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Asian ethnicity and breast cancer subtypes: a study from the California Cancer Registry

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Abstract

The distribution of breast cancer molecular subtypes has been shown to vary by race/ethnicity, highlighting the importance of host factors in breast tumor biology. We undertook the current analysis to determine population-based distributions of breast cancer subtypes among six ethnic

Asian groups in California. We defined immunohistochemical (IHC) surrogates for each breast cancer subtype among Chinese, Japanese, Filipina, Korean, Vietnamese, and South Asian patients diagnosed with incident, primary, invasive breast cancer between 2002 and 2007 in the California Cancer Registry as: hormone receptor-positive (HR+)/HER2– [estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+), human epidermal growth factor receptor 2-negative (HER2–)], triple-negative (ER–, PR–, and HER2–), and HER2-positive (ER±, PR±, and HER2+). We calculated frequencies of breast cancer subtypes among Asian ethnic groups and evaluated their associations with clinical and demographic factors. Complete IHC data were available for 8,140 Asian women. Compared to non-Hispanic White women, Korean [odds ratio (OR) = 1.8, 95% confidence interval (CI) = 1.5–2.2], Filipina (OR = 1.3, 95% CI = 1.2–1.5), Vietnamese (OR = 1.3, 95% CI = 1.1–1.6), and Chinese (OR = 1.1, 95% CI = 1.0–1.3) women had a significantly increased risk of being diagnosed with HER2-positive breast cancer subtypes after adjusting for age, stage, grade, socioeconomic status, histology, diagnosis year, nativity, and hospital ownership status. We report a significant ethnic disparity in HER2-positive breast cancer in a large population-based cohort enriched for Asian-Americans. Given the poor prognosis and high treatment costs of HER2-positive breast cancer, our results have implications for healthcare resource utilization, cancer biology, and clinical care.

Keywords

Breast cancer subtypes; Asian; Ethnicity; HER2-positive breast cancer; Hormone receptor-positive breast cancer; Triple-negative breast cancer

Introduction

Breast tumor gene expression analyses using DNA microarrays have identified distinct breast cancer molecular subtypes that differ markedly in prognosis [1, 2]. Compared to the two hormone receptor-positive (HR+) subtypes (luminal A and luminal B), the human epidermal growth factor receptor 2 (HER2)-positive/estrogen receptor (ER)-negative and basal-like subtypes have been shown to have the least favorable outcomes [2–6]. Combinations of immunohistochemical (IHC) markers have been defined and validated as clinically relevant surrogates for breast cancer subtyping by gene expression [3, 7–9]. Recent population-based studies using IHC data have observed an increased frequency of basal-like or triple-negative (estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative) breast cancers among African [10] and African-American [3, 11, 12] women. These important observations suggest that intrinsic tumor biology varies by race/ethnicity and may be partially responsible for the poor breast cancer outcomes observed among African-American women in the United States.

Asians comprise 57% of the world's population, and breast cancer incidence is increasing rapidly among many Asian populations [13–20]. Among Asians in the U.S., incidence and survival patterns vary considerably across ethnic populations [21, 22], and data from the Surveillance, Epidemiology, and End Results (SEER) cancer registry revealed Asian ethnic differences in hormone receptor positive versus negative breast cancer [23]. Breast cancer subtype distribution among ethnic groups of Asian women, however, has not been

systematically evaluated. Recent studies observed an increased prevalence of HER2-positive breast cancer among Asian-Americans unselected for specific Asian ethnicity [24, 25]. California is home to one of the largest Asian populations outside of Asia, making it a rich geographic region in which to study Asian ethnic differences in breast cancer subtypes. The California Cancer Registry (CCR) has been collecting data on HER2 status on all breast cancers diagnosed statewide since 1999, in addition to ER and PR data. Using this unique data resource, we evaluated differences in the distribution of breast cancer subtypes among the six largest Asian ethnic groups in California.

Methods

Study population

The CCR is a population-based registry that collects data about all cancers diagnosed statewide since 1988. Case ascertainment is estimated to be 99% complete. For the current study, newly diagnosed cases of primary invasive breast cancer in women of all ages were identified from the CCR between January 1, 2002 and December 31, 2007.

Race/ethnicity data in the CCR are based on hospital records, which are in turn based on self-report, assumption of hospital personnel, or inference using information such as birthplace, race/ethnicity of parent, maiden name, or surname [26]. Socioeconomic status (SES) in the CCR was determined using a composite residential neighborhood-level index that combines Census 2000 measures of education, income, occupation, and cost of living within Census block groups, as described previously [27]. This index was categorized into quintiles based on the statewide distribution of neighborhood-level SES (1 = lowest and 5 = highest).

To classify nativity for patients of Asian ethnicity, we used two sources of information about birthplace: (1) registry-based data, which were available for 5,558 (68%) cases; and (2) for those who had unknown birthplace ($n = 2,582$), statistical imputation of immigrant status using the first five digits of the patient's Social Security number (SSN), indicating the state and year of issuance [28, 29]. We classified cases who received their SSN before age 25 years as US-born, whereas those who had received their SSN at or after age 25 were classified as foreign-born. The age cut-point was set at 25 years based on self-reported nativity in previously interviewed cancer patients ($N = 1,836$) [30], and maximization of the area under the receiver-operating characteristic curve. This age cut-point resulted in immigrant status classifications associated with 84% sensitivity and 80% specificity for detecting foreign-born, and was similar across the Asian populations.

American Joint Committee on Cancer (AJCC) stage was used to define disease stage as either I, II, III, IV, or unstaged [31]. Tumor grade was defined as I, II, III, or other/unknown based on Bloom–Richardson criteria [32]. Tumor histology was recorded as ductal (International Classification of Diseases—Oncology, 3rd edition (ICD-O-3) morphology code 8500), lobular (ICD-O-3 morphology code 8520), or mixed/other (all remaining ICD-O-3 morphology codes). Hospital ownership status was recorded as private, public, or unknown based on data obtained from the Office of Statewide Health Planning and Development [33].

Breast cancer subtype definitions

The CCR has mandated statewide collection of breast cancer ER and PR data since 1990 and HER2 status since 1999. In the CCR, ER, PR, and HER2 status are classified as positive, negative, borderline, not tested, not recorded, or unknown based on the laboratory results and pathologist's interpretation in the medical records. In general, ER and PR status are based on the results of conventional dextran-coated charcoal ER and PR assays or IHC (≥ 5% nuclear staining = positive) [34]. HER2 status is recorded on the basis of IHC score (0, 1+ = negative, 2+ = borderline, 3+ = positive) or fluorescence in situ hybridization (≥ 2 copies of *HER2* = negative, >2 copies = positive) [35]. The validity of ER and PR classification in two SEER registries (including Los Angeles County, California) was compared with classification by a single expert pathology laboratory, and the agreement was found to be substantial ($\kappa = 0.70$) for ER and moderate ($\kappa = 0.60$) for PR [36].

For this study, combinations of IHC markers were used as surrogates for molecular breast cancer subtype as follows: HR+/HER2− (ER+ and/or PR+, HER2−), HER2+ (HER2+, ER±, and PR±), and triple-negative (ER−, PR−, and HER2−). Female cases of first, primary, invasive breast carcinoma were included if the status of all the three IHC markers (ER, PR, and HER2) was known. Cases in which any one marker was defined as borderline, not tested, not recorded, or unknown were excluded.

A total of 126,577 incident cases of invasive breast cancer were identified from the CCR between January 1, 2002 and December 31, 2007 among Asian, NH White, NH Black, and Hispanic women. A total of 89,009 (70% of sample) had complete and unequivocal data for all the three IHC markers. In this time period, 11,487 cases belonging to the six largest Asian groups were identified, and 8,140 (71% of sample) had complete IHC marker data. Borderline IHC results accounted for 2% of the cases excluded. We used multivariate logistic regression models to identify associations with missing tumor marker data among Asians. Independent predictors of having missing data on at least one marker included race/ethnicity ($P = 0.05$), age ($P = 0.0002$), stage ($P < 0.0001$), grade ($P < 0.0001$), tumor histology ($P = 0.001$), SES ($P < 0.0001$), year of diagnosis ($P < 0.0001$), place of birth ($P < 0.0001$), and hospital ownership status ($P < 0.0001$).

Statistical analysis

All analyses were conducted using SAS version 9.1 software (SAS Institute Inc, Cary, NC, USA). We first computed the frequencies of the three breast cancer subtypes (HR+/HER2−, HER2+, and triple-negative) among six Asian ethnic groups in the CCR (Japanese, Chinese, Filipina, Korean, Vietnamese, and South Asian). Women belonging to any other Asian or Pacific Islander ethnic group were grouped together as “Other Asian.” Breast cancer subtype frequencies were also calculated in NH White, NH Black, and Hispanic reference populations. Univariate differences in subtype distribution by race/ethnicity, age at diagnosis, stage at diagnosis, tumor grade, tumor histology, year of diagnosis, neighborhood SES, nativity, and public versus private hospital ownership were evaluated using the χ^2 test. Since genetic risk of breast cancer is associated with young age at diagnosis [37], an additional χ^2 test was performed to compare the frequency of breast cancer subtypes by race/ethnicity in two age groups (<40 vs. ≥ 40 years).

We used multivariate logistic regression models to calculate odds ratios (ORs) for the association of either HER2+ or triple-negative breast cancer, compared to HR+/HER2– breast cancer as the referent tumor subtype, for each Asian ethnic group, compared with NH Whites as the referent racial/ethnic group. ORs were adjusted for age at diagnosis, stage at diagnosis, tumor grade, neighborhood SES, year of diagnosis, nativity, and hospital ownership status.

Results

Subtype distribution by race/ethnicity

Frequencies of breast cancer subtype by detailed racial/ethnic group among eligible cases are presented in Table 1. Of 89,009 analyzed cases, 58,555 (66%) belonged to the HR+/HER2– subtype, 18,524 (21%) to the HER2+ subtype, and 11,930 (13%) to the triple-negative subtype. Among Asians, Japanese women had the most favorable subtype distribution, with a relatively high frequency of the HR+/HER2– subtype and a low frequency of HER2+ and triple-negative subtypes. Korean women, by comparison, had the least favorable subtype distribution with a relatively low frequency of the HR+/HER2– subtype and a high frequency of the HER2+ subtype. In contrast to the 19% frequency of HER2+ breast cancer in NH Whites, Korean, Filipina, and Vietnamese women had increased frequencies of HER2+ disease, 36% (95% CI 32–40%), 31% (95% CI 29–32%), and 29% (95% CI 26–33%), respectively. NH Black women had a higher frequency of triple-negative breast cancer (26%, $n = 1,385$) when compared with NH White women (12%, $n = 7,074$). The distribution of subtypes in all the ethnic groups, except Japanese, was significantly different from that among NH Whites at the $P < 0.0001$ level.

Subtype associations with clinical and demographic factors among Asian women

The distribution of breast cancer subtypes varied significantly among Asian women by age, stage at diagnosis, SES, tumor grade, year of diagnosis, histology, nativity, and hospital ownership status (Table 2). HR+/HER2– tumors were less common in younger age groups and had a lower stage distribution than HER2+ and triple-negative subtypes. The majority of triple-negative tumors were of high grade. The frequency of HER2+ breast cancer decreased and HR+/HER2– breast cancer increased with increasing SES. By contrast, the frequency of triple-negative breast cancer remained fairly constant across all the SES groups. In this sample, 78% of Asian cases were foreign-born, and the majority (70%) received treatment from public hospitals. Foreign-born women had increased frequencies of HER2+ breast cancer when compared to US-born women, though the frequency of triple-negative breast cancer was similar regardless of nativity.

Subtype distribution by ethnicity and age at diagnosis

The frequency of breast cancer subtype by Asian ethnic group was further stratified by age group at diagnosis (less than 40 years vs. greater than or equal to 40 years of age). Among Japanese women, HR+/HER2– was the most common subtype in both the younger and older age groups (57 and 71%, respectively). HER2+ and triple-negative tumors were relatively more frequent among younger Japanese women, though these differences were not statistically significant. Young South Asian, Vietnamese, and Filipina women had the least

favorable subtype distributions, with a high frequency of HER2+ breast cancer among young Filipina women (41%) and increased frequencies of triple-negative breast cancer among young Vietnamese (28%) and South Asian (23%) women. The highest frequency of triple-negative breast cancer was observed among younger NH Black women (36%), although relatively high frequencies were also observed among younger Hispanic women (27%), older NH Black women (25%), and younger NH White women (22%).

Multivariate analyses

In multivariate analyses, Korean women were 80% more likely than NH White women to be diagnosed with HER2+ as opposed to HR+/HER2– breast cancer (Table 3). Similarly, Filipina, Vietnamese, and Chinese women were 30, 30, and 10% more likely, respectively, than NH White women to be diagnosed with HER2+ disease. Conversely, Filipina and Chinese women were 30 and 20% less likely, respectively, than NH White women to be diagnosed with triple-negative as opposed to HR+/HER2– breast cancer, whereas South Asian women were 30% more likely. NH Black women had double the rate of triple-negative breast cancer compared with NH White women, and Hispanic women had a 20% higher rate.

Discussion

Our study represents one of the most comprehensive population-based analyses of breast cancer subtypes reported in the literature, with over 89,000 cases included. Furthermore, this is the first study to evaluate breast cancer subtypes in a large and representative dataset enriched for Asian-Americans. Most importantly, we found a significantly increased frequency of HER2-positive breast cancer among four of the largest ethnic groups of Asian-American women. Compared to NH White women, Korean, Filipina, Vietnamese, and Chinese women had a significantly increased risk of being diagnosed with HER2-positive breast cancer. Triple-negative breast cancer, by contrast, was not more common among East Asian, compared to NH White, women in our study. Among Filipina women <40 years of age, HER2-positive breast cancer was especially common (41%).

Like others, we observed a high proportion of breast cancer among young Asian women. In contrast to NH Whites, in whom 4% of all breast cancers developed in women less than age 40, breast cancer developed in 10% of Chinese, 7% of Filipina, 13% of Korean, 12% of Vietnamese, and 15% of South Asian women under the age of 40. Young age at breast cancer diagnosis is highly associated with genetic predisposition to breast cancer, but unlike the association between germline mutations in *BRCA1* and triple-negative breast cancer [38–40], there is as yet no known familial gene mutation that confers increased risk of HER2-positive disease. Most BRCA-associated breast cancers do not demonstrate HER2 positivity [41]. Presumably, similar to *BRCA1* and basal-like breast cancer, ethnic specific genetic factors exist that influence the expression of the HER2-positive phenotype. Our results suggest that further studies are warranted to explore a potential genetic basis for the increased frequency of HER2-positive breast cancer among certain ethnic groups of Asian women.

Asians comprise 57% of the world's population, and thus, our results have particular relevance to the challenges of breast cancer treatment globally [13, 14]. Breast cancer incidence is on the rise in many countries in Asia, as well as among Asian-Americans [15–20]. Breast cancer occurs at a younger age in Asia, and the postmenopausal rise in breast cancer incidence observed in Western populations is not seen in most Asian populations [14, 20, 42]. Classic studies of Japanese and Chinese migrants to the United States, however, highlight the importance of lifestyle factors by demonstrating that breast cancer risk rises over several generations nearly approaching that of U.S. Whites [43]. It is unclear the degree to which the subtype distribution observed in our study population will change over time with increased acculturation to a Western lifestyle and a higher percentage of U.S.-born Asian-Americans. Nonetheless, our results have important implications for current resource utilization and clinical care both in the United States and in Asia. HER2-positive breast cancer has an aggressive clinical course with poorer breast cancer-specific survival than most other breast cancer subtypes [2, 6]. Combination chemotherapy and a year of trastuzumab therapy represent the current standard treatment for this disease, even in patients with early stage disease [44]. As a result, the costs associated with the treatment of HER2-positive breast cancer are much higher than those for other breast cancer subtypes [45]. These high costs of treatment are likely to place a financial burden on the public healthcare system in California that provides care for many Asian-Americans in the state, in addition to the healthcare systems of countries of limited resources providing cancer care in Asia.

Although our study is strengthened by the large size and population-based setting of the CCR, it also has limitations inherent to registry-based data. The CCR does not collect patient-level data on SES or other environmental or lifestyle factors. Although we adjusted for neighborhood SES, which is correlated with individual SES [46], these measures capture different types of exposures and, therefore, may have distinct, independent associations with breast cancer subtypes. Though HER2 data collection was mandated starting in January 1999, uptake was not immediate. As a result, we observed increased absence of HER2 data in earlier diagnosis years with improvements thereafter. Since we could not adjudicate borderline tumor marker test results and there was no centralized pathology review, we were unable to assign a subtype to borderline IHC results (2% of cases excluded), and therefore chose to exclude those cases from the current analysis. Despite these shortcomings, our results for African-Americans and NH Whites were consistent with those from prior studies [3, 12], and clinical features such as stage and grade distribution were as expected according to breast cancer subtype, suggesting that our results are valid and generalizable. Our data source is unique not only in recording HER2 status for a decade, but also in covering a population in which large numbers of Asian women well characterized by ethnicity are represented. Compared to previous studies of breast cancer subtype by ethnicity [3, 12]; our study includes far greater case numbers and thereby lends increased stability and confidence to our results.

In conclusion, we report a significant ethnic disparity in HER2-positive breast cancer among Asian women in a large, population-based cancer registry. Specifically, HER2-positive breast cancer is overrepresented among Korean, Filipina, Vietnamese, and Chinese women when compared to NH White women in California. These results have clinical and

healthcare resource utilization implications, given the poor prognosis of HER2-positive breast cancer and the high costs associated with the treatment of this breast cancer subtype. Future studies to explore the basis for this disparity are warranted and may identify genetic, lifestyle, and environmental risk factors responsible for the differences we observed, with implications for prevention and treatment.

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References

1. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. *Nature*. 2000; 406:747–752. [PubMed: 10963602]
2. Sorlie T, Tibshirani R, Parker J, et al. Repeated observation of breast tumor subtypes in independent gene expression data sets. *Proc Natl Acad Sci U S A*. 2003; 100:8418–8423. [PubMed: 12829800]
3. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA*. 2006; 295:2492–2502. [PubMed: 16757721]
4. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. *Clin Cancer Res*. 2007; 13:4429–4434. [PubMed: 17671126]
5. Rakha EA, El-Rehim DA, Paish C, et al. Basal phenotype identifies a poor prognostic subgroup of breast cancer of clinical importance. *Eur J Cancer*. 2006; 42:3149–3156. [PubMed: 17055256]
6. Slamon DJ, Clark GM, Wong SG, et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. *Science*. 1987; 235:177–182. [PubMed: 3798106]
7. Cheang MC, Voduc D, Bajdik C, et al. Basal-like breast cancer defined by five biomarkers has superior prognostic value than triple-negative phenotype. *Clin Cancer Res*. 2008; 14:1368–1376. [PubMed: 18316557]
8. Nielsen TO, Hsu FD, Jensen K, et al. Immunohistochemical and clinical characterization of the basal-like subtype of invasive breast carcinoma. *Clin Cancer Res*. 2004; 10:5367–5374. [PubMed: 15328174]
9. Tischkowitz M, Brunet JS, Begin LR, et al. Use of immunohistochemical markers can refine prognosis in triple negative breast cancer. *BMC Cancer*. 2007; 7:134. [PubMed: 17650314]
10. Huo D, Ikpat F, Khramtsov A, et al. Population differences in breast cancer: survey in indigenous African women reveals over-representation of triple-negative breast cancer. *J Clin Oncol*. 2009; 27:4515–4521. [PubMed: 19704069]
11. Bauer KR, Brown M, Cress RD, et al. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. *Cancer*. 2007; 109:1721–1728. [PubMed: 17387718]
12. Lund MJ, Trivers KF, Porter PL, et al. Race and triple negative threats to breast cancer survival: a population-based study in Atlanta, GA. *Breast Cancer Res Treat*. 2009; 113:357–370. [PubMed: 18324472]
13. Liede A, Narod SA. Hereditary breast and ovarian cancer in Asia: genetic epidemiology of BRCA1 and BRCA2. *Hum Mutat*. 2002; 20:413–424. [PubMed: 12442265]
14. Yip CH. Breast cancer in Asia. *Methods Mol Biol*. 2009; 471:51–64. [PubMed: 19109774]
15. Seow A, Duffy SW, McGee MA, et al. Breast cancer in Singapore: trends in incidence 1968–1992. *Int J Epidemiol*. 1996; 25:40–45. [PubMed: 8666502]
16. Keegan TH, Gomez SL, Clarke CA, et al. Recent trends in breast cancer incidence among 6 Asian groups in the Greater Bay Area of Northern California. *Int J Cancer*. 2007; 120:1324–1329. [PubMed: 17163416]

17. Yang L, Parkin DM, Ferlay J, et al. Estimates of cancer incidence in China for 2000, projections for 2005. *Cancer Epidemiol Biomarkers Prev.* 2005; 14:243–250. [PubMed: 15668501]
18. Yang L, Parkin DM, Li L, et al. Time trends in cancer mortality in China: 1987–1999. *Int J Cancer.* 2003; 106:771–783. [PubMed: 12866039]
19. Yang L, Parkin DM, Li LD, et al. Estimation and projection of the national profile of cancer mortality in China: 1991–2005. *Br J Cancer.* 2004; 90:2157–2166. [PubMed: 15150609]
20. Son BH, Kwak BS, Kim JK, et al. Changing patterns in the clinical characteristics of Korean patients with breast cancer during the last 15 years. *Arch Surg.* 2006; 141:155–160. [PubMed: 16490892]
21. Miller BA, Chu KC, Hankey BF, et al. Cancer incidence and mortality patterns among specific Asian and Pacific Islander populations in the U.S. *Cancer Causes Control.* 2008; 19:227–256. [PubMed: 18066673]
22. Li CI, Malone KE, Daling JR. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med.* 2003; 163:49–56. [PubMed: 12523916]
23. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by race and ethnicity among women 50 years of age and older. *Cancer Epidemiol Biomarkers Prev.* 2002; 11:601–607. [PubMed: 12101106]
24. Kwan ML, Kushi LH, Weltzien E, et al. Epidemiology of breast cancer subtypes in two prospective cohort studies of breast cancer survivors. *Breast Cancer Res.* 2009; 11:R31. [PubMed: 19463150]
25. Parise CA, Bauer KR, Brown MM, et al. Breast cancer subtypes as defined by the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2) among women with invasive breast cancer in California, 1999–2004. *Breast J.* 2009; 15(6):593–602. E pub 9/22/2009. [PubMed: 19764994]
26. Gomez SL, Le GM, West DW, et al. Hospital policy and practice regarding the collection of data on race, ethnicity, and birthplace. *Am J Public Health.* 2003; 93:1685–1688. [PubMed: 14534222]
27. Yost K, Perkins C, Cohen R, et al. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control.* 2001; 12:703–711. [PubMed: 11562110]
28. Block G, Matanoski GM, Seltser RS. A method for estimating year of birth using social security number. *Am J Epidemiol.* 1983; 118:377–395. [PubMed: 6613981]
29. Shimizu H, Ross RK, Bernstein L, et al. Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. *Br J Cancer.* 1991; 63:963–966. [PubMed: 2069852]
30. Gomez SL, Glaser SL, Kelsey JL, et al. Bias in completeness of birthplace data for Asian groups in a population-based cancer registry (United States). *Cancer Causes Control.* 2004; 15:243–253. [PubMed: 15090719]
31. California Cancer Reporting System Standards. Eighth. Vol. 1. AJCC Stage Group; Cancer Reporting in California Abstracting and Coding Procedures for Hospitals. Revised May, 2008: V. 7.5 http://www.ccrca.org/Vol_1_May_2008_html/Vol_1_08.htm
32. California Cancer Reporting System Standards. Eighth. Vol. 1. Bloom- Richardson Grade for Breast Cancer; Cancer Reporting in California Abstracting and Coding Procedures for Hospitals. Revised May, 2008: V.3.5.8 http://www.ccrca.org/Vol_1_May_2008_html/Vol_1_08.htm
33. Office of Statewide Health Planning and Development (OSHDP). Annual Utilization Report of Hospitals. 2001. <http://www.oshpd.cahwnet.gov>
34. California Cancer Reporting System Standards. Cancer Reporting in California Abstracting and Coding Procedures for Hospitals. 1 Revised May, 2008. http://www.ccrca.org/Vol_1_May_2008_html/Vol_1_08.htm.
35. California Cancer Reporting System Standards. Cancer Reporting in California Abstracting and Coding Procedures for Hospitals. 1 Revised May, 2008: V.6.4 Tumor Marker California-1. http://www.ccrca.org/Vol_1_May_2008_html/Vol_1_08.htm.
36. Ma H, Wang Y, Sullivan-Halley J, et al. Breast cancer receptor status: do results from a centralized pathology laboratory agree with SEER registry reports? *Cancer Epidemiol Biomarkers Prev.* 2009; 18:2214–2220. [PubMed: 19661080]

37. Daly, MB.; Axilbund, JE.; Bryant, E., et al. NCCN clinical practice guidelines in oncology; Genetic/familial high-risk assessment: breast and ovarian, v.1 2010. 2010. p. 18 Available at <http://www.nccn.org>
38. Foulkes WD, Stefansson IM, Chappuis PO, et al. Germline BRCA1 mutations and a basal epithelial phenotype in breast cancer. *J Natl Cancer Inst.* 2003; 95:1482–1485. [PubMed: 14519755]
39. Lakhani SR, Van De Vijver MJ, Jacquemier J, et al. The pathology of familial breast cancer: predictive value of immunohistochemical markers estrogen receptor, progesterone receptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. *J Clin Oncol.* 2002; 20:2310–2318. [PubMed: 11981002]
40. Olopade OI, Grushko T. Gene-expression profiles in hereditary breast cancer. *N Engl J Med.* 2001; 344:2028–2029. [PubMed: 11430337]
41. Grushko TA, Blackwood MA, Schumm PL, et al. Molecular-cytogenetic analysis of HER-2/neu gene in BRCA1-associated breast cancers. *Cancer Res.* 2002; 62:1481–1488. [PubMed: 11888924]
42. Han W, Kim SW, Park IA, et al. Young age: an independent risk factor for disease-free survival in women with operable breast cancer. *BMC Cancer.* 2004; 4:82. [PubMed: 15546499]
43. Ziegler RG, Hoover RN, Pike MC, et al. Migration patterns and breast cancer risk in Asian-American women. *J Natl Cancer Inst.* 1993; 85:1819–1827. [PubMed: 8230262]
44. Carlson RW, Allred DC, Anderson BO, et al. NCCN clinical practice guideline: breast cancer. *J Natl Compr Canc Netw.* 2009; 7:122–192. [PubMed: 19200416]
45. Kurian AW, Thompson RN, Gaw AF, et al. A cost-effectiveness analysis of adjuvant trastuzumab regimens in early HER2/neu-positive breast cancer. *J Clin Oncol.* 2007; 25:634–641. [PubMed: 17308268]
46. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *Am J Public Health.* 1992; 82:703–710. [PubMed: 1566949]

Table 1
Race/ethnicity of women in California diagnosed with incident, invasive breast cancer from 2002 to 2007 with immunohistochemical data for ER, PR, and HER2 ($n = 89,009$)*

	HR+/HER2-		HER2+		Triple-negative		Total
	N	(%) (95% CI)	N	(%) (95% CI)	N	(%) (95% CI)	
Japanese	794	(70%) (67–73%)	221	(19%) (17–22%)	121	(11%) (9–12%)	1136
Chinese	1464	(64%) (62–65%)	591	(26%) (24–27%)	250	(11%) (10–12%)	2305
Filipina	1659	(59%) (57–61%)	859	(31%) (29–32%)	284	(10%) (9–11%)	2802
Korean	310	(49%) (45–53%)	226	(36%) (32–40%)	92	(15%) (12–17%)	628
Vietnamese	375	(57%) (53–60%)	194	(29%) (26–33%)	94	(14%) (12–17%)	663
South Asian	359	(59%) (55–63%)	140	(23%) (20–26%)	107	(18%) (15–21%)	606
Other Asian ^d	566	(58%) (55–61%)	281	(29%) (26–32%)	126	(13%) (11–15%)	973
NH White	42128	(70%) (69–70%)	11296	(19%) (18–19%)	7074	(12%) (11–12%)	60498
NH Black	2706	(51%) (50–52%)	1201	(23%) (22–24%)	1385	(26%) (25–27%)	5292
Hispanic	8194	(58%) (57–59%)	3515	(25%) (24–26%)	2397	(17%) (16–18%)	14106
Total		58555	18524		11930		89009

HR+/HER2- = ER+ and/or PR+, HER2-; HER2+ = ER+, PR+, and HER2+; Triple-negative = ER-, PR-, and HER2-

* All groups, except Japanese, were significantly different from NH Whites with respect to subtype distribution at the $P < 0.0001$ level. All the P values were adjusted for multiple comparisons using the Bonferroni adjustment

Includes women of Asian Indian, Pakistani, Sri Lankan, and Bangladeshi ethnicity_p

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Table 2
Characteristics of Asian women in California diagnosed with incident, invasive breast cancer from 2002 to 2007 with immunohistochemical data for ER, PR, and HER2 (*n* = 8,140)

	HR+/HER2– <i>n</i> = 4,961	HER2+ <i>n</i> = 2231	Triple-negative <i>n</i> = 948	$\chi^2 P$
Age at diagnosis, years (mean)	57.3	54.9	55.2	
Age at diagnosis, grouped years				
0–39	345 (52%)	216 (32%)	107 (16%)	<0.0001
40–49	1272 (60%)	607 (29%)	238 (11%)	
50+	3344 (62%)	1408 (26%)	603 (11%)	
AJCC stage at diagnosis				
I	2404 (68%)	809 (23%)	324 (9%)	<0.0001
II	1853 (58%)	922 (29%)	428 (13%)	
III	450 (51%)	310 (35%)	120 (14%)	
IV	137 (47%)	112 (39%)	41 (14%)	
Unknown	117 (51%)	78 (34%)	35 (15%)	
SES quintile ^a				
1st	316 (54%)	200 (34%)	66 (11%)	<0.0001
2nd	640 (56%)	356 (31%)	139(12%)	
3rd	946 (61%)	427 (27%)	184(12%)	
4th	1310 (61%)	591 (27%)	251 (12%)	
5th	1749 (64%)	657 (24%)	308 (11%)	
Grade				
I	1162 (87%)	142 (11%)	34 (3%)	<0.0001
II	2389 (72%)	759 (23%)	178 (5%)	
III	1111 (38%)	1140 (39%)	662 (23%)	
Other/unknown	299 (53%)	190 (34%)	74 (13%)	
Diagnosis year				
2002	615 (59%)	289 (28%)	143 (14%)	0.01
2003	674 (59%)	316 (28%)	157(14%)	
2004	779 (61%)	338 (26%)	160(13%)	
2005	804 (60%)	387 (29%)	152 (11%)	
2006	962 (62%)	434 (28%)	159 (10%)	
2007	1127 (64%)	467 (26%)	177 (10%)	
Histology				
Ductal	3533 (58%)	1840 (30%)	744 (12%)	<0.0001
Lobular	289 (85%)	39 (11%)	13 (4%)	
Mixed/other	1139 (68%)	352 (21%)	191 (11%)	
Nativity				
US-born	1182 (66%)	405 (23%)	193 (11%)	<0.0001
Foreign-born	3779 (59%)	1826 (29%)	755 (12%)	

	HR+/HER2- n = 4,961	HER2+ n = 2231	Triple-negative n = 948	χ^2 P
Hospital status				
Public	3555 (62%)	1473 (26%)	686 (12%)	<0.0001
Private	583 (57%)	348 (34%)	96 (9%)	
Unknown	823 (59%)	410 (29%)	166 (12%)	

HR+/HER2- = ER+ and/or PR+, HER2-; HER2+ = ER±, PR±, and HER2+; Triple-negative = ER-, PR-, and HER2-

^aNeighborhood-level socioeconomic status (see “methods”): 1st quintile represents those with the lowest SES and the 5th quintile represents those with the highest SES

Table 3

Associations between breast cancer subtype and Asian ethnicity, age at diagnosis, stage at diagnosis, grade, histology, SES, year of diagnosis, nativity, and hospital status as estimated by ORs with 95% confidence intervals (CIs), among women in California diagnosed with incident, invasive breast cancer from 2002 to 2007

	HR+/HER2-		HER2+		Triple-negative	
	OR	95% CI	OR	95% CI	OR	95% CI
Race/ethnicity						
Chinese vs. NH White	1.0		1.1	1.0-1.3	0.8	0.7-1.0
Filipina vs. NH White	1.0		1.3	1.2-1.5	0.7	0.6-0.9
Hispanic vs. NH White	1.0		1.1	1.0-1.2	1.2	1.1-1.3
Japanese vs. NH White	1.0		1.0	0.8-1.2	0.9	0.7-1.1
Korean vs. NH White	1.0		1.8	1.5-2.2	1.2	0.9-1.6
NH Black vs. NH White	1.0		1.2	1.1-1.3	2.0	1.8-2.1
South Asian vs. NH White	1.0		1.0	0.8-1.3	1.3	1.0-1.7
Vietnamese vs. NH White	1.0		1.3	1.1-1.6	1.0	0.8-1.4
Age at diagnosis						
0-39 years vs. 50+ years	1.0		1.4	1.3-1.6	1.5	1.3-1.6
40-49 years vs. 50+ years	1.0		1.2	1.1-1.2	1.0	1.0-1.1
Stage at diagnosis						
AJCC II vs. I	1.0		1.2	1.2-1.3	1.1	1.1-1.2
AJCC III vs. I	1.0		1.6	1.5-1.7	1.1	1.0-1.2
AJCC IV vs. I	1.0		1.8	1.7-2.0	1.0	0.9-1.1
AJCC unknown vs. I	1.0		1.6	1.4-1.7	1.2	1.0-1.3
Grade						
Grade II vs. grade I	1.0		2.3	2.1-2.4	3.2	2.9-3.6
Grade III vs. grade I	1.0		6.8	6.4-7.2	29.5	26.4-33.0
Grade other/unknown vs. grade I	1.0		4.5	4.1-4.9	14.4	12.6-16.4
Histology						
Lobular vs. ductal	1.0		0.4	0.3-0.4	0.2	0.1-0.2
Mixed/other vs. ductal	1.0		0.7	0.6-0.7	0.8	0.7-0.8
SES quintile ^d						

	HR+/HER2-	HER2+		Triple-negative	
	OR	OR	95% CI	OR	95% CI
1 vs. 5	1.0	1.2	1.1-1.3	1.1	1.0-1.2
2 vs. 5	1.0	1.1	1.1-1.2	1.1	1.0-1.2
3 vs. 5	1.0	1.1	1.0-1.2	1.0	1.0-1.1
4 vs. 5	1.0	1.0	1.0-1.1	1.0	1.0-1.1
Year of diagnosis	1.0	1.0	0.9-1.0	1.0	1.0-1.0
Nativity					
US-born vs. foreign-born	1.0	0.9	0.9-1.0	1.1	1.0-1.2
Nativity unknown vs. foreign-born	1.0	0.8	0.8-0.9	0.9	0.8-1.0
Hospital status					
Public vs. private	1.0	0.8	0.7-0.8	1.0	0.9-1.1
Unknown vs. private	1.0	0.8	0.8-0.9	1.1	1.0-1.2

HR+/HER2- = ER+ and/or PR+, HER2-; HER2+ = ER±, PR±, and HER2+; Triple-negative = ER-, PR-, and HER2-

^aNeighborhood-level socioeconomic status (see methods): 1st quintile represents those with the lowest SES and the 5th quintile represents those with the highest SES