Published in final edited form as:
Womens Health (Lond Engl). 2011 November ; 7(6): 677–687. doi:10.2217/whe.11.67.

Ethnic Differences in Breast Cancer Survival: Status and Determinants

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SUMMARY

Ethnic differences in breast cancer survival have been a long-standing concern. The objective of this review is to present relevant studies for all major U.S. racial/ethnic groups including African Americans, Hispanics, Native Americans, Japanese, and Native Hawaiians, and to discuss underlying causes of disparity. In comparison to Caucasian women, African American women continue to experience the poorest breast cancer specific survival of all ethnic groups in the US. The prognosis for Latinas, Native Hawaiians, and Native Americans is intermediate, better than for African Americans but not as good as for Caucasians, whereas Japanese women tend to have better outcomes. The following possible contributors to the observed differences are discussed in detail: unfavorable distribution of stage at diagnosis due to low screening rates, limited access to care and treatment, tumor type, comorbidities, socioeconomic status, obesity, and physical activity.

Keywords

Breast carcinoma; Survival; Ethnicity; Risk factors; Trends; SEER registries

INTRODUCTION

According to the 2010 Surveillance, Epidemiology, and End Results (SEER) report [1], the 5-year breast cancer specific survival rate in the U.S. was 89.2%. The strongest determinant of survival is stage at diagnosis: 98.6% for localized disease, 83.4% for regional disease, and 23.4% for metastasized breast cancer [1]. During the last 20 years, improvements in breast cancer survival have been observed in all ethnic groups [2,3], but substantial differences across ethnic groups have been reported repeatedly with worse outcomes among ethnic groups of low socioeconomic status (SES) [4–8]. Several of the predictors proposed as possible explanations for the ethnic-specific survival differences, e.g., early detection, access to care, pre-existing chronic diseases, obesity, poverty, and lifestyle factors, are related to SES [9–11]. This raises the question whether ethnic disparities may be due to SES rather than biologic differences, such as tumor types or genetic susceptibility [12–15]. The objectives of this review are to compare breast cancer survival rates for all major racial/ethnic groups in the U.S. (African American, Hispanic, Asian, Native Hawaiian/Pacific Islander, and Native American) to rates for Caucasian women and to examine underlying

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CONFLICT OF INTEREST STATEMENT
The authors declare that they have no conflict of interest.

causes. Based on our own expertise, there is a special emphasis on Japanese and Native Hawaiian women. Genetic aspects of susceptibility are not presented as part of this review.

METHODS

Relevant publications were identified in PubMed and in the reference sections of published reports. From the large number of investigations that focused on African American women, we selected the most recent ones and included a large meta-analysis to cover the earlier time period. For the other ethnic groups, we present all available studies even if they were small and published during earlier years. Due to the differences in methodology across studies and the large body of literature, we did not attempt our own meta-analysis or systematic review. Instead, we selected studies that compare breast cancer specific and all cause survival across ethnic groups and illustrate particular causes of disparity. The 24 reports summarized in Table 1 all computed hazard ratios (HR) and 95% confidence intervals (CI). Primarily, they utilized data from one or more cancer registries that participate in the SEER program [5–8,16–22] and sometimes overlap in study population and years of diagnosis. In a number of investigations, this information was enhanced with data from questionnaires, medical records, or Medicare files [23–27]. Also, a few analyses were conducted within a single hospital or institution [28–31], network of health care institutions [32], or large clinical studies [33,34]. First, the results of the review are presented separately by ethnic group (Figure 1); then individual factors that may contribute to ethnic survival differences are discussed in detail.

RESULTS

African Americans

The literature on ethnic-specific survival differences is most abundant for African Americans. The higher breast cancer mortality rates have been a concern for many years, in particular in light of the incidence rates below those for Caucasians [1,3]. Despite some exceptions, the majority of publications show an elevated risk of dying for African Americans compared to Caucasian breast cancer cases with HRs ranging between 1.2 and 2.6 (Figure 1A). A meta-analysis summarizing 20 studies up to 2005 [4] found a higher risk of breast cancer specific mortality for African American women (HR = 1.3; 95% CI 1.2–1.4). Even after controlling for an area-wide measure of SES the association remained significant; the risk estimate was attenuated to 1.2 (95% CI 1.1–1.3). Two earlier investigations that did not have SES information reported risk estimates of 1.5 [8] and 1.3 [32]; the latter study included women with equal access to health care. Since the meta-analysis, a number of conflicting reports have been published. No ethnic differences in outcome were detected in a SEER-Medicare analysis that controlled for SES and comorbidities [26] and in a population of women with low SES who were treated at a single academic center [29]. In a review of medical records within one medical center, no difference in overall survival was observed after adjustment for sociodemographic factors, but the risk for recurrence was non-significantly elevated among African Americans (HR = 1.3; $p = 0.11$) [28]. Although a study limited to metastasized breast cancers found no ethnic difference in survival, an interaction term between ethnicity and year of diagnosis was statistically significant, indicating that the gap for African American relative to Caucasian patients, despite being small, increased over time [20]. A range of elevated risks for breast cancer-specific mortality were described in more recent studies ranging from 1.2 [27] and 1.4 [19,25,30] to 1.5 [6,31], and 2.6 [21]. Although a wide range of covariates were included in the models, the predictors varied across reports, e.g., education, SES, and region [6]; obesity, stage, treatment, comorbidities, and hormone receptor status [25]; or access to care [30]. Therefore, the results in Figure 1 reflect the remaining ethnic differences after accounting for different sets of explanatory factors in each study and are difficult to

compare. The ideal method to control for differences in treatment is clinical trials; however, an analysis of phase III clinical trials conducted by the Southwest Oncology Group (SWOG) showed that African American ethnicity was associated with a 40% higher mortality in patients with early-stage premenopausal breast cancer and a 50% higher mortality among early-stage postmenopausal breast cancer cases, despite treatment on the same protocols and adjustment for multiple prognostic factors [34]. Many of the comparative reports noted the presence of worse predictors of outcome, such as advanced stage, negative ER/PR status, and triple negative tumors, among African American women [11,25,28,29,32].

Asian Americans

Due the large differences in SES across Asian subgroups, mortality differs considerably by subgroup and also by immigrant status. For example, in a California study, foreign born Chinese and Filipino women had poorer outcomes than those born in the US [22]. For women of Japanese and Chinese ancestry, generally more favorable outcomes have been reported than for Caucasians, whereas Filipina, Korean, South Asian, and Vietnamese immigrants tend to experience poorer outcomes [8,16,22]. When risk estimates for Asians as a group were presented, outcomes were better than for Caucasians [21,26]. Given the limited data on most Asian subgroups, we only summarize studies with Japanese Americans in Figure 1B. Whereas the risk of dying from breast cancer was similar as for Caucasians in four investigations [5,16,24,25], two reports described survival advantages in the range of 20% [18] to 40% [8] without adjusting for BMI or other lifestyle factors.

Native Hawaiians/Pacific Islanders

Similar to African Americans, health disparities in Native Hawaiians and other Pacific Islanders due to low SES and lack of access to care have been an area of great concern and active research [35]. Because only one report presented separate results for Samoans [19], all investigations shown in Figure 1C refer to Native Hawaiians. Out of eight studies, all but three [19,24,25] observed statistically significant poorer outcomes. The risk estimates ranged from 1.3 [8] to 1.5 [6,18] and 1.6 [5] when compared to Caucasians; in comparison to Japanese the HR was 1.7 in one report [16]. The higher risk estimates tended to be in SEER-based analyses without additional information on treatment and comorbidity [6,8,18], whereas studies performed in recent years and controlling for more detailed information on lifestyle factors tended to observe less disparity in survival [24,25]. A study linking insurance claims with Hawaii SEER data, thus controlling for comorbidities and adequacy of treatment, also showed little ethnic differences [36]. This indicates that obesity and comorbidities may explain part of the poorer survival observed among Native Hawaiians who suffer from high rates of obesity, hypertension, and diabetes [37,38]. The poor survival of Samoan women as reported by a SEER-based investigation was most likely due to late diagnosis and lack of access to appropriate screening and treatment [6].

Latinas

Of the five studies that included Latinas (Figure 1D), three described poorer breast cancer survival outcomes for Latina women who had immigrated from different countries [6,8,23] and two observed no differences [25,26]. However, in comparison with the risk estimates for African Americans, the HRs for Latinas were relatively small. In a SEER-based report, the risk of dying from breast cancer was 10% higher for Latinas than Caucasians while controlling for stage, age, treatment, ER/PR status, and access to health care [8]. Later research by Ooi [6] and Hill [23], also based on SEER data for Latinas, found an excess risk of 10% in one study after controlling for stage, age, income, education, residence, ER/PR status, and treatment [6]; and 23% in the other study after adjustment for method of detection [23]. Two later studies that detected no ethnic differences controlled for additional

variables, i.e., equal insurance status (Medicare), detection method, comorbidities, SES, surrounding community, and region [26] as well as BMI [25].

Native Americans

We identified five studies (Figure 1E) among Native American women. A 1974–1989 investigation from Washington state [7] reported poorer breast cancer survival among Native Americans than Caucasians in the same area (HR=1.4) after controlling for age, stage, residence, and treatment. Three later reports also showed 30–70% higher risks of dying from breast cancer for Native American women [8,17,19] after adjustment for different predictors. The most recent study that controlled for stage, age, ER/PR status, and treatment in addition to access to health care, poverty, education, and geographic location detected no statistical difference between Native Americans and Caucasians [6].

DISCUSSION

While there is little doubt that mortality from breast cancer has decreased for all ethnic groups during the last 20 years [1,2], it is clear that survival differences between ethnic groups have not been eradicated. Based on many reports confirming disproportionate numbers of late stage disease, lack of screening and early detection due to limited access to health care remain important contributors to this situation [9,23]. Nevertheless, the role of lifestyle factors, such as obesity and physical activity, has become better understood and gained more attention [39]. The differences and time trends across populations are not easily disentangled since the studies do not control for a common set of covariates known to influence survival. As described in an excellent review [10], many of these factors are related to SES and affect prognosis in combination and through multiple pathways. For example, poverty may directly be responsible for lack of screening but also indirectly affect tumor biology because obesity, smoking, and poor nutrition may promote the development of tumors with adverse characteristics. We will consider the major factors that have been identified as contributors to the observed differences and explain the inconsistencies in the reports discussed above.

Early Detection and Access to Care

Given the importance of stage at diagnosis for prognosis [1], screening participation and early detection are the most important predictors of survival. There are many examples of this in the literature, such as the analysis of 229,594 cases from the SEER registries that shows respective rates of 50% and 57% stage I cases among Caucasians and Japanese, compared to 35%, 38%, 42%, and 45% in African Americans, Latinas, Pacific Islanders, and Native Americans [6]. In a study among Latinas, the screen-detected proportion of cancers was only 52% compared to 61% in Caucasians, and adjustment for type of detection reduced the ethnic difference [23]. As described in a large trend analysis for 1987–2005 [2], absolute ethnic disparities declined for mammography screening, stage at diagnosis, and 5-year cause-specific probability of death during this time period; however, relative ethnic disparities in 5-year cause-specific probability of death persisted.

Lack of early detection is further complicated by delay in treatment initiation [9]. Another important issue is compliance with consensus recommendations to treat breast cancer, which have been associated with improved survival [40]. Many reports suggest less surgery, radiation therapy, and hormone treatment and 20–50% rates of inappropriate treatment among African Americans as compared to Caucasians [8,32]. When detailed information from medical charts was used to assess breast cancer treatment [41] or comorbidity and treatment patterns from insurance claims were included as covariates [36], survival times were relatively similar across ethnic groups in Hawaii with a rather unique health care

environment. Because cancer registries do not typically collect information on treatment beyond 6 months, many of the published reports are missing detailed treatment information after initial treatment. However, access to care and health insurance rates [42] are probably not the only reason for these delays; geographic distance from good treatment centers and cultural factors probably also contribute as suggested by the disparate outcome in the SWOG trials [34].

Tumor Type

Advances in molecular classification and characterization of breast tumors into distinct subtypes by using DNA microarrays independent of disease stage has allowed stratification of cases by prognosis [43,44]. Whereas the respective proportions for the major subtypes appear to be similar in Japanese and Chinese Americans as in Caucasians [45], the distribution in African Americans is skewed toward the subtypes with poorer outcomes [46,47]. African American women are more likely to be diagnosed with higher tumor grades as well as ER/PR negative and triple negative tumors than Caucasians, partly as a result of later stage at diagnosis [9,11,33,48]. The same observation was made for Latina women, although to a lesser degree [6]. Interestingly, a study among a socioeconomically deprived population with high obesity rates showed more tumors with poor prognostic features, i.e., late stage, triple negative, and lymph node metastases [49]. This suggests that a low SES regardless of ethnic background is associated with breast cancer tumors that have an unfavorable prognosis [10].

Comorbidity

Closely related to the question of appropriate treatment is the issue of pre-existing conditions. Given the high rates of obesity, diabetes, and hypertension among African American and Hispanic [42] as well as Pacific Islander women [37,38], the presence of these conditions may be responsible for worse breast cancer outcomes, possibly due to less tolerance to cancer treatments. Women with comorbidities may receive less aggressive treatment, as described for diabetic women, due to disease-related complications [50]. The association of comorbidity with lower survival rates among breast cancer patients has been shown repeatedly [36,51,52]; however, comorbidity contributes more to higher overall mortality in breast cancer patients than to breast cancer specific mortality [31]. On the other hand, controlling for comorbidity does not eliminate all ethnic differences as can be seen in several studies within the meta-analysis [4].

Socioeconomic Status

As for many conditions, outcomes tend to be worse for individuals with lower education and income than for those with higher SES [53]. In a recent report on health disparities [42], the persisting ethnic differences in education, health insurance coverage, and poverty status are well documented. Although many survival analyses included SES indicators, the registry-based studies usually only had neighborhood-level SES indicators with well documented limitations available since more accurate individual-level SES data are difficult to collect [54]. Nevertheless, in the meta-analysis of studies among African American women, the area-wide measure of SES narrowed the survival difference considerably [4]. Interestingly, it appears from a limited number of studies within Caucasian populations with low SES that poverty is associated with similar cancer disparities as observed across ethnic groups [2,10,49]. Adjustment for SES probably remains insufficient because a person’s economic and social situation is more complex than just assessing income and education; housing, environmental, dietary, cultural, behavioral, and access to health care issues are additional contributors to health effects and are not easily captured by traditional demographic data [4,53,55]. Since SES is not a biologic risk factor itself and rather a marker for other factors,

such as access to screening and health care, it is also challenging to interpret studies that controlled for SES and true mediating variables, such as obesity, at the same time.

Obesity and Physical Activity

The role of obesity at diagnosis and later has become much clearer over recent years and is important in light of the higher obesity rates in non-Caucasian women [37,42]. There is increasing evidence that obese women with breast cancer experience worse breast cancer survival, as much as 30% higher mortality, than survivors with normal weight [39,56]. This difference appears to be due to estradiol formation in adipose tissue, which stimulates neoplastic cell proliferation in obese women [57] contributing to more biologically aggressive tumors [58]. Estrogen-independent pathways, in particular adipokine production, e.g., adiponectin and leptin, may also contribute to an aggressive breast cancer phenotype [59,60]. Furthermore, obese women may be given lower doses of chemotherapy because the ideal body surface area rather than true body surface area is used to estimate the dose of chemotherapy [61]. Epidemiologic data for other modifiable factors such as physical activity and healthful diets are not as convincing [39], but a growing number of large observational studies have demonstrated that participation in moderate intensity recreational physical activity after diagnosis may improve survival in women with breast cancer [62,63].

Methodological Issues

In the studies included in this review (Table 1), variations in study populations and research methodology appear to be major contributors to the conflicting findings. In general, it appears that smaller ethnic differences in survival are observed when more predictors were included [24] or when patients come from a similar background and are treated in the same institution [28,29]. However, each study controlled for a different combination of covariates, which makes it difficult to determine which factors explain the ethnic disparity across populations. Sample sizes and especially the number of cause-specific deaths were very small in several investigations. Although the studies were based on different populations across the country, the majority relied on data collected by SEER registries. While the SEER data provide information for a large number of cases and follow a standardized protocol for data collection, they lack information on personal and lifestyle factors, such as BMI, SES, access to healthcare, and comorbidities. Another limitation is that the majority of studies with Asians and Pacific Islanders relied on similar datasets or geographic locations because the number of breast cancer patients with Asian and Pacific Islander ancestry in the U.S. is limited. Thus, the multiple SEER analyses are not independent from each other. For example, some of the cases in smaller SEER studies may also be included in the larger or national SEER studies and other reports are updates of earlier investigations with partial overlap. An ideal study would present the association between ethnicity and survival among women with breast cancer in age-adjusted models and compare this to models that control for other predictors of breast cancer survival separately and in combination. These predictors should include stage at diagnosis, hormone receptor status, tumor characteristics, treatment received, comorbidities, insurance status, SES, obesity, and preferably also smoking, physical activity, and other lifestyle factors. This would answer the question what proportion of ethnic differences in survival are explained by individual factors and their combinations and would suggest the most likely interventions to reduce the disparity in breast cancer survival.

CONCLUSIONS

From the existing evidence, it appears that African American women continue to experience the poorest breast cancer specific survival of all ethnic groups in the US. The prognosis for Latinas, Native Hawaiians, and Native Americans is intermediate, better than for African

Americans but not as good as for Caucasians and Japanese. One possible explanation of this evidence is that genetic susceptibility or lifestyle factors predispose some ethnic groups to tumors with more adverse behavior [12–15]. Future genetic investigations may also detect ethnic related genetic polymorphisms of chemotherapy metabolizing enzymes [64]. However, an alternative interpretation is that, regardless of ethnic background, women with low SES and unhealthy lifestyles are more likely to experience late stage disease and to develop more aggressive tumors than more affluent women. This hypothesis is supported by the following pieces of evidence. One, research among Caucasian women with low SES indicates similar tumor types and poor survival as observed in African American populations [49]. Second, improvements in outcomes have occurred over time across ethnic groups [2]. Finally, inclusion of more treatment, comorbidity, SES, and lifestyle information in the statistical analysis appears to diminish the observed ethnic differences (Figure 1).

FUTURE PERSPECTIVE

For the future, Newman et al. [4] proposed two research areas that need to be strengthened in addition to improved early detection and access to care: Methods to measure effects of sociobehavioral issues and poverty, e.g., environmental, economic, cultural, and lifestyle factors, on breast cancer risk and an exploration of associations between ethnicity and variation in primary breast tumor biology. As to efforts in reducing the unequal mortality to breast cancer, improvements in SES, health insurance, and access to care will still achieve great improvements although we do not know at this time whether a part of the observed ethnic differences is due to genetic factors that cannot be modified.

Acknowledgments

One of the authors (SMC) was supported by a postdoctoral fellowship on grant R25 CA 90956.

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EXECUTIVE SUMMARY

Background

- Although breast cancer survival has improved for all ethnic groups over the last 20 years, poor survival rates in some ethnic groups remain an important concern.

Results

- In comparison to other ethnic groups in the US, African Americans have worse breast cancer specific survival rates.
- Breast cancer related mortality among Hispanic, Native Hawaiian, and Native American women is intermediate between African Americans and Caucasians, whereas Japanese and some other Asian groups show better survival rates than Caucasians.
- Adjustment for prognostic predictors reduces ethnic differences in breast cancer survival.
- Lack of early detection, late stage at diagnosis, and limited access to health care are the most important predictors of poor breast cancer survival.
- Low socioeconomic status appears to be associated with tumors showing unfavorable characteristics and higher breast cancer related mortality independent of ethnic background.
- Comorbidities, obesity, and lifestyle factors have emerged as additional significant determinants of prognosis.

Future perspectives

- Improvements in early detection of breast cancer and access to health care will lead to further reductions in breast cancer related mortality.
- Better methods of measuring the effects of sociobehavioral factors and poverty on tumor biology are needed to understand these associations.
- Explorations of tumor biology and genetic susceptibility may be able to identify additional determinants of ethnic differences.

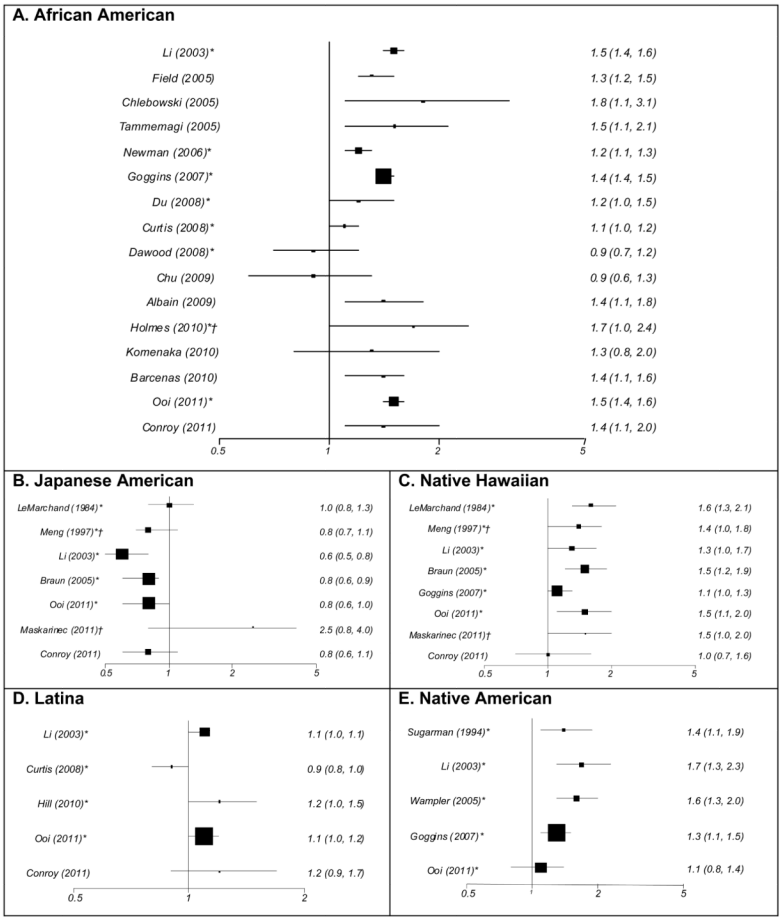

Figure 1.

Summary of breast cancer specific survival by ethnic group^

^Shown are authors, year of publication, and hazard ratios with 95% confidence intervals multivariately adjusted as presented in the original publication (Table 1); the size of symbol reflects the number of study subjects

*Based on SEER data

†Japanese Americans were used as reference group in the original report

Table 1

Selected studies comparing breast cancer specific survival by ethnic group

Author (Year) Population source	N of subjects % Early stage	Cases	Deaths	HR (95% CI)	Covariates
LeMarchand (1984) [5] HTR (1960–1979)	*N*=2,956 58% Loc	W: 1,174		Ref	Age, stage, SES
		J: 973		1.0 (0.8–1.3)	
		H: 458		**1.6 (1.3–2.1)**	
		C: 225		1.0 (0.7–1.4)	
		F: 127		**1.6 (1.1–2.4)**	
Sugarman (1994) [7] Seattle SEER, Portland IHS (1974–1989)	*N*=25,315 59% 0/Loc	W: 25,213	10,038	Ref	Age, stage, urban residence, treatment
		NA: 102	49	**1.4 (1.1–1.9)**	
Meng (1997) [12] HTR (1980–1988)	*N*=3,345 62% Loc Equal access	W: 1,191	172	1.2 (0.9–1.5)	Age, stage, census SES, menopausal status, marital status, geographical residence
		J: 1,130	132	Ref	
		H: 549	122	**1.7 (1.3–2.2)**	
		C: 242	34	1.3 (0.9–1.9)	
		F: 233	46	**1.6 (1.1–2.3)**	
Li (2003) [8] SEER (1992–1998)	*N*=124,934 48% I	W: 97,999	14,089	Ref	Age, stage, ER/PR, surgery, radiation therapy
		B: 10,560	2,393	**1.5 (1.4–1.6)**	
		J: 2,420	187	**0.6 (0.5–0.8)**	
		F: 2,125	227	0.9 (0.8–1.1)	
		C: 1,852	177	0.8 (0.7–1.0)	
		H: 689	88	**1.3 (1.0–1.7)**	
		L: 7,219	1,117	**1.1 (1.0–1.1)**	
		NA: 322	69	**1.7 (1.3–2.3)**	
Wampler (2005) [13] 3 SEER programs (1973–1996)	*N*=2,555 54% Loc	W: 2,044		Ref	Age, marital status, stage, tumor size, lymph nodes, therapy
		NA/AN: 511		**1.6 (1.3–2.0)**	
Field (2005) [27] CRN (1993–1998)	*N*=21,155 67% Loc Equal access	W: 18,879	3,474	Ref	Age, histology, enrollment history, health plan
		B: 2,276	596	**1.3 (1.2–1.5)**	
Chlebowski (2005) [29] WHI (1993–1998)	*N*=156,570 74% Loc	W: 3,455	191	Ref	Age, BMI, tumor stage, study component
		B: 242	21	**1.8 (1.1–3.1)**	

Author (Year) Population source	N of subjects % Early stage	Cases	Deaths	HR (95% CI)	Covariates
Tammemagi (2005) [28] Ford Health System (1985–1990)	*N*=906 35% 0/I	W: 642	115	Ref	Age, tumor stage, ER, therapy, comorbidity
		B: 264	64	**1.5 (1.1–2.1)**	
Braun (2005) [14] HTR (1990–2002)	*N*=7,722 54% I	W: 2,363	239	Ref	Age, stage, ER/PR
		J: 2,666	175	**0.8 (0.6–0.9)**	
		H: 1,330	173	**1.5 (1.2–1.9)**	
		F: 847	110	**1.4 (1.1–1.7)**	
		C: 516	55	0.9 (0.7–1.2)	
Newman (2006) [4] 20 studies (1958–2003)	*N*=90,124	W: 76,111		Ref	Age, stage, SES
		B: 14,013		**1.2 (1.1–1.3)**	
Goggins (2007) [15] SEER (1991–2004)	*N*=348,358 47% I	W: 310,024		Ref	Tumor size, grade, histology, ER/PR
		B: 34,293		**1.4 (1.4–1.5)**	
		H: 1,873		1.1 (1.0–1.3)	
		NA: 1,702		**1.3 (1.1–1.5)**	
		S: 187		**1.6 (1.2–2.1)**	
Du (2008) [23] SEER-Medicare (1992–1999)	*N*=35,029 59% I	W: 30,484		Ref	Age, marital status, tumor details, ER/PR, SES, comorbidity, treatment
		B: 1,971		**1.2 (1.0–1.5)**	
Curtis (2008) [22] SEER-Medicare (1994–1999)	*N*=41,020 56% 0/I	W: 35,878	4,672	Ref	Age, region, screening, tumor type, ER, grade, treatment, comorbidity, community, SES
		B: 2,479	477	1.1 (1.0–1.2)	
		L: 1,172	171	0.9 (0.8–1.0)	
		API: 1,086	82	**0.6 (0.5–0.8)**	
Dawood (2008) [16] SEER (1988–2003)	*N*=15,438 All stage IV	W: 11,049		Ref	Age, grade, ER/PR surgery, marital status,
		B: 2,219		0.9 (0.7–1.2)	
Chu (2009) [25] Louisiana State University (1998–2008)	*N*=786 35% 0/I Equal access	W: 318	46	Ref	Age, stage, therapy, grade, income, SES
		B: 468	86	All deaths 0.9 (0.6–1.3)	
Albain (2009) [30] SWOG Phase III trials	*N*=6.676 Equal access	W: 6,014		Ref	Age, tumor size, number of lymph nodes
		B: 662		**1.4 (1.1–1.8)**	
Holmes (2010) [17] SEER (1992–1998)	*N*=6,951 56% 0/I	W: 5,981		**1.5 (1.1–1.9)**	Age, marital status, stage, surgery, radiation
		B: 506		**2.6 (1.9–3.6)**	

Author (Year) Population source	N of subjects % Early stage	Cases	Deaths	HR (95% CI)	Covariates
		A: 359		Ref	
Gomez (2010) [18] CCR, SEER (1988–2005)	*N*=20,747 13% I	J (US): 2,130	239	Ref	Age, immigrant status, marital status, stage, grade, histology, ER, surgery/treatment, neighborhood SES
		J (foreign): 1,456	159	1.1 (0.9–1.4)	
		C (US): 1,217	114	1.5 (1.3–1.7)	
		C (foreign): 4,437	647	**1.5 (1.3–1.7)**	
		F (US): 614	62	1.2 (0.9–1.5)	
		F (foreign): 6,814	1076	**1.5 (1.3–1.7)**	
Hill (2010) [19] SEER, Mammography Project (1995–2004)	*N*=3,891 49% I	W: 2,881		Ref	Age, detection, income, education, rural residence, tumor size, stage, grade
		L: 1,010		**1.2 (1.0–1.5)**	
Komenaka (2010) [24] Wishard Memorial Hospital, IN (1997–2006)	*N*=574 53% 0/I Equal access	W: 259	30	Ref	Age, stage, ER/PR, employment, comorbidity
		B: 315	55	1.3 (0.8–2.0)	
Barcenas (2010) [26] Medical College, GA (1990–2005)	*N*=1,159 33% 0/I	W: 670	225	Ref	Age, stage, therapy, surgery
		B: 489	217	**1.4 (1.1–1.6)**	
Ooi (2011) [6] SEER (2000–2006)	*N*=229,594 48% I	W: 176,094	10,823	Ref	Age, SEER registry, stage, ER/PR, treatment, poverty, education
		B: 20,486	2,808	**1.5 (1.4–1.6)**	
		L: 14,951	1,188	**1.1 (1.0–1.2)**	
		J: 2,658	105	**0.8 (0.6–1.0)**	
		H: 885	68	**1.5 (1.1–2.0)**	
		NA: 1,004	79	1.1 (0.8–1.4)	
Maskarinec (2011) [20] HTR (1995–1996) Plus interview	*N*=382 65% 0/I Equal access	J: 137	8	Ref	Age, menopausal status, BMI, stage, ER/PR, treatment, toxicity, comorbidity, health insurance
		W: 93	7	0.4 (0.1–1.2)	
		H: 49	16	0.6 (0.2–1.9)	
		C: 45	20	2.3 (0.9–6.0)	
		F: 27	19	1.7 (0.5–5.7)	
Conroy (2011) [21] MEC, CA county cancer surveillance program, CCR, HTR (1993–2007)	*N*=3,842 71% Loc	J: 1,141	65	0.8 (0.6–1.1)	Age, ER/PR, treatment, comorbidity
		W: 991	93	Ref	
		B: 748	115	**1.4 (1.1–2.0)**	
		L: 623	72	1.2 (0.9–1.7)	
		H: 339	31	1.0 (0.7–1.6)	

Abbreviations: SEER=Surveillance Epidemiology End Results, HTR=Hawaii Tumor Registry (part of SEER), IHS=Indian Health Service, CRN=Cancer Research Network, CCR=California Cancer Registry, MEC=Multiethnic Cohort Study, SWOG=South West Oncology Group, SES=Socioeconomic Status, BMI=Body Mass Index

Stages: 0=in situ, Loc=localized, I=stage I; ER/PR=estrogen and progesterone receptor

Ethnic groups: A=Asian , AN=Alaska Native, B=African American, C=Chinese American, F=Filipino, H=Native Hawaiian, J=Japanese American, L=Latino, NA=Native American, PI=Pacific Islander, S=Samoan, W=Caucasian