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John, Esther M
McGuire, Valerie
Kurian, Allison W
et al.

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Racial/ethnic disparities in survival after breast cancer diagnosis by estrogen and progesterone receptor status: A pooled analysis

Esther M. John[1,2,3], Valerie McGuire[1], Allison W. Kurian[1,2,3], Jocelyn Koo[3], Salma Shariff-Marco[4,5], Scarlett Lin Gomez[4,5], Iona Cheng[4,5], Theresa H.M. Keegan[6], Marilyn L. Kwan[7], Leslie Bernstein[9], Cheryl Vigen[8], Anna H. Wu[8]

[1]Department of Epidemiology & Population Health, Stanford University School of Medicine, Stanford, CA 94304

[2]Department of Medicine, Division of Oncology, Stanford University School of Medicine, Stanford, CA 94304

[3]Stanford Cancer Institute, Stanford University School of Medicine, Stanford, CA 94304

[4]Department of Epidemiology & Biostatistics, University of California San Francisco, San Francisco, CA 94158

[5]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA 94158

[6]Division of Hematology and Oncology, UC Davis Comprehensive Cancer Center, University of California, Davis, CA 95817

[7]Division of Research, Kaiser Permanente Northern California, Oakland, CA 94612

[8]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA 90089

[9]Department of Population Sciences, Beckman Research Institute of City of Hope, Duarte, CA 91010

Abstract

Background: Limited studies have investigated racial/ethnic survival disparities for breast cancer (BC) defined by estrogen receptor (ER) and progesterone receptor (PR) status in a multiethnic population.

Methods: Using multivariable Cox proportional hazards models, we assessed associations of race/ethnicity with ER/PR-specific BC mortality in 10,366 Californian women diagnosed with BC from 1993-2009. We evaluated joint associations of race/ethnicity, healthcare, sociodemographic, and lifestyle factors with mortality.

Corresponding author: Esther M. John, PhD, Stanford Cancer Institute, 780 Welch Road, Suite CJ250C, MC 5767, Stanford CA 94304. emjohn@stanford.edu. Phone: 650-497-1221.

Results: Among women with ER/PR+ BC, BC-specific mortality was similar among Hispanic and Asian American women, but higher among African American women (hazard ratio (HR) 1.31, 95% confidence interval 1.05-1.63) compared to non-Hispanic White (NHW) women. BC-specific mortality was modified by surgery type, hospital type, education, neighborhood socioeconomic status (SES), smoking history, and alcohol consumption. Among African American women, BC-specific mortality was higher among those treated at non-accredited hospitals (HR 1.57, CI 1.21-2.04) and those from lower SES neighborhoods (HR 1.48, CI 1.16-1.88) compared to NHW women without these characteristics. BC-specific mortality was higher among African American women with at least some college education (HR 1.42, CI 1.11-1.82) compared to NHW women with similar education. For ER−/PR− disease, BC-specific mortality did not differ by race/ethnicity and associations of race/ethnicity with BC-specific mortality varied only by neighborhood SES among African American women.

Conclusions: Racial/ethnic survival disparities are more striking for ER/PR+ than ER−PR− BC. Social determinants and lifestyle factors may explain some of the survival disparities for ER/PR+ BC.

Impact: Addressing these factors may help reduce the higher mortality of African American women with ER/PR+ BC.

Introduction

Breast cancer (BC) mortality rates in the United States (U.S.) have declined by 40% since 1989, but disparities persist (1,2) and are widening between African American and non-Hispanic White (NHW) women (3). Compared to NHW women, African American women have worse BC survival, Hispanic women have worse or similar survival, and Asian American women have similar or better survival (4–6). Tumor biology, treatment, healthcare, patient characteristics, medical history, behavioral factors, and social determinants have been shown to affect BC survival (7–10), but questions remain about the drivers of the observed survival disparities (6,11–13). Survival is lower for estrogen receptor (ER) negative and progesterone receptor (PR) negative (ER−/PR−) BC than ER or PR positive (ER/PR+) BC (14–18). ER−/PR− BC accounts for about 20% of new BC diagnoses, and is more frequently diagnosed among African American and Hispanic women (19). Studies that examined racial/ethnic survival disparities for BC defined by ER, PR, human epidermal growth factor receptor 2 (HER2), or other tumor markers (14,20–26) and underlying factors are largely limited to comparisons of African American and NHW women; only one study has examined subtype-specific survival in a more diverse sample of BC patients (11). Less is known about the factors contributing to the generally better BC survival of Hispanic and Asian American women compared to NHW and African American women. A better understanding of the contributing factors that may be specific to particular racial/ethnic groups is critical for guiding tailored approaches aimed at reducing BC survival disparities.

To address these gaps in knowledge, especially for Hispanic and Asian American women, we pooled multiethnic data from the California Breast Cancer Survivorship Consortium (CBCSC) (27) and the Northern California Breast Cancer Family Registry (NC-BCFR) (28). Using the wealth of cancer registry and questionnaire data that have been harmonized across

the studies in CBCSC, we assessed associations of race/ethnicity with ER/PR-specific mortality and variations by selected healthcare, sociodemographic, and lifestyle characteristics.

Materials and Methods

Study sample

The CBCSC harmonized cancer registry and questionnaire data from six population-based BC studies conducted in California (27). The present analysis is based on three population-based case-control studies of BC [the Asian American Breast Cancer Study (AABCS) (29); the Women's Contraceptive and Reproductive Experiences Study (CARE) (30); and the San Francisco Bay Area Breast Cancer Study (SFBCS) (31)] and two cohort studies [the California Teachers Study (CTS) (32); and the Multiethnic Cohort (MEC) (33)], and includes 9,701 women diagnosed from 1993-2007 with an invasive BC and more than 30 days of follow-up. In addition, we included data from the NC-BCFR which enrolled women newly diagnosed with BC into a prospective family study (28). After excluding women who also participated in SFBCS (n=320) or CTS (n=23), the NC-BCFR contributed data on 2,647 invasive BC cases diagnosed from 1995-2009 with more than 30 days of follow-up. Cases who did not self-identify as African American, Asian American, Hispanic, or NHW were excluded (N=80), leaving 12,268 in the pooled dataset. Of these, 15.5% had missing ER or PR status. ER/PR-specific analyses were based on 8,163 ER/PR+ cases and 2,203 ER−/PR− cases. We could not classify the BC cases by HER2 status, because the California Cancer Registry (CCR) did not collect data on HER2 until 1999, and data were substantially incomplete before 2005 (23,34).

BC cases were linked to the CCR to ascertain vital status and underlying cause of death, if deceased. The CCR conducts follow-up by linking cancer cases to state and national databases, including the National Death Index. Follow-up time was defined as the time from diagnosis to study end date (December 31, 2010), last known contact, or death, whichever occurred first. Mean follow-up time was 8.7 years. Study participants consented by written informed consent or receipt by mail of a completed questionnaire. The studies were approved by the Institutional Review Board of each participating institution and the California State Committee for the Protection of Human Subjects.

Study variables

Each parent study collected data using its own structured questionnaire. Questionnaire and cancer registry data were harmonized according to common definitions developed for the CBCSC (27) and applied to the NC-BCFR. CCR data included ER and PR status, age and year at diagnosis, American Joint Committee on Cancer stage, histology, grade, nodal involvement, tumor size, subsequent cancers, receipt of first-course treatment (surgery type, radiation, chemotherapy), hospital type, marital status and neighborhood socioeconomic status (SES) at diagnosis. Neighborhood SES is a composite measure at the census block-group level of seven SES indicators, including education, occupation, employment, household income, poverty, rent, and house value (35), which were linked to CCR geocodes of address at diagnosis. Neighborhood SES was based on 1990 U.S. Census data for cases

diagnosed prior to 1996, and on 2000 Census data for cases diagnosed from 1996-2007. For NC-BCFR cases, those diagnosed from 2006-2009 were assigned neighborhood SES values based on 2010 Census data. Neighborhood SES was categorized into quintiles based on California state-wide distributions. The CCR records the first facility reporting each cancer case. As previously described (36), hospitals were categorized as i) National Cancer Institute-designated Cancer Centers (NCI-CC) as of 2010 (37), ii) American College of Surgeons Cancer Program (ACOS-CP; i.e., Academic Comprehensive Cancer Program, Comprehensive Community Cancer Program, Community Cancer Program) (38), or iii) other. Information was collected by structured questionnaires administered by interview or submitted by mail on self-identified race/ethnicity, education, and pre-diagnosis parity, weight, height, smoking history, and alcohol consumption. Body mass index (kg/m^2, BMI) was calculated using reported or measured weight (kg) at least 6 months before BC diagnosis divided by height squared (m^2).

Statistical analysis

Multivariable Cox proportional hazards models were fit to data to estimate hazard ratios (HR) and 95% confidence intervals (CI) for BC-specific mortality and all-cause mortality. Given that survival is relatively high for BC, we considered both mortality outcomes. We assessed mortality by race/ethnicity separately for i) all BC cases combined (including cases with unknown ER/PR status), ii) ER+ cases, iii) ER− cases, iv) PR+ cases, v) PR− cases, vi) ER/PR+ cases and stratified by stage (I/II vs. III/IV), and vii) ER−/PR− cases and stratified by stage. To examine the influence of different sets of prognostic factors on racial/ethnic survival disparities, we conducted three models in sequence. Model 1, the base model, included age and year of diagnosis. Model 2 included variables in Model 1 and histology, grade, nodal involvement, tumor size, subsequent tumors, and receipt of first course treatment (surgery, radiation, chemotherapy). Model 3 included variables in Model 2 and marital status, education, neighborhood SES, parity, BMI, smoking history, and alcohol consumption. The Cox models used attained age as the time scale, and were stratified by study and stage to allow the baseline hazard functions within each model to vary by study and stage. Covariates included in the models followed the analytic approach developed for the CBCSC analyses (27,36,39–42). All covariates included a category for missing data and were categorized as shown in the footnotes of Table 3. Heterogeneity in HR estimates by race/ethnicity was assessed using the Wald test.

For both case groups (ER/PR+ BC and ER−/PR− BC), we evaluated associations of race/ethnicity with BC-specific and all-cause mortality and variations by healthcare factors (surgery type, hospital type), sociodemographic characteristics (age at diagnosis, marital status, education, neighborhood SES), and lifestyle factors (BMI, smoking history, alcohol consumption). Cases were classified jointly by race/ethnicity and each dichotomized explanatory variable (8 subgroups for each mortality outcome). In models for each factor, we examined racial/ethnic variation in mortality associated with each dichotomized factor (low vs. high risk) and estimated HRs and 95% CIs for each combination of race/ethnicity x factor, with NHW women and the lower-risk level of each factor as the referent category. Analyses were performed using SAS, version 9.4, software (SAS Institute, Inc., Cary, North Carolina).

Results

Patient characteristics

African American women were more likely to be diagnosed with BC stage II or higher and less likely to receive initial care at a NCI-CC or ACOS-CP hospital, whereas Asian American women were most likely to have received a mastectomy (Table 1). NHW women were more likely to have a college degree or higher alcohol consumption; Hispanic women were more likely to have lower education and higher parity; African American women were more likely to be unmarried at diagnosis, a current smoker, or live in lower SES neighborhoods; and Asian American women were more likely to be married, have a BMI <25 kg/m^2, and not smoke or consume alcohol (Table 2). Differences in patient characteristics by joint ER/PR status are shown in Supplemental Tables 1 and 2.

Breast cancer-specific and all-cause mortality by race/ethnicity

For all BCs combined, compared to NHW women, BC-specific mortality was greater among African American women (HR 1.54, 95% CI 1.33-1.78) in a minimally adjusted model (Model 1, Table 3), but did not differ for Hispanic and Asian American women. Additional adjustment for tumor characteristics and treatment (Model 2), and for sociodemographic and lifestyle characteristics in addition to Model 2 factors (Model 3), had the biggest impact on mortality of African American women, reducing the HR to 1.27 (CI 1.08-1.49). Compared to NHW women, mortality was marginally lower among Hispanic women (HR 0.85, CI 0.70-1.02), but did not differ among Asian American women. In the fully adjusted Model 3, all-cause mortality was lower among Hispanic women (HR 0.76, CI 0.63-0.87) than among NHW women, but did not differ from NHW women for African American or Asian American women.

Mortality patterns across racial/ethnic groups were similar for women with ER+, PR+, or ER/PR+ BC. In Model 3, for ER/PR+ BC, BC-specific mortality was greater among African Americans (HR 1.31, CI 1.05-1.63), and all-cause mortality was lower among Hispanics (HR 0.74, CI 0.61-0.88). Analyses stratified by stage at diagnosis showed heterogeneity by race/ethnicity for women with stage I/II BC, but not for those with stage III/IV BC. For ER−/PR− BC, racial/ethnic mortality differences were less pronounced than for ER/PR+ BC, and there were no differences by race/ethnicity in the fully adjusted models.

ER/PR+ breast cancer: Mortality and modifying factors

For ER/PR+ BC, joint associations of race/ethnicity and selected healthcare, sociodemographic, and lifestyle factors with mortality are presented in Supplemental Table 3. For associations with each dichotomized factor presented below, we compared women in each racial/ethnic group who had that characteristic (e.g., obese) or did not have that characteristic (e.g., not obese) to the reference group of NHW women who did not have that characteristic (e.g., not obese). Several factors modified BC-specific mortality among African American women (Figure 1). Mortality was higher among African American women who had a mastectomy (HR 1.62, CI 1.18-2.23), received initial care at a non-accredited (HR 1.57, CI 1.21-2.04), were not married (HR 1.39, CI 1.07-1.80), were from lower SES neighborhoods (HR 1.48, CI 1.16-1.88), or were obese (HR 1.52, CI 1.14-2.03),

ever smokers (HR 1.51, CI 1.10-2.07), or alcohol consumers (HR 1.53, CI 1.15-2.05), compared to NHW women without these characteristics, whereas BC-specific mortality was similar for NHW and African American women without these characteristics. BC-specific mortality was also higher among African American women who were married (HR 1.44, CI 1.08-1.91), more educated (HR 1.42, CI 1.11-1.82), from higher SES neighborhoods (HR 1.34, CI 1.00-1.80), or non-obese (HR 1.34, CI 1.05-1.73), than among NHW women with comparable characteristics.

Among Hispanic women, few factors modified BC-specific mortality. Women treated with breast-conserving surgery (HR 0.64, CI 0.44-0.92) or from higher SES neighborhoods (HR 0.67, CI 0.48-0.92) had better survival than NHW women with comparable characteristics. Among Asian American women, BC-specific mortality did not vary by any of the factors we examined. Among NHW women, BMI was the only characteristic that modified BC-specific mortality; mortality was marginally higher among obese compared to non-obese NHW women (HR 1.27, CI 0.96-1.69) (Supplemental Table 3).

For all-cause mortality (Figure 2), similar patterns emerged, although differences in HR estimates were not as pronounced. Characteristics associated with higher BC-specific mortality were also associated with higher all-cause mortality among African American women (i.e., treatment with mastectomy, receipt of initial care at a non-accredited hospital, unmarried, lower education, residence in lower SES neighborhood, obesity, and smoking history), compared to NHW women without these characteristics. HR estimates ranged from 1.24 (CI 1.03-1.49) for initial care at a non-accredited hospital to 1.47 (CI 1.17-1.85) for smoking history. All-cause mortality was also higher among African American women who were more educated (HR 1.18, CI 0.98-1.42) or non-obese (HR 1.31, CI 1.10-1.57) than NHW women with comparable characteristics. Compared to NHW women, Hispanic women had lower all-cause mortality, regardless of hospital type, age at diagnosis, marital status, or alcohol consumption. Furthermore, all-cause mortality was not higher among Hispanics who had a mastectomy, had lower education, or were obese or from lower SES neighborhoods, when compared to NHW women without these characteristics. Among Asian American women, all-cause mortality did not vary by any of the factors we examined. Among NHW women, all-cause mortality was higher among those who were not married (HR 1.18, CI 1.02-1.37), obese (HR 1.42, CI 1.18-1.70), or ever smokers (HR 1.26, CI 1.08-1.46) compared to NHW women without these characteristics (Table 2).

ER−/PR− breast cancer: Mortality and modifying factors

For women with ER−/PR− BC, the association of race/ethnicity with BC-specific and all-cause mortality varied by few factors (Supplemental Table 4). Compared to NHW women from higher SES neighborhoods, BC-specific mortality was higher among women from lower SES neighborhoods, both among NHW women (HR 1.39, CI 1.01-1.90) and African American women (HR 1.34, CI 0.96-1.85). BC-specific mortality was also higher among African American women (HR 1.62, CI 1.01-2.60) who never smoked compared to NHW never smokers (Figure 3). All-cause mortality (Figure 4) was higher among African American women (HR 1.42, CI 1.05-1.94) and NHW women (HR=1.45, CI 1.07-1.95) from lower SES neighborhoods compared to NHW women from higher SES neighborhoods.

Discussion

In this study of over 10,000 Californian women with BC, enriched for racial/ethnic minority groups, we found differential racial/ethnic patterns in mortality by ER/PR status. For women with ER/PR+ BC, we found higher BC-specific mortality among African American women compared to NHW women and lower all-cause mortality among Hispanic women compared to NHW women, whereas for women with ER−/PR− BC, mortality did not differ by race/ethnicity. Assessing the joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics with mortality, we identified several factors (surgery type, marital status, neighborhood SES, BMI, smoking history, and alcohol consumption) that modified associations with race/ethnicity, except for Asian American women. In contrast, for ER−PR− BC, we found that associations of race/ethnicity with mortality varied only by neighborhood SES. Through analyses that considered the joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics, we gained additional insights into factors that may modify mortality differently across the four racial/ethnic groups, particularly in African American and Hispanic women.

Although the inclusion of sociodemographic and lifestyle characteristics attenuated the increased relative hazards for mortality among African American women, BC-specific mortality remained higher for BC overall and for ER/PR+ BC, which is consistent with other reports of higher mortality among African American women with BC (11,21–24). Among women with ER/PR+ BC, African American women with stage I/II disease had slightly higher BC-specific mortality than NHW women with the same stage disease (HR=1.27, CI 0.99-1.62). That finding is consistent with data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) registries (43) and clinical trials (44) where African American women with stage I disease (all BCs combined) had higher BC-specific mortality, compared to NHW women. After excluding triple negative cases in the SEER-wide study (43), findings were similar and the authors partly attributed the higher mortality of African American women with stage I BC to more aggressive tumor features, such as a higher likelihood that African American women with small tumors (less than 2 cm) present with lymph node metastases or distant metastases.

The higher BC-specific mortality among African American women with stage I/II disease may also be related to differences in receipt of guideline-concordant treatment, although we were not able to directly assess this possibility in the SEER registry. African American women diagnosed with stage I/II BC have been shown to be less likely to receive breast-conserving surgery compared to NHW women (4). In our study, however, the proportion of women with stage I/II BC who had breast-conserving surgery was comparable among African American (65%), Hispanic (61%), and NHW (66%) women, but lower among Asian American women (52%). Compared to NHW women with breast-conserving surgery, BC-specific and all-cause mortality was higher among women who received a mastectomy among African American women only. Treatment with mastectomy may be a proxy for restricted care options among African American women: for example, care at centers with less expertise in coordinating multidisciplinary interventions such as breast conserving surgery and radiation, or limited access to the transportation or time off from work needed to complete radiation therapy. Other factors may also modify the higher mortality among

African Americans, such as more extensive disease or comorbidities that may contraindicate breast-conserving surgery.

While we did not have information on access to health care after diagnosis, we were able to examine associations of mortality with hospital type. African American women diagnosed with ER/PR+ BC had BC-specific mortality that was similar to that of NHW women if initial care was at a hospital affiliated with NCI-designated Cancer Centers or the ACOS Cancer Program, whereas those who received initial care at other hospitals had higher BC-specific and all-cause mortality. This finding was unique to African American women, suggesting that lack of access to care or systemic barriers to high-quality care may disproportionately affect African American BC patients and their survival outcomes (45). We previously reported an association between hospital type and mortality for BC overall (36), and we show here the same association for ER/PR+ BC, but not for ER−/PR− BC. These findings suggest that interventions specific to the diagnosis and treatment of ER/PR+ BC might be delivered more effectively by accredited hospitals, which tend to have higher standards of adherence to treatment best practices for BC patients (46). Candidate interventions might include the quality of pathology laboratories in identifying ER/PR+ tumor status; referral to medical oncology for discussion and prescription of endocrine therapy; and clinical expertise in managing side effects of endocrine therapy, which may facilitate adherence. Research is needed to identify and implement key interventions that could improve access of African American women with ER/PR+ BC to higher quality care, thereby improving their survival.

Sociodemographic characteristics have been associated with survival of BC patients (9), including better survival of married women with BC (6,47). Consistent with those findings, we found for ER/PR+ BC that unmarried women, except among Hispanic women, had higher BC-specific mortality compared to married NHW women. A similar pattern was seen for all-cause mortality. However, married African American women also had higher BC-specific and all-cause mortality, whereas married Hispanic women had a greater overall survival benefit than married NHW women. Better survival of married BC patients may be related to greater social and/or economic support or other socially mediated factors (47–49). Our findings suggest that the mechanisms linking marital status to cancer survival may differ across racial/ethnic groups (50).

Better BC survival has also been associated with higher levels of education (51), and living in higher SES neighborhoods (6). However, we did not see such a pattern among African American women with ER/PR+ BC. BC-specific mortality was higher among those who were more educated or from higher SES neighborhoods than NHW women with comparable education or neighborhood SES. These findings are consistent with prior findings of higher BC-specific mortality among African American women than NHW women across all levels of census tract SES (52,53), and of lower BC-specific mortality associated with higher county-level income and education among NHW women, but not among African American women (54). Additionally, we found that more educated Hispanic women and those from higher SES neighborhoods had a greater survival benefit than NHW women with comparable education and neighborhood SES. These findings warrant a deeper understanding of the factors underlying education and neighborhood SES that might

disproportionately affect survival of African American women with ER+/PR+ BC. Education and neighborhood SES may be related to quality of health care received and complex social determinants (9).

Consistent with other reports of higher mortality among obese women with BC (55,56), for ER/PR+ BC, we found a pattern of higher BC-specific mortality among obese women, except among Hispanic women, and higher all-cause mortality among obese NHW and African American women, compared to non-obese NHW women. However, BC-specific and all-cause mortality was also elevated among non-obese African American women relative to non-obese NHW women. As for other lifestyle-related factors, NHW and African American women who were never smokers or consumers of alcohol had similar mortality. While smoking and alcohol consumption were associated with higher BC-specific mortality, this was seen only among African American women. Other studies have found higher BC-specific mortality associated with current smoking (57,58), but evidence for alcohol consumption is inconclusive (59). The proportions of women who were current or past smokers or obese were highest among African American women, whereas the proportion of women consuming alcohol was highest among NHW women. The present findings suggest that certain lifestyle behaviors around the time of diagnosis were associated with better survival of women diagnosed with ER/PR+ BC. Because data on lifestyle factors after diagnosis were not available across all studies, we could not investigate the impact of post-diagnosis lifestyle factors on survival disparities.

In contrast to our findings for ER/PR+ BC, few factors modified all-cause mortality among women with ER−/PR− BC. Risk was greater among African American and NHW women from lower SES neighborhoods compared to NHW women from higher SES neighborhoods. This finding is consistent with a Michigan study of ER−/PR− BC, where clinical characteristics did not explain the higher all-cause mortality among African American women compared to NHW women, but there were no differences by race/ethnicity after adjustment for neighborhood SES (25).

In the U.S., African American and other communities of color are more likely to experience adverse conditions and toxic stressors throughout their life, and often need to exert more effort for basic daily activities. Effectively, the resulting increased and prolonged levels of social stress eventually impact emotional and physical health. Although the CBCSC has previously investigated neighborhood social and built environment factors (13,36,40,41), finding complex interactions with individual-level factors, research on cancer health disparities needs to acknowledge that health inequities are rooted in and continue to be maintained by structural factors as upstream social determinants of health. Research needs to focus on structural racism, interpersonal discrimination, and medical mistrust as drivers of cancer health inequities, and policies and measures to address disparities must fundamentally start with addressing structural factors.

Several limitations need to be considered when interpreting these results. They include: the relatively small sample size of ER−/PR− BC in each racial/ethnic group, the possibility of selection bias, as not all eligible women chose to participate in the parent case-control and cohort studies; incomplete cancer registry information on HER2 status, with only 669 triple

negative (ER−, PR−, HER2−) cases in the pooled dataset; incomplete data on receipt of radiotherapy and chemotherapy (60), and limited to first-course treatment; and lack of data on receipt of endocrine therapy, guideline-concordant treatment, treatment delays, or adherence to treatment. Information on comorbidities, physical activity, health care access, health insurance, and behavioral factors such as diet was not available across all studies that were pooled (27). We had only limited data on social determinants of health, such as education and neighborhood SES (41). Other social determinants that may drive survival disparities for ER/PR+ BC warrant in-depth investigation (e.g., unemployment, income, neighborhood disadvantage, lack of social support, social isolation, racial discrimination, and systemic racism) (9). Nevertheless, our study has several important strengths, including a long follow-up of an average 8.7 years, a high follow-up rate in the CCR, population-based design, the highly racially/ethnically diverse study sample with a large number of African American, Hispanic, and Asian American women with BC accounting for 57% of the study sample. The sample size was sufficient for race/ethnicity-specific analyses by ER/PR status, and assessing associations of ER/PR+ BC mortality with a wide range of modifying factors, including lifestyle factors that are not available in cancer registries. However, larger multiethnic studies are warranted to investigate mortality for ER−/PR− BC and triple negative BC.

In conclusion, in this large multiethnic study of women diagnosed with invasive BC, BC-specific and all-cause mortality differed by race/ethnicity for BC overall and ER/PR+ BC, but not for ER−/PR− BC. We found that healthcare, sociodemographic, and lifestyle factors may contribute to racial/ethnic survival disparities among women with ER/PR+ BC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AABCS	Los Angeles County Asian American Breast Cancer Study
ACOS-CP	American College of Surgeons Cancer Program
BC	breast cancer
CARE	Women's Contraceptive and Reproductive Experiences study
CBCSC	California Breast Cancer Survivorship Consortium
CCR	California Cancer Registry
CI	confidence intervals
CTS	California Teachers Study
ER	estrogen receptor status
HR	hazard ratio
MEC	Multiethnic Cohort study
NC-BCFR	Northern California Breast Cancer Family Registry
NCI-CC	National Cancer Institute Cancer Center
NHW	non-Hispanic White
PR	progesterone receptor status
SES	socioeconomic status
SFBCS	San Francisco Bay Area Breast Cancer Study
U.S.	United States

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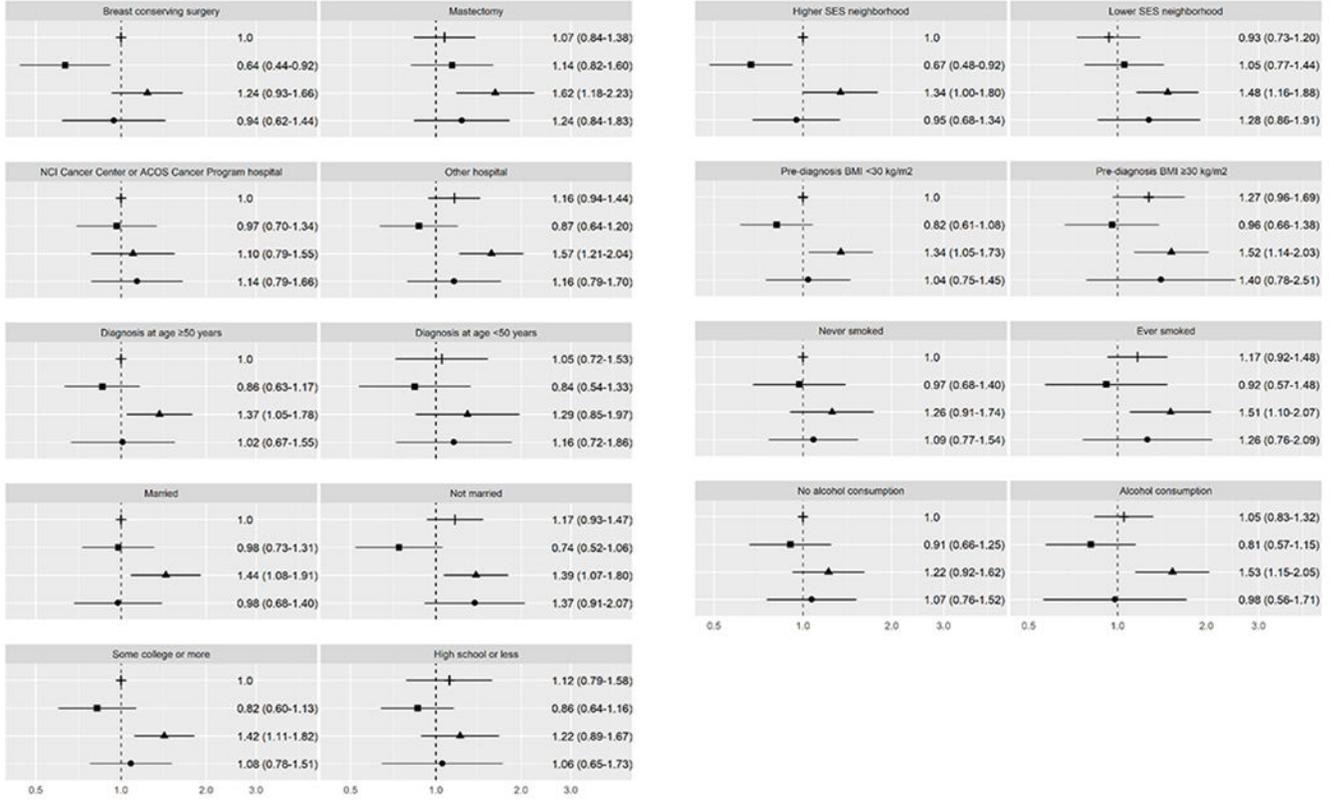
Figure 1.
Breast cancer-specific mortality for ER+ or PR+ breast cancer. This figure depicts hazard ratios and 95% confidence intervals for joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics with breast cancer-specific mortality. The following symbols are used for each racial/ethnic group: ┼ for non-Hispanic Whites, ■ for Hispanics, ▲ for African Americans, ● for Asian Americans.
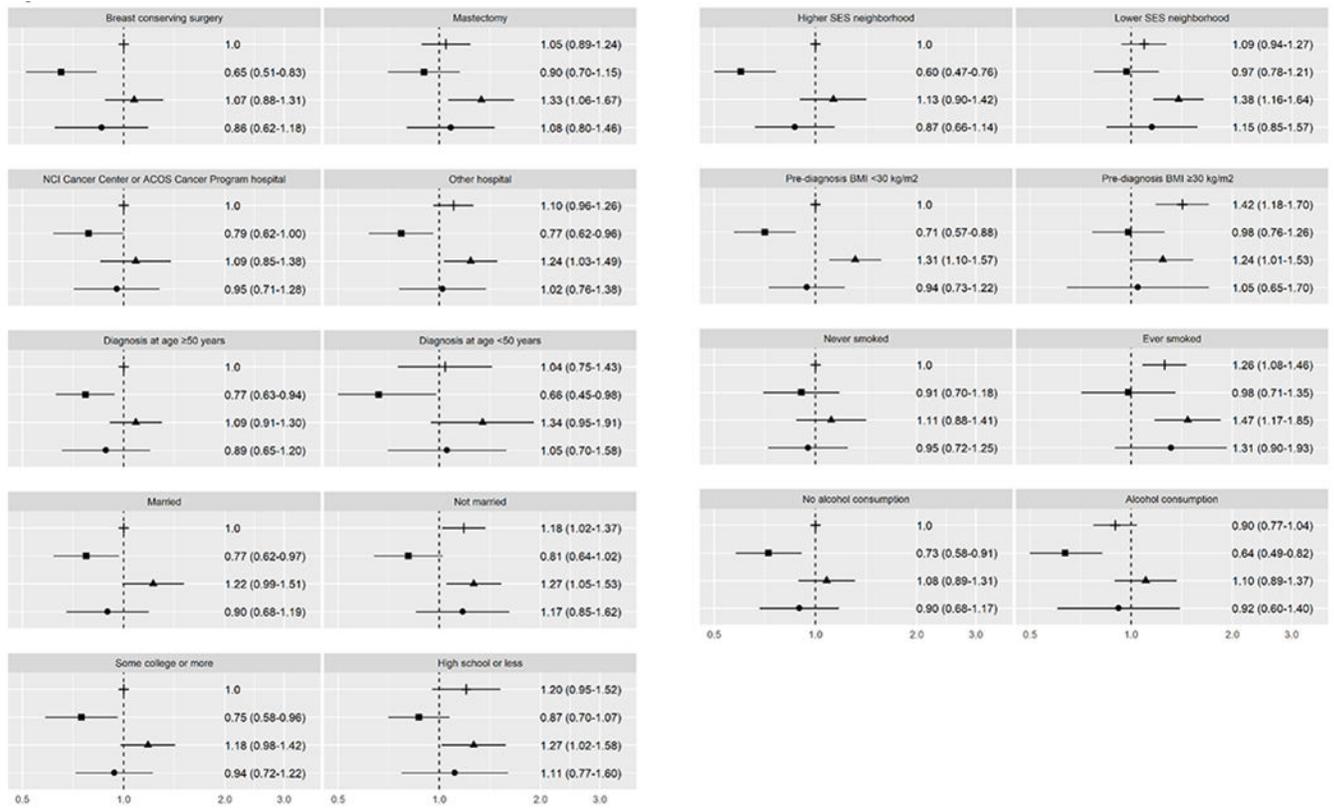
Figure 2.
All-cause mortality for ER+ or PR+ breast cancer. This figure depicts hazard ratios and 95% confidence intervals for joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics with all-cause mortality. The following symbols are used for each racial/ethnic group: ┼ for non-Hispanic Whites, ■ for Hispanics, ▲ for African Americans, ● for Asian Americans.
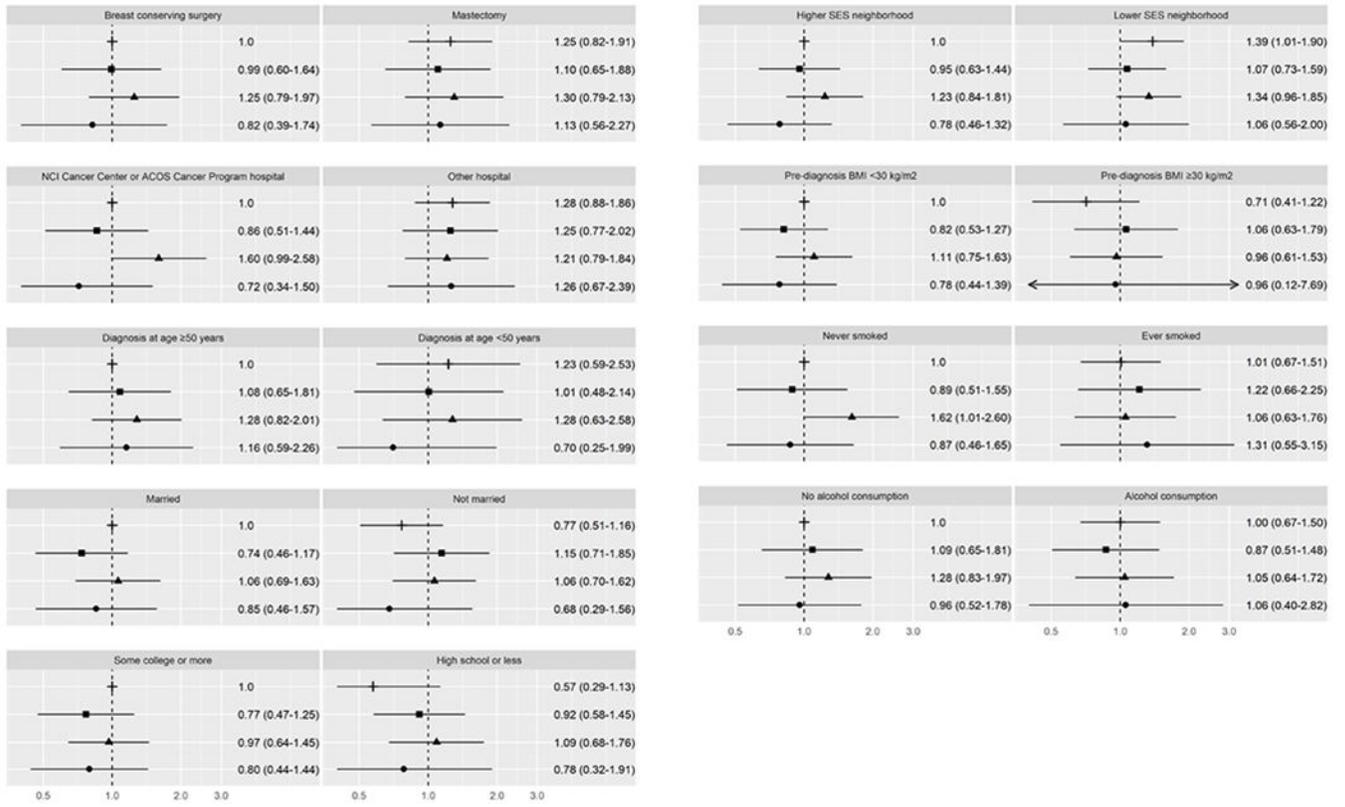
Figure 3.
Breast cancer-specific mortality for ER− and PR− breast cancer. This figure depicts hazard ratios and 95% confidence intervals for joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics with breast cancer-specific mortality. The following symbols are used for each racial/ethnic group: ┼ for non-Hispanic Whites, ▪ for Hispanics, ▲ for African Americans, ● for Asian Americans.
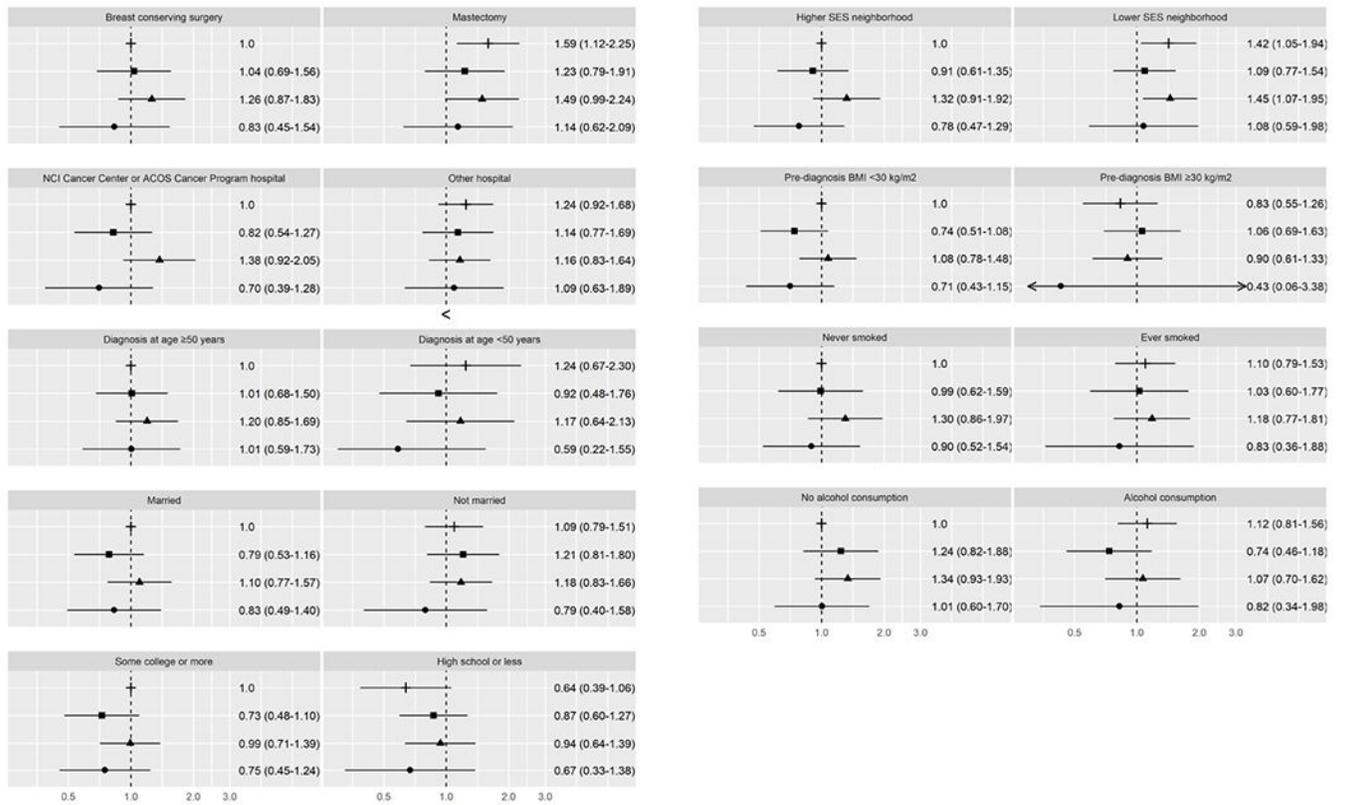
Figure 4.
All-cause mortality for ER– and PR– breast cancer. This figure depicts hazard ratios and 95% confidence intervals for joint associations of race/ethnicity and healthcare, sociodemographic, and lifestyle characteristics with all-cause mortality. The following symbols are used for each racial/ethnic group: ┼ for non-Hispanic Whites, ▪ for Hispanics, ▲ for African Americans, ● for Asian Americans.

Table 1.

Clinical and healthcare characteristics of women with breast cancer [1], by race/ethnicity

	Non-Hispanic White N=4487		Hispanic N=2,263		African American N=1,972		Asian American N=1,644		Total N=10,366	
	N	%	N	%	N	%	N	%	N	%
Study [2]										
AABCS	0	0	0	0	0	0	817	50	817	8
CARE	428	10	61	3	374	19	0	0	863	8
CTS	2,701	60	79	3	62	3	85	5	2,927	28
MEC	301	7	467	21	558	28	116	7	1,442	14
NC-BCFR	568	13	684	30	530	27	626	38	2,408	23
SFBCS	489	11	972	43	448	23	0	0	1,909	18
AJCC stage at diagnosis										
I	2,365	53	983	43	789	40	750	46	4,887	47
II	1,672	37	987	44	920	47	749	46	4,328	42
III	261	6	215	10	144	7	103	6	723	7
IV	85	2	35	2	53	3	23	1	196	2
Unknown	104	2	43	2	66	3	19	1	232	2
Histology										
Ductal	3,214	72	1,754	78	1,519	77	1,281	78	7,768	75
Lobular	899	20	322	14	261	13	214	13	1,696	16
Other	374	8	187	8	192	10	149	9	902	9
Grade										
I	1,040	23	363	16	276	14	240	15	1,919	19
II	1,798	40	845	37	634	32	682	41	3,959	38
III or IV	1,279	29	875	39	882	45	618	38	3,654	35
Unknown	370	8	180	8	180	9	104	6	834	8
Nodal involvement										
No nodes	3,007	67	1,352	60	1,171	59	1,006	61	6,536	63
Positive nodes	1,363	30	862	38	731	37	608	37	3,564	34
Unknown	117	3	49	2	70	4	30	2	266	3

	Non-Hispanic White N=4487		Hispanic N=2,263		African American N=1,972		Asian American N=1,644		Total N=10,366	
	N	%	N	%	N	%	N	%	N	%
Tumor size (cm)										
<1	897	20	333	15	229	12	257	16	1,713	17
1–<5	3,146	70	1,670	74	1,480	75	1,221	74	7,517	73
5	274	6	187	8	185	9	135	8	781	8
Unknown	173	4	73	3	78	4	31	2	355	3
Had 1 or more subsequent cancers										
No	3,677	82	1,977	87	1,650	84	1,387	84	8,691	84
Yes	810	18	286	13	322	16	257	16	1,675	16
Surgery [3]										
No surgery	58	1	28	1	64	3	16	1	166	2
Mastectomy	1,652	37	941	42	753	38	840	51	4,186	40
Breast-conserving surgery	2,772	62	1,288	57	1,152	58	786	48	5,998	58
Other	5	<1	6	<1	3	<1	2	<1	16	<1
Radiation therapy [3]										
No	1,881	42	952	42	963	49	869	53	4,665	45
Yes	2,606	58	1,311	58	1,009	51	775	47	5,701	55
Chemotherapy [3]										
No	2,659	59	991	44	1,001	51	745	45	5,396	52
Yes	1,761	39	1,246	55	939	48	872	53	4,818	46
Unknown	67	1	26	1	32	2	27	2	152	1
Hospital type										
NCI Cancer Center	249	6	130	6	87	4	123	7	589	6
ACOS Cancer Program	2,040	45	828	37	484	25	683	42	4,035	39
Other	2,198	49	1,305	58	1,401	71	838	51	5,742	55

Abbreviations: ACOS, American College of Surgeons; AJCC, American Joint Committee on Cancer; ER, estrogen receptor status; PR, progesterone receptor; NCI, National Cancer Institute.

[1] Analysis based on 8,163 women with ER/PR+ breast cancer and 2,203 women with ER−/PR− breast cancer.

[2] AABCS, Asian American Breast Cancer Study; CARE, Women's Contraceptive and Reproductive Experiences Study; CTS, California Teachers Study; MEC, Multiethnic Cohort Study; NC-BCFR, Northern California Breast Cancer Family Registry; SFBCS, San Francisco Bay Area Breast Cancer Study.

[3]Receipt of first-course treatment.

Table 2.

Sociodemographic and lifestyle characteristics of women with breast cancer[1], by race/ethnicity

	Non-Hispanic White N=4487		Hispanic N=2,264		African American N=1,972		Asian American N=1,644		Total N=10,366	
	N	%	N	%	N	%	N	%	N	%
Age at diagnosis (years)										
<35	105	2	96	4	41	2	82	5	324	3
35-49	783	17	744	33	541	27	615	37	2,683	26
50-64	2,019	45	933	41	861	44	683	42	4,496	43
65-79	1,283	29	467	21	467	24	249	15	2,466	24
80	297	7	23	1	62	3	15	1	397	4
Marital status [2]										
Never married	561	13	345	15	459	23	234	14	1,599	15
Married	2,822	63	1,372	61	776	39	1,212	74	6,182	60
Separated/divorced	514	11	281	12	415	21	82	5	1,292	12
Widowed	520	12	217	10	271	14	103	6	1,111	11
Unknown	70	2	48	2	51	3	13	1	182	2
Education										
Some high school or less	78	2	812	36	244	12	108	7	1,242	12
High school graduate	336	7	493	22	431	22	180	11	1,440	14
Some college or technical school	622	14	566	25	774	39	392	24	2,354	23
College graduate or higher degree	3,445	77	383	17	514	26	962	59	5,304	51
Unknown	6	<1	9	<1	9	<1	2	<1	26	<1
Neighborhood SES (quintiles) [2]										
1 (low)	125	3	257	11	452	23	91	6	925	9
2	375	8	416	18	501	25	209	13	1,501	14
3	699	16	479	21	413	21	272	17	1,863	18
4	1,188	26	524	23	366	19	415	25	2,493	24
5 (high)	1,991	44	551	24	214	11	638	39	3,394	33
Unknown	109	2	36	2	26	1	19	1	190	2
Number of full-term pregnancies										

	Non-Hispanic White N=4487		Hispanic N=2,264		African American N=1,972		Asian American N=1,644		Total N=10,366	
	N	%	N	%	N	%	N	%	N	%
Nulliparous	1,080	24	316	14	334	17	417	25	2,147	21
1	646	14	296	13	377	19	282	17	1,601	15
2	1,471	33	565	25	462	23	521	32	3,019	29
3	788	18	458	20	361	18	261	16	1,868	18
4	462	10	617	27	424	22	154	9	1,657	16
Unknown	37	1	11	<1	14	1	12	1	74	1
BMI (kg/m^2)[3]										
<25	2,514	56	729	32	563	29	1,118	68	4,924	48
25-29.9	1,169	26	735	32	645	33	392	24	2,941	28
30	655	15	754	33	712	36	116	7	2,237	22
Unknown	149	3	45	2	52	3	18	1	264	3
Pre-diagnosis smoking history										
Never	2,231	50	1,173	52	780	40	1,351	82	5,535	53
Past	1,426	32	375	17	452	23	203	12	2,456	24
Current	366	8	162	7	323	16	82	5	933	9
Unknown[4]	464	10	553	24	417	21	8	<1	1,442	14
Pre-diagnosis alcohol consumption (drinks/week)										
0	1,452	32	1,380	61	1,176	60	1,409	86	5,417	52
2	813	18	345	15	302	15	76	5	1,536	15
>2	2,080	46	511	23	447	23	155	9	3,193	31
Unknown	142	3	27	1	47	2	4	<1	220	2

Abbreviations: BMI, body mass index; ER, estrogen receptor status; PR, progesterone receptor; SES, socioeconomic status.

[1] Analysis based on 8,163 women with ER/PR+ breast cancer and 2,203 women with ER−/PR− breast cancer.

[2] At diagnosis.

[3] In year before diagnosis (case-control studies) or within 6 months of diagnosis (cohort studies).

[4] Smoking history was not assessed in an early component of SFBCS and therefore unknown for 14% of cases.

Table 3.

Breast cancer-specific and all-cause mortality, for breast cancer overall and by tumor estrogen receptor and progesterone receptor status, stage at diagnosis, and race/ethnicity

	Cases	Deaths	Breast cancer-specific mortality			Deaths	All-cause mortality		
			Model 1 HR (95% CI) [1]	Model 2 HR (95% CI) [2]	Model 3 HR (95% CI) [3]		Model 1 HR (95% CI) [1]	Model 2 HR (95% CI) [2]	Model 3 HR (95% CI) [3]
	n	n				N			
All breast cancer [4]	12,268	1,686				3,052			
Non-Hispanic White	5,245	627	1.0	1.0	1.0	1,330	1.0	1.0	1.0
Hispanic	2,596	303	0.90 (0.76-1.07)	0.88 (0.74-1.04)	0.85 (0.70-1.02)	512	0.87 (0.77-0.99)	0.88 (0.77-1.00)	0.76 (0.63-0.87)
African American	2,403	514	1.54 (1.33-1.78)	1.45 (1.25-1.68)	1.27 (1.08-1.49)	853	1.44 (1.29-1.60)	1.38 (1.23-1.54)	1.11 (0.98-1.25)
Asian American	2,024	242	0.91 (0.71-1.17)	0.87 (0.68-1.12)	0.91 (0.70-1.18)	357	0.83 (0.69-1.02)	0.81 (0.66-0.99)	0.84 (0.68-1.03)
			P < 0.01	*P < 0.01*	*P < 0.01*		*P < 0.01*	*P < 0.01*	*P < 0.01*
ER+ breast cancer	7,890	920				1,827			
Non-Hispanic White	3,621	362	1.0	1.0	1.0	861	1.0	1.0	1.0
Hispanic	1,343	254	0.86 (0.68-1.09)	0.83 (0.66-1.06)	0.83 (0.64-1.07)	458	0.89 (0.75-1.05)	0.89 (0.75-1.05)	0.74 (0.62-0.89)
African American	1,656	153	1.72 (1.42-2.10)	1.69 (1.39-2.07)	1.42 (1.13-1.78)	287	1.59 (1.38-1.83)	1.57 (1.35-1.81)	1.20 (1.02-1.41)
Asian American	1,270	151	1.03 (0.76-1.41)	1.00 (0.73-1.37)	1.09 (0.79-1.51)	221	0.94 (0.74-1.20)	0.91 (0.71-1.16)	0.96 (0.74-1.24)
			P<0.01	*P<0.01*	*P<0.01*		*P<0.01*	*P<0.01*	*P<0.01*
ER- breast cancer	2,521	475				693			
Non-Hispanic White	875	169	1.0	1.0	1.0	252	1.0	1.0	1.0
Hispanic	648	149	0.92 (0.67-1.27)	0.93 (0.67-1.28)	0.89 (0.62-1.28)	221	0.86 (0.66-1.12)	0.90 (0.69-1.17)	0.83 (0.61-1.12)
African American	618	103	1.07 (0.80-1.42)	1.13 (0.84-1.51)	1.00 (0.73-1.37)	144	1.10 (0.87-1.39)	1.16 (0.91-1.47)	0.97 (0.75-1.27)
Asian American	380	54	0.87 (0.53-1.42)	0.84 (0.51-1.38)	0.86 (0.51-1.45)	76	0.72 (0.48-1.09)	0.71 (0.47-1.09)	0.75 (0.48-1.16)
			P=0.72	*P=0.47*	*P=0.85*		*P=0.08*	*P=0.05*	*P=0.38*
PR+ breast cancer	6,456	717				1,428			
Non-Hispanic White	2,944	280	1.0	1.0	1.0	678	1.0	1.0	1.0
Hispanic	1,063	198	0.81 (0.62-1.05)	0.82 (0.63-1.08)	0.79 (0.59-1.06)	347	0.87 (0.72-1.05)	0.90 (0.75-1.09)	0.74 (0.59-0.91)
African American	1,390	121	1.54 (1.24-1.92)	1.54 (1.23-1.93)	1.30 (1.00-1.68)	227	1.51 (1.29-1.78)	1.51 (1.28-1.78)	1.14 (0.95-1.37)
Asian American	1,059	118	0.98 (0.69-1.38)	0.95 (0.67-1.35)	1.03 (0.72-1.49)	176	0.91 (0.69-1.19)	0.87 (0.66-1.15)	0.95 (0.71-1.26)
			P<0.01	*P<0.01*	*P<0.01*		*P<0.01*	*P<0.01*	*P<0.01*

	Cases	Deaths	Breast cancer-specific mortality			Deaths	All-cause mortality		
			Model 1 HR (95% CI)[1]	Model 2 HR (95% CI)[2]	Model 3 HR (95% CI)[3]		Model 1 HR (95% CI)[1]	Model 2 HR (95% CI)[2]	Model 3 HR (95% CI)[3]
	n	n				N			
PR− breast cancer	3,428	625				966			
Non-Hispanic White	1,349	235	1.0	1.0	1.0	387	1.0	1.0	1.0
Hispanic	774	183	0.92 (0.70-1.22)	0.88 (0.67-1.18)	0.80 (0.59-1.10)	281	0.86 (0.69-1.08)	0.86 (0.69-1.08)	0.76 (0.59-0.98)
African American	821	132	1.27 (0.99-1.63)	1.23 (0.96-1.59)	1.05 (0.79-1.38)	193	1.24 (1.02-1.51)	1.24 (1.02-1.52)	1.00 (0.80-1.25)
Asian American	484	75	0.95 (0.63-1.43)	0.91 (0.60-1.37)	0.89 (0.58-1.38)	105	0.87 (0.62-1.23)	0.85 (0.60-1.21)	0.83 (0.58-1.19)
			P=0.06	*P=0.06*	*P=0.30*		*P<0.01*	*P<0.01*	*P=0.07*
ER/PR+ breast cancer	8,163	964				1,890			
Non-Hispanic White	3,709	381	1.0	1.0	1.0	888	1.0	1.0	1.0
Hispanic	1,703	161	0.85 (0.68-1.07)	0.84 (0.67-1.06)	0.84 (0.65-1.08)	295	0.87 (0.74-1.03)	0.88 (0.75-1.04)	0.74 (0.61-0.88)
African American	1,419	264	1.59 (1.31-1.92)	1.58 (1.30-1.92)	1.31 (1.05-1.63)	475	1.51 (1.31-1.73)	1.50 (1.30-1.72)	1.14 (0.97-1.33)
Asian American	1,332	158	0.98 (0.73-1.33)	0.96 (0.71-1.30)	1.06 (0.77-1.46)	232	0.90 (0.71-1.15)	0.88 (0.69-1.12)	0.94 (0.73-1.20)
			P< 0.01	*P< 0.01*	*P< 0.01*		*P< 0.01*	*P< 0.01*	*P< 0.01*
Stage I or II	7,355	676				1,520			
Non-Hispanic White	3,388	271	1.0	1.0	1.0	738	1.0	1.0	1.0
Hispanic	1,499	100	0.86 (0.66-1.13)	0.80 (0.61-1.04)	0.73 (0.54-0.98)	217	0.88 (0.73-1.05)	0.87 (0.73-1.05)	0.70 (0.57-0.86)
African American	1,246	189	1.84 (1.48-2.29)	1.63 (1.31-2.04)	1.27 (0.99-1.62)	381	1.64 (1.41-1.91)	1.57 (1.35-1.83)	1.16 (0.97-1.37)
Asian American	1,222	116	0.93 (0.66-1.31)	0.85 (0.60-1.21)	0.94 (0.65-1.35)	184	0.87 (0.67-1.13)	0.83 (0.63-1.08)	0.90 (0.68-1.18)
			P< 0.01	*P< 0.01*	*P< 0.01*		*P< 0.01*	*P< 0.01*	*P< 0.01*
Stage III or IV	634	263				320			
Non-Hispanic White	240	104	1.0	1.0	1.0	129	1.0	1.0	1.0
Hispanic	173	54	0.87 (0.57-1.33)	1.04 (0.67-1.62)	1.23 (0.75-2.02)	70	0.90 (0.61-1.32)	1.08 (0.72-1.60)	1.05 (0.67-1.64)
African American	127	65	1.34 (0.91-1.97)	1.39 (0.92-2.11)	1.28 (0.80-2.04)	75	1.27 (0.89-1.82)	1.27 (0.87-1.86)	1.04 (0.68-1.61)
Asian American	94	40	1.03 (0.55-1.92)	1.08 (0.56-2.08)	1.04 (0.52-2.08)	46	0.91 (0.50-1.65)	0.96 (0.51-1.79)	0.89 (0.46-1.70)
			P=0.14	*P=0.37*	*P=0.74*		*P=0.24*	*P=0.58*	*P=0.97*
ER−/PR− breast cancer	2,203	420				613			
Non-Hispanic White	778	145	1.0	1.0	1.0	220	1.0	1.0	1.0
Hispanic	560	94	0.98 (0.69-1.39)	0.98 (0.69-1.40)	0.95 (0.64-1.42)	134	0.91 (0.68-1.22)	0.96 (0.72-1.29)	0.90 (0.65-1.25)
African American	553	135	1.25 (0.92-1.70)	1.29 (0.94-1.77)	1.16 (0.82-1.64)	195	1.24 (0.96-1.60)	1.31 (1.01-1.70)	1.09 (0.82-1.45)

	Cases n	Deaths n	**Breast cancer-specific mortality** Model 1 HR (95% CI)[1]	Model 2 HR (95% CI)[2]	Model 3 HR (95% CI)[3]	Deaths N	**All-cause mortality** Model 1 HR (95% CI)[1]	Model 2 HR (95% CI)[2]	Model 3 HR (95% CI)[3]
Asian American	312	46	0.92 (0.55-1.55)	0.88 (0.52-1.50)	0.89 (0.51-1.55)	64	0.79 (0.51-1.23)	0.80 (0.51-1.25)	0.80 (0.50-1.29)
			P=0.29	P=0.19	P=0.60		P=0.03	P=0.02	P=0.42
Stage I or II	1,860	297				462			
Non-Hispanic White	649	100	1.0	1.0	1.0	163	1.0	1.0	1.0
Hispanic	471	62	1.01 (0.68-1.51)	1.00 (0.67-1.50)	0.92 (0.59-1.44)	97	0.91 (0.66-1.25)	1.00 (0.72-1.38)	0.86 (0.60-1.23)
African American	463	101	1.51 (1.08-2.12)	1.45 (1.03-2.05)	1.27 (0.86-1.86)	153	1.38 (1.05-1.81)	1.45 (1.10-1.91)	1.13 (0.83-1.55)
Asian American	277	34	0.96 (0.55-1.69)	0.91 (0.51-1.62)	0.93 (0.50-1.72)	49	0.78 (0.49-1.25)	0.85 (0.52-1.38)	0.87 (0.52-1.45)
			P=0.03	P=0.06	P=0.34		P<0.01	P<0.01	P=0.30
Stage III or IV	285	113				131			
Non-Hispanic White	106	43	1.0	1.0	1.0	48	1.0	1.0	1.0
Hispanic	77	28	0.95 (0.48-1.88)	1.09 (0.52-2.28)	1.20 (0.46-3.09)	33	0.91 (0.66-1.25)	1.25 (0.63-2.49)	1.35 (0.55-3.34)
African American	70	30	1.10 (0.58-2.08)	1.26 (0.61-2.62)	1.02 (0.42-2.48)	35	1.05 (0.55-2.00)	1.27 (0.64-2.52)	0.92 (0.40-2.11)
Asian American	32	12	0.66 (0.20-2.11)	0.62 (0.18-2.20)	0.54 (0.11-2.68)	15	0.80 (0.28-2.32)	0.67 (0.22-2.08)	0.46 (0.11-1.95)
			P=0.84	P=0.71	P=0.84		P=0.85	P=0.64	P=0.56

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, body mass index; CCR, California Cancer Registry; CI, confidence interval; ER/PR+, estrogen receptor-positive or progesterone receptor-positive; ER−/PR−, estrogen receptor-negative and progesterone receptor-negative; HR, hazard ratio; NHW, non-Hispanic white; SES, socioeconomic status.

[1] Model 1 used delayed entry Cox proportional hazards regression with attained age (days) as the time scale. Entry date into the risk set is the later of date of questionnaire completion or date of BC diagnosis. The exit date is earliest of date of death, last follow-up date in CCR, or December 31, 2010. The Cox model was stratified by study (AABCS, CARE, CTS, MEC, NC-BCFR, SFBCS) and AJCC stage (I, II, III, IV, unknown) and included age at diagnosis (years), log transformed age at diagnosis, and year of diagnosis.

[2] Model 2 included Model 1 variables and histology (ductal, lobular, other), grade (I, II, III/IV, unknown), nodal involvement (no, yes, unknown), availability of tumor size as continuous measure (yes, no) and tumor size (continuous), diagnoses of subsequent cancers (yes, no), time between diagnoses of subsequent tumors (days), surgery type (none, mastectomy, breast conserving surgery, other), radiation therapy (yes, no), and chemotherapy (yes, no, unknown).

[3] Model 3 included Model 2 variables and marital status at diagnosis (single or never married, married, separated or divorced, widowed, unknown), education (some high school or less, high school graduate, some college or technical school, college graduate or higher degree, unknown), neighborhood SES at diagnosis (quintiles, unknown), number of full-term pregnancies (nulliparous, 1, 2, 3, 4, unknown), BMI (<25, 25-29.9, 30 kg/m², unknown) in year before diagnosis (case-control studies) or within 6 months of diagnosis (cohort studies), pre-diagnosis smoking history (never, past, current, unknown), and alcohol consumption (0, 2, >2 drinks per week, unknown) in year before diagnosis (case-control studies) or within 6 months of diagnosis (cohort studies).

[4] Includes all women regardless of ER or PR status.