.00, 0.95–1.04).

**DISCUSSION:** Nativity does not explain lower dementia incidence in Asian Americans vs. whites, but may contribute to heterogeneity across Asian ethnicities. Future research should explore differential impacts of social and cardiometabolic factors.

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#### Keywords

Dementia; Nativity; Incidence; Racial/Ethnic Disparities

#### Introduction

The limited available evidence on dementia incidence among Asian Americans suggests Asian Americans have lower dementia risk than whites, and that incidence varies across Asian American subgroups.(1–6) Understanding this reduced risk could help identify strategies to reduce dementia risk for all racial/ethnic groups. One hypothesis is that differences in nativity (Asian Americans being more likely foreign-born than whites (7)) could explain lower dementia incidence in Asian Americans vs. whites and variability across Asian American subgroups. Lower incidence among foreign-born individuals could be due to selection factors (healthier individuals more likely to migrate)(8); higher incidence in US-born Asian Americans could also be due to more closely sharing the health behaviors and profiles of white Americans, elevating dementia risk.(9–11) We compared dementia incidence among US- and foreign born individuals in a cohort of Asian and non-Latino white older adults.

#### Methods

#### Study population

Our study population comprised Kaiser Permanente Northern California (KPNC) health plan members who completed one of two harmonized health surveys: California Men's Health Study (CMHS; administered 2002–2003 (12)) or Kaiser Permanente Research Program on Genes, Environment, and Health Survey (RPGEH; administered 2007–2009 (13,14)). The cohort included 184,929 Asian and non-Latino white individuals age 60 and <90 and had two continuous years of health plan coverage as of their survey date. Data comparing this cohort to both KPNC membership broadly and the general population are in Supplement 1.

We excluded individuals with electronic health record (EHR) dementia diagnosis (Alzheimer's disease, vascular, and non-specific dementias) between 1996 (start of EHR at KPNC) and survey date (n=4,454, 2.4%). To examine nativity within ethnic subgroups, we excluded participants with unknown/missing country of birth (n=8,376, 4.6%), and restricted to subgroups with adequate sample size (n=40 dementia cases) of both US-born and foreign-born participants (Chinese, Japanese, Filipino, and non-Latino white, final n=155,536); excluded ethnicities all had <15 cases among US- or foreign-born. Cohort members were followed for incident dementia from survey completion until death, lapse in health plan membership 90 days, or end of study period (2/29/2020). All data were de-identified. Survey participants provided informed consent at participation; the analytic study was approved by the University of California, Los Angeles institutional review board (#19-000794).

#### **Measures**

Incident dementia outcome—Incident dementia diagnoses during follow-up were identified from EHR using International Classification of Diseases 9<sup>th</sup> and 10<sup>th</sup> Revision codes (Supplement 2) for Alzheimer's disease, vascular dementia, and non-specific dementia from inpatient, emergency, and outpatient settings excluding lab-only and radiology-only encounters. Censoring events included death, lapse in health plan coverage 90 days, or end of study period. Deaths were identified from the KPNC mortality database, which aggregates mortality records from KPNC clinical and administrative sources, the National Death Index, California State death records, and Social Security Administration records. Because ages of events occurring after age 90 were top-coded for de-identification, we imputed event times after age 90 using Weibull distributions derived from analyses of the identifiable data housed at KPNC (details in Supplement 3).

**Other measures**—Age at survey and sex (male/female) were identified from EHRs. Other measures were self-reported in the CMHS and RPGEH surveys. Nativity (US-born or foreign-born) was defined by birth in the US (yes/no). Race/ethnicity measures were derived from survey questions asking participants to mark all groups that best described their race or ethnicity. Asian Americans were classified by the Asian ethnicities they reported ("Asian Indian/South Asian," "Chinese," "Filipino," "Japanese," "Korean," "Vietnamese," and/or "other Southeast Asian"). Participants who reported one Asian ethnicity with or without white/European-American ethnicity were classified as the Asian ethnicity they reported, and participants who endorsed multiple Asian ethnicities (with or without white/European-American) were classified as multi-ethnic Asian. Participants who reported only white/ European-American ethnicity were classified as non-Latino white. Participants reported educational attainment (1-8 years, some high school, high school/GED, technical/trade school/some college, college degree, graduate school), per-capita income (household income divided by square root of household size), marital status (married/living as married vs. other), health status (fair/poor vs. good/very good/excellent), and family history of dementia (yes/no).

**Statistical analysis**—We estimated age-adjusted dementia incidence rates, standardized to the 2000 US Census population ages 60+, and age-specific rates (60–64, 65–69, 70–74, 75–79, 80–84, 85+) by race/ethnicity and nativity. Sex-adjusted Cox proportional hazards models with age as the timescale (starting at survey age) estimated effects of nativity on dementia incidence rate. Analyses were stratified by race/ethnicity, conducted for specific Asian ethnicities (Chinese, Filipino, Japanese), and all Asians in the sample combined. Sensitivity analyses were conducted restricted to non-multiracial Asians and stratified by sex. Statistical code is available (https://github.com/Mayeda-Research-Group/Asian\_dementia\_nativity).

#### Results

Our analytic sample included 155,536 participants (6,243 Chinese, 4,879 Filipino, 3,256 Japanese, and 141,158 white participants, Table 1). The proportion US-born differed substantially by race/ethnicity (30.9% of Chinese, 10.1% of Filipino, 71.5% of Japanese,

and 90.8% of white participants). Baseline age, sex, and educational attainment also showed racial/ethnic variability.

Age-adjusted incidence rates were lower in Asian than white participants, and varied across Asian ethnicities (highest in Filipinos, lowest in Chinese) (Figure 1A, Table S7). Among white and Chinese participants, age-adjusted dementia incidence rates were similar by nativity, while incidence rates were higher among foreign-born vs. US-born Filipino and to a lesser extent, Japanese participants (Figure 1B, Table S7). Age-specific incidence rates followed the same pattern (Table S8).

Age- and sex-adjusted Cox proportional hazards models yielded similar findings: foreignborn Filipino individuals experienced 1.39 (95% confidence interval [CI] 1.02–1.89) times the rate of dementia compared with US-born counterparts. The hazard ratios were smaller among Chinese (HR 1.07, 95% CI 0.92–1.24) and Japanese (HR 1.07, 95% CI 0.88–1.30). In pooled analyses of all Asians, dementia incidence rates were 1.09 times higher among those with foreign- vs US-birth (95% CI 0.99–1.20). Dementia incidence did not differ between foreign- vs. US-born whites (HR 1.00, 95% CI 0.95–1.04).

Sensitivity analyses restricted to non-multiracial Asians showed similar results, and sex-stratified analyses generally showed larger HRs among women, but estimates were imprecise (Supplement 5).

#### **Discussion**

We aimed to assess whether nativity explained lower dementia incidence in Asian Americans versus whites and heterogeneity between Asian American subgroups. Our findings confirmed prior work reporting lower incidence in Asian Americans than whites and heterogeneity across Asian subgroups,(1–6) but did not support nativity as a factor explaining Asian-white differences. For all Asian ethnicities, age-adjusted dementia incidence was similar or higher in foreign-born than US-born individuals. Chinese individuals and US-born Filipinos and Japanese had the lowest dementia incidence rates.

Despite rapid growth in the Asian American population (15), most cohorts do not contain large enough Asian American samples to examine dementia incidence, especially among specific ethnic groups. Our study includes robust samples of three of the six largest Asian ethnic groups in the US (15), and is the first to assess the impact of nativity on dementia incidence in multiple groups. Prior work has examined the related but distinct concept of immigration's effect on dementia-related outcomes, showing lower cognitive test scores among first-generation versus third-generation immigrants,(16) and that immigration-related factors (e.g., migration age, reason) did not impact cognitive impairment in Chinese-Americans near Chicago (17). Our results generally agree with these findings. However, being Japanese-born appeared protective against cognitive decline in the Kame cohort (18). In contrast, we found foreign birth was associated with similar or slightly higher dementia incidence among Japanese individuals. The difference between our results and Kame findings could be due to cohort and period effects (Kame includes predominantly earlier birth cohorts than our study), including birth cohort differences in socioeconomic

factors (e.g. greater education in the US-born in our study). Foreign birth was associated with increased dementia incidence in Filipinos, a group that has not been studied previously.

Differences in our findings between Asian ethnic groups may also reflect differences in historical immigration patterns for each group, which were shaped by economic and political factors in the US and countries of origin. Most Japanese immigration occurred in the early  $20^{th}$  century when US laws largely prohibited immigration from other Asian countries. As of 2010, less than one-third of Japanese in the US were foreign-born (7). In contrast, 76% of Chinese and 69% of Filipinos in the US were foreign-born, reflecting that migration in these groups predominantly occurred after the 1965 Immigration and Nationality Act, which substantially expanded immigration opportunities for Asians (7). More recent Asian immigrants also tend to be more highly educated and skilled than those from earlier periods (7). As a result of these contextual differences, potential contributions of healthy migration, adoption of American health behaviors, and other factors to dementia risk by nativity may differ by ethnic group.

Limitations of our work include our being limited to assessing nativity; details on immigration (e.g. age) and measures of adoption of typical US health behaviors that may influence dementia risk were unavailable, so we could not assess whether these constructs influenced the impact of nativity on dementia incidence. Further, our sample over-represents US-born Asian Americans compared to the California population of adults 60+, and likely under-represents non-English speakers from other ethnic groups (Supplement 1). If non-English speakers have lower dementia risk, our results could overestimate diagnosed dementia incidence in the foreign born, and reduce generalizability of our results to Asian Americans 60+ in California. This is less likely to occur for Filipinos, who predominantly speak English. Mortality and dementia incidence rates suggest our cohort is somewhat healthier than the broader KPNC membership and California general population (Supplement 1). Finally, we were unable to look at additional Asian ethnic groups due to few US-born participants.

In conclusion, nativity does not seem to drive lower dementia risk among Asian Americans versus whites, but may contribute to heterogeneity between Asian ethnic groups. Testing other hypotheses for lower dementia incidence rates among Asian Americans vs. whites was beyond the scope of this paper, but future studies should evaluate possible differential impacts of social and cardiometabolic factors on dementia risk.

### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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#### **Research in Context**

#### **Systematic review:**

The authors reviewed the literature for evidence on differences in late-life cognition and dementia incidence by nativity among Asian Americans. Although there is limited evidence on this topic, reports on patterns of dementia incidence in Asian American ethnic groups, as well as literature on the impact of immigration-related factors among Asian Americans are cited.

#### **Interpretation:**

Our findings agree with prior work reporting lower incidence in Asian Americans than whites and heterogeneity across Asian subgroups, but did not support nativity as explaining Asian-white differences. For all Asian ethnicities, age-adjusted dementia incidence was similar or higher in foreign-born than US-born individuals.

#### **Future directions:**

Future studies should evaluate other hypotheses for lower dementia incidence rates among Asian Americans vs. whites, such as possible differential impacts of social and cardiometabolic factors on dementia risk.

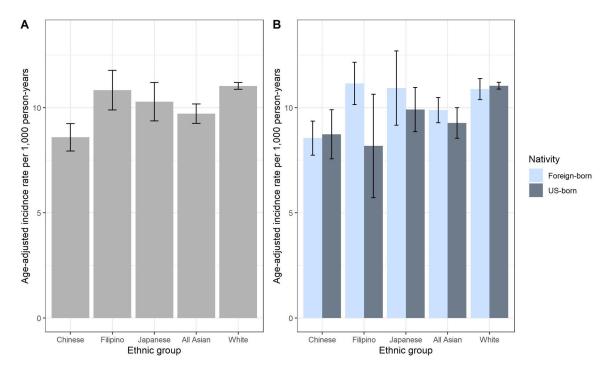


Figure 1.

Age-adjusted (age-standardized to the 2000 US Census population ages 60+) dementia incidence rates per 1000 person-years for Chinese, Filipino, Japanese, and white participants in the California Men's Health Study and the Kaiser Permanente Research Program on Genes, Environment, and Health Survey, showing (A) overall rates by ethnicity, and (B) rates for each group stratified by nativity

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Characteristics of Chinese, Filipino, Japanese, and White CMHS and RPGEH survey participants

Table 1.

	Chinese	ıese	Filipino	omo	Japanese	nese	W	White
	n=6,243	243	n=4	n=4,879	n=3	n=3,256	n=14	n=141,158
Born in the US (%)	1,930	(30.9)	494	(10.1)	2,327	(71.5)	128,232	(8.06)
Age, years (mean [SD])	70.5	(7.2)	69.4	(8.8)	72.6	(7.7)	71.5	(7.7)
Female (%)	3,159	(50.6)	2,792	(57.2)	2,042	(62.7)	81,921	(58.0)
Education (%)								
1st-8th grade	471	(7.5)	263	(5.4)	59	(1.8)	1,796	(1.3)
9th-12th grade	537	(8.6)	215	(4.4)	147	(4.5)	5,283	(3.7)
High school diploma or equivalent	855	(13.7)	493	(10.1)	289	(21.1)	24,965	(17.7)
Some college or technical school	1,346	(21.6)	948	(19.4)	840	(25.8)	40,867	(29.0)
Bachelor's degree	1,620	(25.9)	2,099	(43.0)	608	(24.8)	29,409	(20.8)
Master's degree or higher	1,147	(18.4)	587	(12.0)	530	(16.3)	29,504	(20.9)
Missing	267	(4.3)	274	(5.6)	184	(5.7)	9,334	(9.9)
Marital Status (%)								
Married/Living as married	4,827	(77.3)	3,489	(71.5)	2,144	(65.8)	92,079	(65.2)
Missing	74	(1.2)	36	(0.7)	21	(0.6)	1,180	(0.8)
Annual per capita income								
Income, dollars (mean [SD])	\$ 47,380	(29,393)	\$ 39,812	(24,851)	\$ 54,279	(28,145)	\$ 56,101	(28,761)
Missing (%)	787	(12.6)	637	(13.1)	535	(16.4)	18,810	(13.3)
General Health Status (%)								
Excellent/very good/good	4,332	(69.4)	3,282	(67.3)	2,520	(77.4)	111,802	(79.2)
Fair/poor	1,493	(23.9)	1,263	(25.9)	621	(19.1)	23,820	(16.9)
Missing	418	(6.7)	334	(8.9)	115	(3.5)	5,536	(3.9)
Family history of dementia (%)								
Reported family history of dementia	284	(4.5)	202	(4.1)	288	(8.8)	17,268	(12.2)
Missing	1,115	(17.9)	538	(11.0)	339	(10.4)	12,100	(8.6)

Abbreviations: CMHS, California Men's Health Study; RPGEH, Research Program on Genes, Environment, and Health.

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