

## AN EXCESS OF BREAST CANCER AMONG YOUNG CALIFORNIA-BORN ASIAN WOMEN

**Objective:** To compare breast cancer risk among young Asian and Pacific Islander (API) women to White women, all of whom were born in California during the 1960s.

**Design:** We used previously-collected data from a population-based case-control study in which breast cancer cases were linked to their California birth records.

**Setting:** California, US.

**Participants:** Invasive breast cancer cases diagnosed 1988–2004 among women aged <45 were identified from the population-based California Cancer Registry. Breast cancer cases ( $n=3,799$ ) were linked to their California birth records. Controls ( $n=17,461$ ) were randomly selected from California birth records for females, frequency matched to cases by birth year.

**Main Outcome Measures:** Odds ratios (ORs) and 95% confidence intervals (95% CI) were estimated using logistic regression.

**Results:** Among young women born in California, API women had higher risks of breast cancer than Whites (OR=1.62, 95% CI: 1.35–1.94). Among APIs, the risks were highest for women of Filipina (OR=1.72, 95% CI: 1.15–2.56) and Japanese ancestry (OR=1.59, 95% CI 1.20–2.10).

**Conclusions:** Our finding of breast cancer risk among young API women who were born in California that exceeds that of young White women highlights the need for further evaluations of breast cancer risk among young API women and underscores the need to consider both ancestry and migration status in such evaluations. (*Ethn Dis.* 2011;21(2):196–201)

**Key Words:** Breast Neoplasms, Health Status Disparities, Case Control Studies

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### INTRODUCTION

Race/ethnicity and geographic location are among the most powerful predictors of breast cancer risk with the highest rates of breast cancer typically observed among White women living in the United States and the lowest rates among Asian women living in Asia.<sup>1,2</sup> Asian women who move to the United States gradually acquire the higher breast cancer rates of their adoptive country, increasing with time since migration and with generational status, suggesting a strong influence of acculturation on breast cancer risk.<sup>3–8</sup>

Historically, national cancer surveillance data report that Asian and Pacific Islander (API) women living in the United States have substantially lower breast cancer incidence rates than US White and Black women.<sup>9–13</sup> More recent studies, however, that have focused on disaggregating the large and heterogeneous group of Asian and Pacific Islander women into distinct populations based on ethnic ancestry, have suggested previously unrecognized elevated risks among some ethnic subpopulations.<sup>14–19</sup> Furthermore, recent detailed temporal analyses have shown disproportionate increases in incidence among some API ethnic subpopulations<sup>16,19</sup> and have underscored the importance of birth place and generational status in determining breast cancer risk among the API population living in the United States.<sup>15,19</sup> Efforts to study the role of nativity and immigration status on breast cancer risk have been hampered by limitations in cancer surveillance data that often contain inaccurate or incomplete data on place of birth. In a recent study that used an innovative approach utilizing social se-

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curity numbers to impute immigration status for records missing birthplace information, Gomez and colleagues reported elevated rates of breast cancer incidence among US-born API women in California, that among younger women, exceeded those of non-Hispanic Whites.<sup>15</sup>

The analysis presented here takes advantage of data collected as part of a broader case control study designed to evaluate the relationship between selected perinatal characteristics and breast cancer risk in young women. The objective of our present analysis was to compare the risk of breast cancer among very young Asian and Pacific Islander women to that of White women, all of whom were born in California during the 1960s. Because all women in this study were known to have been born in the United States by virtue of their linkage to a California birth certificate, our analysis offered the opportunity to confirm the provocatively elevated rates of breast cancer among US born API women reported by Gomez et al using alternative methods for ascertaining place of birth.

## METHODS

This analysis was conducted as part of a broader case control study in which probabilistic record linkage techniques were used to link cases of invasive breast cancer diagnosed in young California women to their own California birth records to obtain information on perinatal characteristics of interest. Population controls were selected from 1960s California birth records. The analyses presented here are based on the cases and controls selected for this larger study as described below.

### Study Population

All cases of primary invasive breast cancer (SEER site code=26000) were identified from California's statewide Cancer Registry (CCR) for the period 1988 through 2004.<sup>20</sup> Because the perinatal characteristics of interest for the broader study were to be derived from California birth certificates, cases were limited to those who were born in California. Registry data on birthplace, however, is incomplete for a large proportion of cases, making identification of California births problematic. Therefore, we limited our initial pool of potentially eligible cases to primary invasive breast cancers diagnosed in California women who had either a California or unknown birthplace listed in the CCR record. For the time period of this study, approximately 15% of primary invasive breast cancer cases had a California birthplace and 44% had an unknown birthplace. Furthermore, because of limitations in the availability of automated California birth data, we only included breast cancer cases who were born in the decade of the 1960s. Thus, our initial pool of eligible cases for linkage to birth records consisted of 7,866 cases of primary invasive breast cancer among California women born in the 1960s who had either a California ( $n=2,792$ ) or unknown birthplace ( $n=5,074$ ) listed in their CCR record.

### Record Linkage

Probabilistic record linkage was used to identify California births by linking eligible breast cancer cases to their own California birth records. Additional linkages to other data sources were used to augment the missing information on birth place and maiden name in the CCR database prior to linking the CCR data to the birth data.<sup>21</sup> All record linkages were performed using AUTOMATCH software.<sup>22</sup> Overall, we linked 48% (3,799/7,866) of our eligible breast cancer cases to a California birth certificate. As would be expected, linkage success was substantially better among those with a California birthplace listed in the CCR (76%) than among those with a missing or unknown birthplace (32%). Linkage success also varied by ethnicity (52% for Whites; 57% for Blacks; 45% for Hispanics; and 17% for Asian/Pacific Islanders). This variation in linkage success by ethnicity appeared primarily to be a function of the lower success for records with unknown birthplace. Among those with a California birthplace listed in the CCR, linkage success rates did not vary greatly by ethnicity (ranging from a low of 75% for Asian/Pacific Islanders to a high of 80% for Blacks). Linkage success also differed marginally by age (59% for women in their twenties versus 41% for women in their forties) and by marital status (55% for never married women compared to 47% among ever married women).

### Control Selection

Population-based controls were selected from California birth records, maintained by the California Office of Vital Records. To identify these controls, we randomly selected approximately four live female births, frequency matched to the breast cancer cases on year of birth. Controls who had died prior to the age of 21 (the youngest age of our cases) were identified by linking the birth certificate controls to California mortality files 1960–1989. Controls

who had died were excluded and each was replaced with another randomly-selected live birth from the same birth year.

### Classification of Ethnicity

Although the CCR collects detailed information on race and ethnicity, California birth records from the 1960s offer much less detailed information. In order to apply uniform methods for race/ethnicity classification to both cases and controls, we needed to rely on data from the birth records for classification. Because information on race/ethnicity in the electronic birth files was not uniformly available at the same level of detail throughout the course of our study, race/ethnicity classification was manually abstracted from birth certificate images based on parental ethnicity. For birth certificates that were missing ethnicity information and to identify appropriate API subgroups, a characteristic surnames approach<sup>23,24</sup> was used to categorize individuals into 4 broad categories (White, Black, Asian/Pacific Islander, Other) and API ancestry into the 3 most prevalent groups in California during that time period (Japanese, Chinese, Filipina). Since Hispanic origin was not systematically reported on the birth certificates, it was not possible to separately categorize Hispanic ethnicity.

### Statistics

Odds ratios (ORs) and 95% confidence intervals for each category of ethnicity and API ancestry were obtained from unconditional logistic regression models, with White as the referent group, adjusting for birth year. Analyses were conducted using SAS, version 9.2.<sup>25</sup> All statistical tests were two-sided and  $P<.05$  was considered statistically significant.

### Results

The analytic data set consisted of the 3,799 breast cancer cases who linked to a 1960s California birth record and

**Table 1. Distribution of demographic characteristics among breast cancer cases and population controls (n=21,260)**

Characteristic	Breast cancer cases		Population controls	
	n	%	n	%
Total	3,799	100	17,461	100
Ethnicity				
White	3,119	82	15,287	88
Black	472	12	1,454	8
Asian/Pacific Islander	164	4	496	3
Other	44	2	224	1
Asian/Pacific Islander Ancestry				
Japanese	67	41	207	41
Chinese	32	19	127	26
Filipina	33	20	94	19
Other Asian/Pacific Islander	32	19	68	14
Birth year				
1960	751	20	3,562	20
1961	630	17	2,979	17
1962	553	14	2,557	15
1963	467	12	2,146	12
1964	372	10	1,709	10
1965	294	8	1,334	8
1966	226	6	994	5
1967	186	5	822	5
1968	159	4	687	4
1969	161	4	671	4

17,461 population controls. The demographic characteristics of our study population are shown in Table 1. As reflective of California in the decade of the 1960's, the study population is predominantly White, born in the early 1960s and all are very young women. Age among study subjects ranged from 20 to 44 years with a mean age at diagnosis among breast cancer cases of 36 years (data not shown). Compared to breast cancer cases, the population controls were slightly more likely to be White (Table 1). Among the APIs, Japanese ancestry was most common, followed by Chinese and Filipina ancestry. No "other" category of API ancestry had sufficient numbers of individuals for meaningful analysis and thus was included in the other category. The distribution of API ancestry was similar between the breast cancer cases and population controls, although there was a slightly lower proportion of Chinese women among the breast cancer cases (19%) than among the

controls (26%). The birth year distribution of the breast cancer cases and population controls did not differ as our study design frequency matched the population controls to the breast cancer cases by birth year.

The odds ratios for race and API ancestry, comparing the risk of breast cancer to population controls are shown in Table 2. As expected, the risk for breast cancer among young Black women was elevated (OR = 1.59, 95% CI=1.42–1.78) compared to Whites. The risk for API women was similarly elevated (OR=1.62, 95% CI=1.35–1.94). In considering ancestral origins among Asians and Pacific Islanders, young women of Filipina (OR=1.72, 95% CI=1.15–2.56) and Japanese descent (OR=1.59, 95% CI 1.20–2.10) had significantly higher risks than young White women. Further analyses demonstrated similar risk patterns for early (localized) and late stage diagnoses and for estrogen/progesterone positive and negative tumors (data not shown).

**Table 2. Odds ratios and 95% confidence intervals (95% CI) for invasive breast cancer (n=3,799) associated with ethnicity and Asian/Pacific Islander (API) ancestry, compared to population controls (n=17,461), adjusted for birth year**

	Cases	Odds ratio	95% CI
Ethnicity			
White	3,119	1.00	-
Black	472	1.59	1.42, 1.78
Asian/Pacific Islander	164	1.62	1.35, 1.94
Other	44	0.96	0.69, 1.32
API Ancestry			
Japanese	67	1.59	1.20, 2.10
Filipina	33	1.72	1.15, 2.56
Chinese	32	1.23	0.84, 1.82
Other API	32	2.29	1.50, 3.49

## DISCUSSION

Our results suggest that among young women born in California, Asian and Pacific Islander women may have higher risks of breast cancer than young White women, and in fact some groups (eg, Filipina) may have higher risks than Blacks. These findings contradict the perception that API women are at a much lower risk of breast cancer than White women. This perception, however, is fueled largely by the lower rates of breast cancer incidence reported by

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national cancer surveillance data among API women overall, regardless of age or migration status. Limited age-specific national surveillance data suggest that among younger women, the rate of breast cancer among API women is more similar to, albeit, still lower than that in Whites.<sup>12,13,26,27</sup> National cancer surveillance data, however, are not able to account for place of birth due to the large proportion of missing information on this factor. US Census data indicate that the majority (69%) of Asian Pacific Islanders living in the United States are foreign-born.<sup>14</sup> In contrast our study, by design, included only women born in the United States, specifically in California. While the importance of nativity in determining breast cancer risk has long been recognized,<sup>3,5,8,15,28</sup> our findings of an elevated risk of breast cancer among young California-born API women that exceeds that of young White women, highlights the need to further evaluate breast cancer risks among this rapidly growing segment of the US population.

Beyond the likely importance of nativity, there are a number of other potential explanations for the apparent conflict of our findings with reports from national cancer surveillance data. Notably, the distribution of API ancestral populations within our study population is not reflective of that in the US population. A much higher proportion of our study population of API women were of Japanese descent (41%) than is represented in the US API population (8%).<sup>14</sup> The Japanese, who were among the first wave of large-scale Asian immigration to the United States, are more likely than any other API population to be born in the United States, and are considered one of the most highly-aculturated groups, demonstrating breast cancer risk factor profiles most similar to White women.<sup>14</sup> Furthermore, more recent analyses of cancer registry data that have utilized disaggregated API data, have documented high rates of breast cancer among

Japanese women, both nationally,<sup>17,29</sup> and within California.<sup>16,18,19</sup> The observation in our study of elevated risks among all API ancestral subpopulations examined (Japanese, Filipina, Chinese, and other), however, suggests that our finding for the broad group of API women was not singularly driven by the excess risk among the large proportion of Japanese women in our study.

Most research to date that has focused on explaining racial/ethnic disparities in breast cancer incidence has addressed the degree to which they can be accounted for by the prevalence of known risk factors.<sup>28,30-36</sup> While results from these studies report risk factor profiles (ie, differences in parity, age at first birth, diet and other lifestyle factors) that are generally consistent with racial/ethnic patterns in incidence, exceptions and inconsistencies are numerous, suggesting a complex interplay of multiple factors that are likely to be modified by place of birth and acculturation.<sup>35-37</sup> Furthermore, this research generally has not focused on young women and thus is likely not applicable to the population being studied here.<sup>28,30,36</sup> Characterization of breast cancer risk profiles specifically among young API women, taking into consideration migration status, is an important area for future research. The potential role of environmental toxicants, for which there are well-documented ethnic disparities with both Blacks and Asians shouldering the burden of heavy exposures,<sup>38</sup> is one neglected but potentially important area for future inquiry.

Because this study was not specifically initiated to look at ethnicity and relied on pre-existing data sources, there are a number of limitations to our study worth noting. Because information on Hispanic origin was not available on the birth certificates in the 1960s, our study was unable to separately identify Hispanic women. An examination of Hispanic ancestry among the breast cancer cases in the CCR database suggests that

as much as 19% of the White women in our study may be of Hispanic origin. While inclusion of these women in our referent group (Whites) would likely have the effect of upwardly biasing our risk estimates for the API women, it is unlikely to fully explain the 60 to 70% increase in risks observed. Although information is sparse on breast cancer incidence among young Hispanic women, there is some evidence that rates among younger<sup>39</sup> and US born<sup>40</sup> Hispanics are more similar to those of non-Hispanic White women, further suggesting that the bias, if any, caused by including them in our referent group is likely to be minimal.

Another limitation of our study was the use of controls identified from the California birth certificate records, which assumes that controls were still alive and residing in California during the follow-up period (1988-2004). While we removed and replaced controls that had died prior to follow-up, differential migration patterns between ethnic groups could affect estimates of risk. Unfortunately, detailed California-specific migration information for the full follow-up period of our study is not available. Recent department of finance data, however, suggest that migration rates among the California population do not differ substantially by ethnicity (ranging from 15.7 percent for Whites to 14.4 percent for APIs) and in fact most residential mobility (85%) is confined to within California's borders.<sup>41</sup> Furthermore, to evaluate the potential bias introduced by the use of population-based birth controls, we conducted a sensitivity analysis where we recalculated odds ratios using an alternative set of cancer controls. This analysis, based on controls who consisted of other cancer cases diagnosed during the same time period and who were born in California during the 1960s, yielded remarkably similar risk estimates with an odds ratio of 1.58, 95% CI 1.22-2.06 for women of API ancestry compared to White women

(data not shown). Furthermore, it is important to note that these sensitivity analyses, which were completely based on CCR data for which Hispanic origin is known, were able to separate Hispanics from Whites, and yet yielded almost identical risk estimates as from our analyses based on population controls.

Finally, our results should be interpreted with caution as they are based on a very small and specific subset of breast cancer cases (ie, women aged <45 born in the 1960s whose CCR record linked to a California birth record). It is difficult to ascertain the degree to which these results are generalizable to the population of women at risk in this age group. It is, however, important to emphasize that our results are consistent with the recent analysis of California breast cancer surveillance data conducted by Gomez and colleagues, in which social security data were used to impute missing nativity (US vs foreign born) and age-adjusted rates were calculated separately for US-born and foreign-born Asian women.<sup>15</sup> To our knowledge, that study is the only other study that has reported rates of breast cancer among young US-born API women exceeding those of non-Hispanic Whites.<sup>15</sup> Consistent with our findings, the elevated rate was only observed among women aged <55 years and was most pronounced in women <45, particularly among Filipina women. The consistency of our findings with the Gomez study, which used entirely different methods for ascertaining birthplace, and was based on a much larger proportion of the full population of breast cancer cases recorded in the cancer registry, suggests our findings are not likely due to a systematic bias introduced by our study design.

It is estimated that by 2050 Asian/Pacific Islanders will be 8% of the US population, a tripling of the proportion observed in 2000.<sup>14</sup> In the context of the rapidly growing number of young US-born API women, our findings, if replicated, could have major public

health implications for cancer control efforts in this historically understudied population. Evaluating whether such risks persist in other birth cohorts and beyond California should be a research priority. It is essential that such evaluations take into account birth place and API ancestry.

**ACKNOWLEDGMENTS**

This research was supported by funding from the California Breast Cancer Research Program (Grant #10PB-0165A). The authors would like to thank the following people for their technical or administrative support: Michael Layefsky for overseeing and performing the data linkages; Robert Gunier for his consultation on potential environmental factors of interest; Andrew Hertz for geocoding the case data; Phat Bui for directing the manual data abstraction of the birth records data; Theresa Saunders for her administrative support; the staff of the California Cancer Registry for providing statewide cancer files and the staff at the California Office of Vital Records for access and coordination of the birth records data abstraction.

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