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Competing Causes of Death for Women With Breast Cancer and Change Over Time From 1975 to 2003

Xianglin L. Du, MD, PhD^{*}, Erin E. Fox, PhD^{*,†}, and Dejian Lai, PhD[‡]

^{*}From the Division of Epidemiology, School of Public Health, University of Texas Health Science Center, Houston, TX

[†]Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin, TX

[‡]Division of Biostatistics, School of Public Health, University of Texas Health Science Center, Houston, TX.

Abstract

This study was to determine whether the proportion of death due to breast cancer changed over time in different cohorts of women diagnosed with breast cancer. We identified 316,149 women with breast cancer at age 20 or older during 1975–2003 from the Surveillance, Epidemiology, and End Results 9 tumor registries in the United States. Logistic regression models were used to assess the effects of time period on the likelihood of dying because of breast cancer as underlying cause of death, adjusting for other factors. Overall, underlying cause of death was 52.8% due to breast cancer, 17.8% due to heart disease, and 4.9% due to stroke. Percentage of death due to breast cancer did not change significantly from 1975 to 2003 in those who died <12 months after diagnosis, but decreased significantly in women who died between 1 and 15 years. Risk of death due to breast cancer in women diagnosed during 1995–1998 was significantly lower than those in 1975–1979 (odds ratio = 0.79, 95% confidence interval = 0.70 – 0.89), after adjusting for age, race, ethnicity, and tumor stage. Percentage of death due to breast cancer decreased significantly with age from 87.5% in women <40% to 30.7% in those 80 or older, which was not significantly affected by year of diagnosis. Proportion of death due to breast cancer increased with advanced tumor stage and was similar in various racial/ethnic groups of population. The findings demonstrated that the impact of breast cancer on overall death was reduced after 1 year of diagnosis, but suggested the need for continued cancer surveillance.

Keywords

breast cancer; cause of death; women; SEER; tumor registry; temporal trend

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death in women.^{1–4} According to the American Cancer Society data, it was estimated that 212,920 women will be diagnosed with and 40,970 women will die of breast cancer in 2006.³ During the past decade, mortality for patients with breast cancer decreased significantly,¹ largely because of early detection or screening for breast cancer and advances in medical care and treatments.^{5–17} As a result, many patients with breast cancer can live much longer than ever before, and many of these women will die of causes other than breast cancer when they are getting older. However, there is little information on how the main underlying causes of death changed over time during the past several decades for women with breast cancer, although

several studies have examined competing causes of death for women with breast cancer and found that other causes of death increased with age.^{18–22} Schairer et al found that the probability of death from breast cancer relative to the probability of death from other causes declined with age.²² However, it is unknown if the proportion of death from breast cancer relative to other causes changed over time in different cohorts of women diagnosed with breast cancer from 1975 to 2003. This study used data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) cancer registries, one of the most often referred data sources on cancer, to examine the causes of death for women diagnosed with breast cancer from 1975 to 2003, to determine the percentage of women who died of breast cancer and percentages of women who died of heart disease, stroke, pneumonia, or other causes, and to determine how the competing causes of death changed over time. With improvement in medical care and early diagnosis for this disease in recent decades, the postdiagnosis life span increased substantially.^{1–4,9–17} Hence, women with breast cancer may have been subject to other competing risks of death for a longer period of time, which would result in a relatively lower proportion of deaths due to breast cancer in recent years compared with earlier cohorts.^{18–22} On the basis of evidence from previous randomized trials^{9–17} and observational studies,^{18–22} it would be reasonable to hypothesize that the majority of women with breast cancer died of causes other than breast cancer and that the proportion of women whose underlying cause of death was breast cancer decreased over time from 1975 to 2003.

PATIENTS AND METHODS

Data Sources

Data used in this article were from the SEER 1975–2003 Public Use Data Set (CD-ROM) released in April 2006.²³ The SEER program supports the 9 population-based tumor registries in 4 metropolitan areas (San Francisco/Oakland, Detroit, Atlanta, Seattle) and 5 states (Connecticut, Iowa, New Mexico, Utah, and Hawaii) since 1975, covering over 14% of the US population.¹ The registries ascertain all newly diagnosed (incident) breast cancer cases from multiple reporting sources such as hospitals, outpatient clinics, laboratories, private medical practitioners, nursing/convalescent homes/hospices, autopsy reports, and death certificates. Information in the data set includes tumor location and demographic characteristics such as age, gender, race, and marital status. The SEER public use data set also includes information on the types of surgical procedures and radiation therapy received. The Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston approved this study.

Study Population

We identified 316,149 women who were diagnosed with invasive breast cancer at all ages between 1975 and 2003 in 9 SEER areas, in whom breast cancer was the first and only primary tumor. By the date of last follow-up (December 31, 2003), 136,450 (43.2%) patients died, of whom 72,064 (52.8%) died of breast cancer.

Study Variables

Causes of Death—The SEER data set provided the underlying cause of death for women with breast cancer who died. The leading causes of death included breast cancer, heart disease, stroke, other cancers, other cardiovascular diseases, respiratory diseases, and other causes. About 3.7% of cases had missing or unknown information on the causes of death.

Patient and Tumor Characteristics—Other variables examined in the analysis included age at diagnosis (<44, 40–49, 50–59, 60–69, 70–79, ≥80 years), race (white, African American, American Indian, Asian, or unknown), Hispanic ethnicity (yes or no), tumor stage (local, regional, distant stage, or unstaged), year of diagnosis (1975–2003), and geographic area (9

SEER regions).²³ Variables on tumor size, grade, and hormone receptor status, which were available since 1988, were also adjusted in the analysis.

Treatment for Breast Cancer—Breast-conserving surgery (BCS) was defined as receiving segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy unspecified (SEER surgery codes 10–29).²³ Mastectomy was defined as subcutaneous, total (simple), modified radical, radical, or extended radical mastectomy (codes 30–70).²³ Radiation therapy included beam radiation, radioactive implants, brachytherapy, radioisotopes, or other radiation. Clinical guidelines recommend that patients with invasive breast cancer receive mastectomy or receive BCS followed by subsequent radiation therapy.²⁴ The “no cancer-directed surgery” included either no surgical procedures, or only incisional, needle, or aspiration biopsy.²⁴ Therefore, patients were categorized into 4 groups: no cancer-directed surgery (codes 0-9), BCS only without radiation therapy, BCS with radiation therapy, and mastectomy.

Statistical Analysis

Descriptive analyses generated the number of women diagnosed with breast cancer from 1975 to 2003 and the number and proportion of cases that died during these time periods, by patient and tumor characteristics, the year of diagnosis, and SEER region. The competing causes of death were stratified by the time period during which patients died. This was to ensure that comparisons were made among cases with a similar length of follow-up after diagnosis. A χ^2 test of trend was used to assess the time trend of the proportion of death due to breast cancer in the 5 time periods. Logistic regression models were used to assess the effect of time period on the likelihood of dying because of breast cancer. In these multiple logistic regression analyses, odds ratios were adjusted for age, race, Hispanic ethnicity, and tumor stage. Logistic regression analyses were also performed to determine the effect of age and tumor stage on the competing cause of death while adjusting for the year of diagnosis. A simple linear regression was used to test the significance of odds ratio trend over time. All analytical procedures were performed using the SAS software package (Cary, NC)²⁵ and Stata (version 9.2; College Station, TX).²⁶

RESULTS

Table 1 presents the number of patients who were diagnosed with invasive breast cancer from 1975 to 2003 in the 9 SEER areas, the number of cases who died of all causes of death combined, and the number of cases who died of breast cancer only. Of 316,149 cases diagnosed with breast cancer, 43.2% died of all causes by the last date of follow-up, and 22.8% died of breast cancer specifically that accounted for 52.8% of all deaths. Mean age at diagnosis was 61 years. Over 75% of breast cancer cases occurred in women aged ≥ 50 and over 53% occurred in women aged ≥ 60 . White women represented 86.1% of these cases, 8.0% were African Americans, and 5.2% were Asians. Over 96% of all breast cancer cases were non-Hispanic. The majority of breast cancer cases were diagnosed at localized stages (56.4%) or at regional stages (33.1%). Only 6.6% of women were diagnosed with advanced distant stage breast cancer. Of those who died of breast cancer as the underlying cause of death, 47% were regional stages, 24% were local stages, and 20.5% were distant stages. Those with distant stage who died of breast cancer as underlying cause of death accounted for 82.9% (14,803 of 17,854) of all deaths with distant stage. Most cases received mastectomy, and approximately 30% received BCS, but 8.6% of patients received BCS without radiation therapy.

Table 2 presents the causes of death stratified by the years of follow-up and by the length of survival time (<1, 1–3, 4–5, 6–10, 11–15, >15 years). Overall, among patients who died, 52.8% of deaths were due to breast cancer, 17.8% were due to heart disease, 4.9% were due to stroke,

3.4% were due to other cancers besides breast, 20.2% were due to other causes, and 3.7% of deaths were unknown. Among those cases that died within 1 year of diagnosis, the proportion of death due to breast cancer was relatively stable over time (60%–66%). The proportions of death due to heart disease and stroke decreased slightly whereas death due to other causes increased. In women who survived longer, the percentage of death due to breast cancer decreased over time. For example, in those who died between 13 and 36 months after diagnosis, the percentage of death due to breast cancer decreased from 71.2% in the cohort of patients diagnosed in 1975–1979 to 62.7% in patients diagnosed in 1995–1999. In those who died between 61 and 120 months after diagnosis, the percentage of death due to breast cancer decreased from 53% in patients diagnosed in 1975–1979 to 39% in patients diagnosed in 1990–1994. In those who died 10 or more years after diagnosis, the majority of deaths were due to causes other than breast cancer, mostly cardiovascular diseases (heart disease or stroke). During all time periods, the percentage of patients with missing information on the cause of death was relatively stable. The proportion of death due to various causes was presented in Figure 1 for those who died within 1 year and in Figure 2 for those died after 1 or more years after diagnosis. From these figures, it was found that the proportion of death due to breast cancer was stable in those who died less than 1 year and slightly increased over time in those who died after 1 year of diagnosis.

Table 3 presents the odds ratios of dying of breast cancer from simple and multiple logistic regression models by the 6 different time periods. Model 1 was the unadjusted odds ratio without controlling for other factors. Model 2 adjusted for age, race, and Hispanic ethnicity. Model 3 adjusted for tumor stage in addition to the previous factors. Among patients with breast cancer who died within 12 months after diagnosis, those diagnosed in 1980–1989 were slightly less likely to die of breast cancer as underlying cause of death compared with those diagnosed in 1975–1979, whereas those diagnosed in 1990–2002 did not vary significantly after adjusting for age, race, Hispanic ethnicity, and tumor stage. Among cases who died between 13 and 120 months after diagnosis, those diagnosed in later years were significantly less likely to die of breast cancer as the underlying cause of death than those in the late 1970s (1975–1979). For example, the adjusted risk of death due to breast cancer between 37–60 months in women diagnosed in 1995–1998 was significantly lower than those in 1975–1979 (odds ratio = 0.79, 95% confidence interval = 0.70–0.89). The trend of odds ratio over time was significant ($P < 0.01$). However, those long-term survivors who were diagnosed in 1980–1988 and died 15 years later were more likely to die of breast cancer as the underlying cause of death than those in 1975–1979.

To assess the potential bias because of missing information on the cause of death, further analyses excluded those cases (Table 4). After excluding those with missing data on the cause of death, the magnitude and trend of odds ratios were similar to that presented in Table 3.

Table 5 presents the proportion and adjusted odd ratios of death due to breast cancer by factors other than the year of diagnosis, including age, race, Hispanic ethnicity, tumor stage, treatment, and geographic location. Model 1 adjusted for age, race, Hispanic ethnicity, tumor stage, treatment, and geographic area, whereas model 2 adjusted for the variables in model 1 and year of diagnosis. The percentage of death due to breast cancer decreased significantly with age. For example, 87.9% of deaths in women aged <40 were because of breast cancer compared with 30.7% in those aged 80 or older. Women aged 40 to 49 were 40% less likely and those aged >70 were over 90% less likely to die of breast cancer compared with those <40 years of age (model 1). When additionally controlling for the year of diagnosis, the risk of death due to breast cancer by age groups was almost unchanged (model 2). There was no significant racial/ethnic variation in the likelihood of death due to breast cancer. As expected, women diagnosed with advanced stage were more likely to die of the disease. For example, those with distant stage were over 8 times more likely to die of breast cancer than those with local stage

disease (odds ratio = 8.84, 95% confidence interval = 8.41–9.28). The odds ratio of death due to breast cancer was significantly lower in women receiving cancer-directed surgeries than those who did not. In those with no cancer-directed surgery, 31.4% were of local stage, 21.0% were of regional stage, 26.5% were of distant stage, and 21.1% were of unknown stage. There were also some geographic variations across the 9 SEER areas.

Adjusting for hormone receptor status (estrogen or progesterone receptor positivity), tumor size and grade in addition to other confounders for cases in later time periods (after 1988 when these data became available) did not alter the results (Table 6). This table also shows that the proportion of death due to breast cancer was higher in women with negative hormone receptor, larger tumor size, and poorer tumor grade, after controlling for the year of diagnosis, demographics, tumor stage, treatment, and geographic area.

DISCUSSION

This study examined the competing causes of death and changes over time among women diagnosed with invasive breast cancer. Overall, among all patients who were diagnosed with breast cancer and died between 1975 and 2003, the underlying cause of death was 52.8% due to breast cancer, 17.8% due to heart disease, 4.9% due to stroke, 3.4% due to other cancers, and 20.2% due to other causes. The percentage of death due to breast cancer did not change significantly over time from 1975 to 2003 in those who died within 12 months of diagnosis, but decreased significantly in women who died between 1 and 15 years after diagnosis. The percentage of death due to breast cancer significantly decreased with age and increased with advanced tumor stage, but did not vary significantly by race or ethnicity.

Thanks to advances in technology and medical care for early detection and treatment, many women diagnosed with breast cancer can survive longer than ever before.^{5–17} Studies have shown that breast cancer mortality decreased and relative survival increased over the past decades,^{1–3} which may be inflated because of overdiagnosis.^{27,28} However, the trend in competing causes of death in women with breast cancer over the past 30 years has not been well documented. Schairer et al²² reported the probabilities of death from breast cancer and other causes among female patients with breast cancer and concluded that these probabilities varied substantially by tumor stage and age at diagnosis. Diab et al²⁰ studied the tumor characteristics of elderly women with breast cancer and found that relative contribution of breast cancer death to the overall causes of mortality decreased by age from 73% in women aged 50 to 54 to 29% in women aged 85 or older. However, whether the competing causes of death for patients with breast cancer changed over time was not addressed in these studies. We found that about half of women with breast cancer died of causes other than breast cancer, and the proportion of death due to breast cancer decreased significantly over time after 1 year of diagnosis. This finding is important because breast cancer now may not be perceived as life-threatening as it used to be because patients with this disease can survive for more years than ever before.

Among patients with breast cancer who died of other causes, heart disease and stroke are the leading causes of death. Because the risk of heart disease and stroke increases dramatically with age, the proportion of cases who died of heart disease and stroke increases significantly with age.²⁹ This pattern is similar to the cause of death for general population aged ≥ 65 in the United States and around the world.^{30–36} Particularly, in the population aged 80 or older, the significant majority will die of heart disease, stroke, or other causes such as fall and dementia.²⁹ Other diseases such as diabetes and obesity are increasingly becoming a concern. Therefore, prevention and treatment of these diseases are critically important for both patients with cancer and for general population. The main risk factors of these leading causes of deaths are tobacco (18.1% of total US deaths), poor diet and physical inactivity (16.6%), and alcohol consumption

(3.5%).^{30,34} These leading causes of death were also the main contributors to disparities in mortality in relation to socioeconomic status and race or ethnicity, whereas cancer accounted for 3.3% of racial disparities in mortality.³³ Implications of these studies are that prevention and treatment of heart disease, stroke, and associated risk factors will benefit people with or without cancer.

Several limitations of this study should be considered. First, the cause of death for patients with breast cancer was obtained from the National Death Index, which was primarily based on death certificates from local hospitals. These death certificates may not accurately reflect the true cause of deaths.^{37–39} Therefore, nondifferential misclassification of the cause of death is likely. Second, over the past 30 years, the definitions of diseases and technology in ascertaining the cause of disease have changed substantially. These changes might have affected the classification of the causes of death. Third, although the 9 SEER registries accounted for 14% of the US population, the results from these studies may not be generalizable to the entire nation. In addition, over the past decade, mammography screening has been effective in detecting in situ tumors and shifting invasive tumor toward earlier stages and smaller tumor sizes. Because our study population included women who had breast cancer as the first invasive tumor, those with in situ cases were excluded from the study. However, tumor stages were adjusted for in this study. Also, when tumor size, grade, and hormone receptor status were controlled for in the analysis, the results remained similar. Furthermore, we only include women who were diagnosed with breast cancer as the only primary tumor. Those patients with presence of other primary malignancies may have had more complicated competing causes of death. Finally, information on adjuvant chemotherapy and hormonal therapy is not available in SEER data. Although these adjuvant therapies have been effective in reducing all-cause and disease-specific mortality in women with breast cancer, no studies have shown that this will alter the patterns of competing causes of death over time. However, some chemotherapy regimens, particularly anthracycline-containing agents, are known to have cardiac toxicity.^{40–42} The risk of heart disease is relatively small and the impact of this toxicity on the overall patterns of competing causes of deaths over time may be minimal, if any.

In conclusion, overall, the underlying cause of death was 52.8% due to breast cancer, 17.8% due to heart disease, and 4.9% due to stroke. The percentage of death due to breast cancer as the underlying cause of death significantly decreased over time from 1975 to 2003 in women with breast cancer after 1 year of diagnosis, decreased significantly with age, and increased with advanced tumor stage, but did not vary by race or ethnicity. The findings demonstrated that the impact of breast cancer on the risk of overall death was reduced after 1 year of diagnosis, but suggested the need for continued cancer surveillance.

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FIGURE 1.

Proportion of deaths due to various causes by year of diagnosis for breast cancer patients who died within 12 months of diagnosis, 1975–2003.

FIGURE 2.

Proportion of deaths due to various causes by year of diagnosis for breast cancer patients who died more than 1 year after diagnosis, 1975–2003.

TABLE 1
Number of Patients Diagnosed With Breast Cancer and the Number of Deaths due to All Causes or Breast Cancer Only During 1975–2003

	Breast Cancer Cases (N = 316,149)		All Causes of Death (N = 136,450)		Breast Cancer Deaths (N = 72,064)	
	N	%	N	%	N	%
Year of diagnosis						
1975–1979	36,129	11.4	28,883	21.2	15,099	21.0
1980–1984	40,852	12.9	29,828	21.9	15,753	21.9
1985–1989	51,183	16.2	30,305	22.2	15,291	21.2
1990–1994	58,299	18.4	24,894	18.2	12,810	17.8
1995–1999	69,119	21.9	17,280	12.7	9,829	13.6
2000–2003	60,567	19.2	5,260	3.9	3,282	4.6
Age						
<40	22,453	7.1	7,464	5.5	6,564	9.1
40–49	55,716	17.6	14,488	10.6	11,867	16.5
50–59	68,787	21.8	21,969	16.1	15,912	22.1
60–69	69,795	22.1	30,067	22.0	16,372	22.7
70–79	61,357	19.4	33,869	24.8	12,576	17.5
80+	38,041	12.0	28,593	21.0	8,773	12.2
Race						
White	272,117	86.1	119,008	87.2	61,256	85.0
Black	25,249	8.0	12,395	9.1	7,768	10.8
Asian	16,339	5.2	4,413	3.2	2,682	3.7
American Indian	1,077	0.3	417	0.3	276	0.4
Missing	1,367	0.4	217	0.2	82	0.1
Hispanic origin						
Non-Hispanic	303,943	96.1	132,332	97.0	69,591	96.6
Hispanic	10,713	3.4	3,756	2.8	2,319	3.2
Missing	1,493	0.5	362	0.3	154	0.2
Historic stage						
Localized	178,236	56.4	55,087	40.4	17,293	24.0
Regional	104,696	33.1	53,842	39.5	33,919	47.1
Distant	20,967	6.6	17,854	13.1	14,803	20.5
Missing	12,250	3.9	9,667	7.1	6,049	8.4
Treatment						
No cancer-directed surgery	36,713	11.6	18,960	13.9	13,295	18.5
BCS only	27,066	8.6	10,625	7.8	4,033	5.6
BCS + RT	70,195	22.2	12,035	8.8	5,938	8.2
Mastectomy	182,175	57.6	94,830	69.5	48,798	67.7
SEER location						
San Francisco, CA	52,878	16.7	22,588	16.6	11,449	15.9
Connecticut	52,638	16.7	24,240	17.8	12,565	17.4
Detroit, MI	53,856	17.0	25,937	19.0	14,298	19.8
Hawaii	12,492	4.0	3,880	2.8	2,146	3.0
Iowa	40,592	12.8	19,455	14.3	9,866	13.7
New Mexico	16,799	5.3	6,847	5.0	3,893	5.4
Seattle, WA	44,924	14.2	16,911	12.4	8,707	12.1
Utah	15,923	5.0	6,525	4.8	3,415	4.7
Atlanta, GA	26,047	8.2	10,067	7.4	5,725	7.9
Total	316,149	100.0	136,450	100.0	72,064	100.0

TABLE 2
Causes of Death and Change Over Time, Stratified by Survival and Follow-up Time

Causes of Death	Percentage of Causes of Death, by Year of Diagnosis and Length of Follow-up					
	1975–1979	1980–1984	1985–1989	1990–1994	1995–1999	2000–2002
Died ≤12 mo in those with follow-up of ≥12 mo (N = 21,363)						
Breast cancer	65.8	61.7	59.9	62.9	62.4	64.0
Other cancer	3.5	3.6	3.7	3.5	4.0	3.4
Heart disease	14.7	17.3	17.8	14.6	14.1	11.8
Stroke	4.7	4.5	3.9	3.5	3.8	3.1
Other CVD	0.5	0.5	0.7	0.7	0.8	0.8
Respiratory	1.9	2.6	3.0	4.0	3.5	2.3
Other	7.1	8.3	9.2	9.6	10.1	12.6
Missing	1.8	1.5	1.8	1.3	1.2	1.9
Total N	3,702	3,685	3,876	3,669	4,045	2,386
Died during 13–36 mo in those with follow-up of ≥36 mo (N = 32,178)						
Breast cancer	71.2	70.8	67.8	65.2	62.7	59.4
Other cancer	2.5	2.4	2.5	2.6	2.8	2.8
Heart Disease	11.9	12.9	12.8	13.2	13.0	13.9
Stroke	3.5	2.8	3.1	3.7	4.0	3.1
Other CVD	0.5	0.3	0.6	0.5	0.9	0.7
Respiratory	1.5	2.1	2.9	3.3	3.7	3.9
Other	5.7	6.0	7.9	9.4	10.9	12.6
Missing	3.3	2.7	2.5	2.1	2.1	3.8
Total N	5,886	6,355	6,556	6,343	5,963	2,386
Died during 37–60 mo in those with follow-up of ≥60 mo (N = 22,539)						
Breast cancer	65.8	64.2	60.5	55.8	54.8	-
Other cancer	2.6	2.6	2.8	2.6	3.5	-
Heart disease	15.3	15.6	15.1	16.9	14.5	-
Stroke	3.8	3.4	4.4	4.4	4.6	-
Other CVD	0.6	0.5	0.8	0.9	0.8	-
Respiratory	2.4	2.8	3.6	4.4	4.5	-
Other	6.5	7.3	10.2	12.4	14.3	-
Missing	2.9	3.6	2.8	2.7	2.9	-
Total N	4,258	4,735	4,962	4,860	3,724	-
Died during 61–120 mo in those with follow-up of ≥120 mo (N = 28,385)						
Breast cancer	53.0	52.2	45.4	39.0	-	-
Other cancer	2.9	2.8	3.3	4.2	-	-
Heart disease	20.7	19.0	20.5	21.6	-	-
Stroke	4.9	5.1	5.7	6.4	-	-
Other CVD	0.9	0.6	0.9	1.2	-	-
Respiratory	3.4	4.7	5.5	6.1	-	-
Other	10.1	11.5	14.8	17.5	-	-
Missing	4.3	4.2	3.8	4.1	-	-
Total N	6,380	7,201	8,205	6,599	-	-
Died during 121–180 mo in those with follow-up of ≥180 mo (N = 12,218)						
Breast cancer	37.0	34.6	28.5	-	-	-
Other cancer	3.9	4.1	5.5	-	-	-
Heart disease	24.9	25.8	24.3	-	-	-
Stroke	7.2	6.6	8.0	-	-	-
Other CVD	1.0	0.7	1.2	-	-	-
Respiratory	6.2	7.3	7.3	-	-	-
Other	14.2	15.3	19.6	-	-	-
Missing	5.6	5.6	5.6	-	-	-
Total N	3,662	4,202	4,354	-	-	-
Died ≥181 mo in those with follow-up of ≥180 mo (N = 9,979)						
Breast cancer	18.8	20.0	21.4	-	-	-

Causes of Death	Percentage of Causes of Death, by Year of Diagnosis and Length of Follow-up					
	1975–1979	1980–1984	1985–1989	1990–1994	1995–1999	2000–2002
Other cancer	5.2	5.6	5.5	-	-	-
Heart disease	30.3	26.6	24.0	-	-	-
Stroke	7.8	8.0	7.1	-	-	-
Other CVD	1.7	1.8	1.7	-	-	-
Respiratory	8.1	7.5	8.0	-	-	-
Other	20.4	22.8	24.1	-	-	-
Missing	7.8	7.6	8.3	-	-	-
Total N	4,995	3,650	1,134	-	-	-

CVD indicates cardiovascular disease.

TABLE 3
Crude and Adjusted Odds Ratios for the Likelihood of Death due to Breast Cancer in Different Time Periods

Year of Diagnosis	Model 1*			Model 2†			Model 3‡		
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR
Survived ≤12 mo and followed-up for ≥12 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	0.81	0.73–0.90	0.86	0.77–0.96	0.88	0.77–0.96	0.88	0.78–0.99	0.88
1985–1989	0.75	0.68–0.83	0.79	0.68–0.83	0.79	0.71–0.88	0.79	0.70–0.89	0.79
1990–1994	0.82	0.74–0.92	0.89	0.80–0.99	0.92	0.80–0.99	0.92	0.81–1.04	0.92
1995–1999	0.83	0.75–0.93	0.90	0.81–1.00	0.93	0.81–1.00	0.93	0.82–1.05	0.93
2000–2002	0.81	0.72–0.92	0.92	0.81–1.04	0.96	0.81–1.04	0.96	0.83–1.10	0.96
Survived 13–36 mo and followed-up for ≥36 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	0.99	0.92–1.08	1.05	0.92–1.08	1.04	0.96–1.15	1.04	0.95–1.15	1.04
1985–1989	0.87	0.81–0.94	0.93	0.85–1.01	0.96	0.85–1.01	0.96	0.88–1.06	0.96
1990–1994	0.77	0.71–0.83	0.87	0.80–0.95	0.94	0.80–0.95	0.94	0.86–1.04	0.94
1995–1999	0.68	0.63–0.74	0.80	0.73–0.87	0.89	0.73–0.87	0.89	0.81–0.97	0.89
2000	0.59	0.51–0.67	0.74	0.63–0.86	0.80	0.63–0.86	0.80	0.68–0.95	0.80
Survived 37–60 mo and followed-up for ≥60 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	0.93	0.85–1.01	0.98	0.88–1.08	0.98	0.88–1.08	0.98	0.88–1.08	0.98
1985–1989	0.80	0.73–0.87	0.91	0.83–1.01	0.96	0.83–1.01	0.96	0.86–1.06	0.96
1990–1994	0.65	0.60–0.71	0.77	0.60–0.71	0.86	0.70–0.85	0.86	0.77–0.95	0.86
1995–1998	0.62	0.56–0.68	0.73	0.66–0.81	0.79	0.66–0.81	0.79	0.71–0.89	0.79
Survived 61–120 mo and followed-up for ≥120 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	0.97	0.91–1.04	1.04	0.96–1.13	1.03	0.96–1.13	1.03	0.95–1.12	1.03
1985–1989	0.74	0.69–0.79	0.88	0.81–0.95	0.93	0.81–0.95	0.93	0.86–1.00	0.93
1990–1993	0.56	0.52–0.60	0.67	0.61–0.72	0.73	0.61–0.72	0.73	0.67–0.79	0.73
Survived 121–180 mo and followed-up for ≥180 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	0.93	0.84–1.02	1.01	0.90–1.12	1.00	0.90–1.12	1.00	0.90–1.12	1.00
1985–1988	0.69	0.63–0.76	0.80	0.72–0.89	0.84	0.72–0.89	0.84	0.75–0.94	0.84
Survived ≥181 mo and followed-up for ≥180 mo									
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent	1.00
1980–1984	1.12	1.00–1.25	1.30	1.19–1.50	1.32	1.19–1.50	1.32	1.17–1.49	1.32
1985–1988	1.21	1.04–1.41	1.60	1.40–1.95	1.66	1.40–1.95	1.66	1.40–1.96	1.66

* Model 1 did not adjust for other factors.

† Model 2 adjusted for age (continuous), race, and Hispanic ethnicity.

‡ Model 3 adjusted for age (continuous), race, Hispanic ethnicity and tumor stage.

TABLE 4

Crude and Adjusted Odds Ratios for the Likelihood of Death due to Breast Cancer in Different Time Periods, by Excluding Cases With Missing Information on Cause of Death

Year of Diagnosis	Model 1		Model 2 [†]		Model 3 [‡]	
	OR	95% CI	OR	95% CI	OR	95% CI
Died ≤12 mo in those with follow-up of ≥12 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	0.80	0.72–0.89	0.86	0.77–0.96	0.87	0.77–0.98
1985–1989	0.74	0.67–0.82	0.78	0.70–0.87	0.77	0.68–0.87
1990–1994	0.81	0.72–0.90	0.87	0.78–0.98	0.89	0.79–1.01
1995–1999	0.82	0.74–0.91	0.88	0.79–0.99	0.90	0.80–1.02
2000–1902	0.81	0.72–0.92	0.93	0.81–1.05	0.96	0.84–1.11
Died during 13–36 mo in those with follow-up of ≥36 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	0.97	0.89–1.05	1.03	0.94–1.13	1.02	0.92–1.12
1985–1989	0.83	0.77–0.90	0.89	0.81–0.97	0.92	0.83–1.01
1990–1994	0.72	0.66–0.78	0.82	0.75–0.90	0.89	0.80–0.98
1995–1999	0.63	0.58–0.69	0.75	0.68–0.82	0.83	0.75–0.92
2000	0.57	0.49–0.66	0.73	0.62–0.87	0.81	0.68–0.97
Died during 37–60 mo in those with follow-up of ≥60 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	0.95	0.87–1.04	1.01	0.91–1.12	1.02	0.91–1.13
1985–1989	0.79	0.72–0.86	0.90	0.81–1.00	0.95	0.85–1.06
1990–1994	0.64	0.58–0.70	0.77	0.69–0.85	0.86	0.77–0.96
1995–1998	0.61	0.55–0.67	0.72	0.65–0.81	0.79	0.70–0.89
Died during 61–120 mo in those with follow-up of ≥120 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	0.97	0.90–1.04	1.04	0.95–1.12	1.03	0.95–1.12
1985–1989	0.72	0.68–0.78	0.86	0.80–0.93	0.91	0.84–0.99
1990–1993	0.55	0.51–0.59	0.66	0.60–0.72	0.72	0.66–0.78
Died during 121–180 mo in those with follow-up of ≥180 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	0.93	0.84–1.02	1.01	0.91–1.13	1.01	0.90–1.12
1985–1988	0.68	0.62–0.75	0.80	0.72–0.90	0.84	0.75–0.94
Died ≥181 mo in those with follow-up of ≥180 mo						
1975–1979	1.00	Referent	1.00	Referent	1.00	Referent
1980–1984	1.12	1.00–1.25	1.36	1.21–1.54	1.35	1.19–1.52
1985–1988	1.22	1.05–1.43	1.74	1.47–2.06	1.74	1.47–2.06

* Model 1 did not adjust for other factors.

[†] Model 2 adjusted for age (continuous), race, and Hispanic ethnicity.

[‡] Model 3 adjusted for age (continuous), race, Hispanic ethnicity and tumor stage.

TABLE 5
Breast Cancer as the Underlying Cause of Death Among All Deaths, by Patient and Tumor Characteristics, 1975–2003

Characteristics	Deaths (N)	Deaths Due to Breast Cancer (%)	Odds Ratio* of Death Due to Breast Cancer (Model 1)		Odds Ratio† of Death Due to Breast Cancer (Model 2)	
			OR	95% CI	OR	95% CI
Age						
<40	7,464	87.9	1.00	Referent	1.00	Referent
40–49	14,488	81.9	0.60	0.55–0.65	0.60	0.55–0.65
50–59	21,969	72.4	0.34	0.31–0.36	0.34	0.31–0.37
60–69	30,067	54.5	0.15	0.14–0.17	0.15	0.14–0.17
70–79	33,869	37.1	0.08	0.07–0.08	0.08	0.07–0.08
80+	28,593	30.7	0.05	0.05–0.06	0.05	0.05–0.05
Race						
White	119,008	51.5	1.00	Referent	1.00	Referent
Black	12,395	62.7	1.01	0.97–1.06	0.98	0.94–1.03
Asian	4,413	60.8	1.06	0.97–1.16	1.01	0.92–1.10
American Indian	417	66.2	1.10	0.87–1.40	1.05	0.82–1.34
Missing	217	37.8	0.45	0.29–0.69	0.48	0.31–0.74
Hispanic ethnicity						
Non-Hispanic	132,332	52.6	1.00	Referent	1.00	Referent
Hispanic	3,756	61.7	1.04	0.96–1.13	1.00	0.92–1.09
Missing	362	42.5	0.82	0.59–1.15	0.76	0.54–1.06
Historic stage						
Localized	55,087	31.4	1.00	Referent	1.00	Referent
Regional	53,842	63.0	3.13	3.04–3.22	3.11	3.03–3.20
Distant	17,854	82.9	9.00	8.57–9.46	8.84	8.41–9.28
Missing	9,667	62.6	3.94	3.72–4.18	3.93	3.71–4.16
Treatment						
No cancer-directed surgery	18,960	70.1	1.00	Referent	1.00	Referent
BCS only	10,625	38.0	0.57	0.54–0.61	0.54	0.50–0.57
BCS + RT	12,035	49.3	0.69	0.65–0.73	0.64	0.60–0.68
MRM	94,830	51.5	0.63	0.60–0.66	0.66	0.63–0.70
SEER location						
San Francisco-CA	22,588	50.7	1.00	Referent	1.00	Referent
Connecticut	24,240	51.8	1.12	1.07–1.17	1.11	1.07–1.16
Detroit-MI	25,937	55.1	1.12	1.07–1.17	1.11	1.06–1.15
Hawaii	3,880	55.3	1.00	0.91–1.10	0.99	0.90–1.09
Iowa	19,455	50.7	1.32	1.26–1.38	1.30	1.24–1.36
New Mexico	6,847	56.9	1.21	1.14–1.30	1.18	1.11–1.26
Seattle-WA	16,911	51.5	1.13	1.08–1.19	1.11	1.06–1.17
Utah	6,525	52.3	1.19	1.11–1.27	1.15	1.07–1.22
Atlanta-GA	10,067	56.9	1.09	1.03–1.15	1.06	1.00–1.12
Total	136,450	52.8	-	-	-	-

* Adjusted for age, race, Hispanic ethnicity, tumor stage, treatment, and geographic area.

† Adjusted for the above variables plus year of diagnosis.

TABLE 6
Breast Cancer as the Underlying Cause of Death Among All Deaths, by Patient and Tumor Characteristics, 1988–2003

Characteristics	Deaths (N)	Deaths Due to Breast Cancer (%)	Odds Ratio* of Death Due to Breast Cancer	
			OR	95% CI
Age				
<40	3,184	89.9	1.00	Referent
40–49	6,406	85.1	0.64	0.56–0.74
50–59	7,778	77.6	0.40	0.35–0.46
60–69	10,742	58.6	0.19	0.17–0.21
70–79	15,071	39.2	0.09	0.08–0.11
80+	15,608	32.0	0.06	0.05–0.07
Race				
White	49,631	51.6	1.00	Referent
Black	6,444	65.5	0.91	0.85–0.98
Asian	2,367	62.7	1.04	0.75–1.45
American Indian	254	68.9	0.94	0.82–1.06
Missing	93	39.8	0.48	0.27–0.87
Hispanic ethnicity				
Non-Hispanic	56,473	53.3	1.00	Referent
Hispanic	2,071	63.3	0.92	0.82–1.04
Missing	245	44.9	0.69	0.48–0.98
Historic stage				
Localized	23,930	29.4	1.00	Referent
Regional	20,547	65.3	2.69	2.57–2.82
Distant	9,511	84.1	6.70	6.21–7.24
Missing	4,801	64.1	3.73	3.38–4.12
Treatment				
No cancer-directed surgery	10,218	71.9	1.00	Referent
BCS only	7,882	38.1	0.66	0.60–0.72
BCS + RT	8,715	48.4	0.80	0.73–0.88
MRM	31,974	53.1	0.69	0.64–0.75
SEER location				
San Francisco-CA	9,018	52.3	1.00	Referent
Connecticut	9,909	51.4	1.08	1.00–1.16
Detroit-MI	11,047	55.1	1.07	1.00–1.15
Hawaii	1,863	56.4	0.98	0.85–1.13
Iowa	8,045	50.4	1.19	1.10–1.28
New Mexico	3,294	57.9	1.21	1.09–1.34
Seattle-WA	7,607	53.2	1.13	1.05–1.22
Utah	3,092	53.1	1.18	1.07–1.31
Atlanta-GA	4,914	59.8	1.06	0.97–1.16
Hormone receptor status [†]				
Positive	24,921	47.3	1.00	Referent
Negative	9,278	73.4	1.77	1.66–1.89
Unknown	24,590	52.6	1.02	0.97–1.08
Tumor grade				
Well differentiated	3,434	19.9	1.00	Referent
Moderately differentiated	13,191	43.3	1.83	1.65–2.04
Poorly differentiated	20,348	67.6	2.82	2.54–3.13
Unknown	21,816	52.2	1.83	1.65–2.04
Tumor size				
<1.0	4,432	23.4	1.00	Referent
1.0–1.99	13,124	34.9	1.46	1.33–1.60
2.0–2.99	11,644	50.6	2.09	1.91–2.29

Characteristics	Deaths (N)	Deaths Due to Breast Cancer (%)	Odds Ratio* of Death Due to Breast Cancer	
			OR	95% CI
3.0–3.99	6,574	59.9	2.50	2.26–2.77
4.0+	12,952	72.6	2.91	2.64–3.20
Unknown	10,063	66.3	2.46	2.21–2.73
Total	58,789	53.6	-	-

* Adjusted for age, race, Hispanic ethnicity, tumor stage, treatment, geographic area, year of diagnosis, hormone receptor status, tumor grade, and tumor size.

† Positive hormone receptor status represents either estrogen or progesterone receptor positive.