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# Use of and Mortality After Bilateral Mastectomy Compared With Other Surgical Treatments for Breast Cancer in California, 1998–2011

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### Abstract

**IMPORTANCE**—Bilateral mastectomy is increasingly used to treat unilateral breast cancer. Because it may have medical and psychosocial complications, a better understanding of its use and outcomes is essential to optimizing cancer care.

**OBJECTIVE**—To compare use of and mortality after bilateral mastectomy, breast-conserving therapy with radiation, and unilateral mastectomy.

**DESIGN, SETTING, AND PARTICIPANTS**—Observational cohort study within the population-based California Cancer Registry; participants were women diagnosed with stages 0–III unilateral breast cancer in California from 1998 through 2011, with median follow-up of 89.1 months.

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**Author Contributions:** Drs Kurian and Gomez had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Kurian, Clarke, Gomez.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Kurian, Nelson, Clarke, Gomez.

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**MAIN OUTCOMES AND MEASURES**—Factors associated with surgery use (from polytomous logistic regression); overall and breast cancer—specific mortality (from propensity score weighting and Cox proportional hazards analysis).

**RESULTS**—Among 189 734 patients, the rate of bilateral mastectomy increased from 2.0% (95% CI, 1.7%–2.2%) in 1998 to 12.3% (95% CI, 11.8%–12.9%) in 2011, an annual increase of 14.3% (95% CI, 13.1%–15.5%); among women younger than 40 years, the rate increased from 3.6% (95% CI, 2.3%-5.0%) in 1998 to 33% (95% CI, 29.8%-36.5%) in 2011. Bilateral mastectomy was more often used by non-Hispanic white women, those with private insurance, and those who received care at a National Cancer Institute (NCI)-designated cancer center (8.6% [95% CI, 8.1%-9.2%] among NCI cancer center patients vs 6.0% [95% CI, 5.9%-6.1%] among non-NCI cancer center patients; odds ratio [OR], 1.13 [95% CI, 1.04–1.22]); in contrast, unilateral mastectomy was more often used by racial/ethnic minorities (Filipina, 52.8% [95% CI, 51.6%-54.0%]; OR, 2.00 [95% CI, 1.90–2.11] and Hispanic, 45.6% [95% CI, 45.0%–46.2%]; OR, 1.16 [95% CI, 1.13–1.20] vs non-Hispanic white, 35.2% [95% CI, 34.9%–35.5%]) and those with public/Medicaid insurance (48.4% [95% CI, 47.8%-48.9%]; OR, 1.08 [95% CI, 1.05-1.11] vs private insurance, 36.6% [95% CI, 36.3%-36.8%]). Compared with breast-conserving surgery with radiation (10-year mortality, 16.8% [95% CI, 16.6%-17.1%]), unilateral mastectomy was associated with higher all-cause mortality (hazard ratio [HR], 1.35 [95% CI, 1.32–1.39]; 10-year mortality, 20.1% [95% CI, 19.9%–20.4%]). There was no significant mortality difference compared with bilateral mastectomy (HR, 1.02 [95% CI, 0.94–1.11]; 10-year mortality, 18.8% [95% CI, 18.6%–19.0%]). Propensity analysis showed similar results.

**CONCLUSIONS AND RELEVANCE**—Use of bilateral mastectomy increased significantly throughout California from 1998 through 2011 and was not associated with lower mortality than that achieved with breast-conserving surgery plus radiation. Unilateral mastectomy was associated with higher mortality than were the other 2 surgical options.

Randomized trials have demonstrated similar survival for patients with early-stage breast cancer treated with breast-conserving surgery and radiation or with mastectomy. <sup>1,2</sup> However, older data show increasing use of mastectomy, and particularly bilateral mastectomy, among US patients with breast cancer. <sup>3–5</sup> Bilateral mastectomy represents both treatment (for the affected breast) and prevention (for the contralateral breast), with the uncommon exception of patients having bilateral tumors. The causes of the increasing use of bilateral mastectomy are unknown; one possibility is the dissemination of sensitive diagnostic tests such as breast magnetic resonance imaging and genetic testing of *BRCA1* (unigene cluster number Hs. 194143) and *BRCA2* (unigene cluster number Hs.34012). <sup>4,6</sup> Although it may be cited as a justification for bilateral mastectomy, evidence for a survival benefit appears limited to rare patient subgroups, including women with *BRCA1/2* mutations or strong family history of cancer. <sup>7–9</sup>

Because bilateral mastectomy is an elective procedure for unilateral breast cancer and may have detrimental effects in terms of complications and associated costs<sup>10,11</sup> as well as body image and sexual function, <sup>12,13</sup> a better understanding of its use and outcomes is crucial to improving cancer care. Because patients' preferences drive its use, patients are unlikely to accept randomization to a less extensive surgical procedure in a clinical trial; thus, observational studies offer a feasible alternative to address an important clinical question. To

minimize selection bias, we designed a population-based study of the use and outcomes of bilateral mastectomy compared with other surgical treatments, using the California Cancer Registry (CCR, part of the National Cancer Institute [NCI] Surveillance, Epidemiology and End Results [SEER] program), which comprises about 99% of all breast cancer cases statewide.

# **Methods**

## **Case Ascertainment and Data Collection**

The study population consisted of all female California residents newly diagnosed with a first primary breast cancer (International Classification of Diseases-Oncology, 3rd edition, morphology codes C50.0-50.9), of American Joint Commission on Cancer stages 0-III, from January 1, 1998, through December 31, 2011. Approval for human subjects research was obtained from the Cancer Prevention Institute of California institutional review board. We obtained CCR data routinely abstracted from medical records on age at diagnosis, race/ ethnicity (from patients' medical records and registry categorization; assessed because prior research indicates that the use of and survival after surgical procedures vary by race/ ethnicity, and because we aimed to evaluate these associations in a population-based context), marital status, stage, tumor grade, tumor size, histology, lymph node involvement, metastasis, and biomarkers. 14 Tumors with histologic morphology codes 8500-8508 and 8521-8523 were coded as ductal and those with codes 8520 and 8524-8525 as lobular. We also obtained CCR information on initial treatment (surgery, chemotherapy, and radiation therapy), primary health insurance, census block group of residence at diagnosis, and vital status (determined by CCR through hospital follow-up and database linkages, including the Social Security Administration) as of December 31, 2010, and, for the deceased, the underlying cause of death.

### **Tumor Biomarker Information**

Estrogen-receptor and progesterone-receptor status were each categorized as positive ( 5% nuclear staining), negative, borderline, not tested, not recorded, or unknown. Tumors were considered estrogen receptor—/progesterone receptor—positive if they were estrogen receptor—positive, progester-one receptor—positive, or both, and as estrogen receptor—/ progesterone receptor—negative if both were negative. Given that CCR did not systematically collect v-erb-b2 avian erythroblastic leukemia viral oncogene homologue 2 (*ERBB2*, also known as *HER-2/neu*, unigene cluster number Hs.446352) testing results before 2006, *ERBB2* data are not included.

### **Neighborhood Socioeconomic Information**

For each case, we assigned a previously developed measure of neighborhood socioeconomic status (SES). For cases diagnosed in 1998–2005, we used a measure of neighborhood-level SES quintiles based on distribution across California, incorporating block group-level data from the 2000 Census on income, education, housing costs, and occupation. For cases diagnosed in 2006–2010, we used data from the American Community Survey of the US Census to derive a similar index.

# **Hospital-Level Information**

The CCR records the facility reporting each case. Using the aforementioned index, we determined the SES distribution of all cases for each facility and identified facilities that were NCI-designated cancer centers.

### **Statistical Analysis**

We used polytomous logistic regression to model surgery use. Survival time was measured in days from diagnosis to death. Women who died from other causes were censored at time of death for the analysis of breast cancer–specific mortality. Women alive at the time of last follow-up or December 31, 2010, were censored then. We used Cox proportional hazards to model the association of various factors with overall and breast cancer–specific mortality. The proportional hazards assumption was confirmed by testing the correlation of Schoenfeld residuals with time. For both models (surgery use and mortality), covariates included age, race/ethnicity, tumor size, grade, histology, nodal and estrogen receptor/progesterone receptor status, receipt of adjuvant chemotherapy and radiation, neighbor hood SES quintile, marital and insurance status, the SES composition of patients at the reporting hospital, care at an NCI-designated cancer center, and diagnosis year. Stage was included as a stratifying variable in the Cox regression, allowing baseline hazards to vary by stage. Multicol-linearity in the models was assessed using the variance inflation factor. We did not test for a priori interactions but did conduct stratified analyses by age and stage. Missing data were coded as unknown and retained as a separate category for analyses.

We used SAS version 9.3 for all analyses except those of surgical use trends, for which we used Joinpoint (Joinpoint Regression Program version 4.0.4 [Statistical Research and Applications Branch, NCI]). This program uses Monte Carlo Permutation tests to model data and identify up to 3 points ("joinpoints") at which there was a statistically significant change in linear trend. <sup>16</sup> Results of joinpoint analysis were used to inform grouping of diagnosis years in logistic regression analysis.

Propensity score analyses defined surgery type as the patient attribute for which scores were calculated. <sup>17</sup> We used generalized boosting models, a nonparametric machine-learning classifier, in the R package twang, setting the search limit to 15 000 trees. <sup>18</sup> All independent variables in Table 1 and Table 2 were used to calculate per-patient scores, except 3 variables highly correlated with others (radiation therapy with surgery type; chemotherapy and adjuvant treatment with administration of chemotherapy before or after the surgical procedure).

We used graphical analysis to assess the postbalance maximum standardized effect difference for each variable  $^{17}$  and calculated weights for the average treatment effect (average outcome for the whole population after one surgery vs another); and average treatment effect for those treated (average out come for those treated after one surgery vs another). The svykm and svylogrank functions from the survey package  $^{19}$  were used to calculate weighted Kaplan-Meier curves and P values; the svycoxph function was used for weighted Cox proportional hazard models, with outcome regressed on treatment and

stratified by stage. Weighted CIs for mortality rates were calculated by the survfit function in the R survival package.

# Results

# **Patient Characteristics**

A total of 291 117 stages 0–III breast cancer cases were diagnosed and reported to CCR from January 1, 1998, through December 31, 2011. Cases were excluded if missing essential data for categorization or if ineligible for breast-conserving surgery with radiation according to practice guide lines,  $^{20}$  as follows: diagnosed by death certificate or autopsy only (n = 33); tumor larger than 5 cm or unknown, microscopic or diffuse tumor, Paget disease of breast or mammographic diagnosis only, or inflammatory carcinoma (n = 41 853); no pathology report confirmation (n = 283); unknown lymph node involvement (n = 1771); surgery other than bilateral mastectomy, breast-conserving surgery with radiation, or unilateral mastectomy (n = 52 343); and diagnosis of bilateral tumors or a second primary breast tumor within 60 days (n = 5100), resulting in 189 734 women included in analyses of surgery use. Mortality analyses excluded women diagnosed after 2010 because of incomplete mortality data for 2011 (n = 14 331), those having zero or invalid survival time (n = 11), and those having unknown cause of death (n = 475). Mortality analyses included 174 917 women; median follow-up time was 89.1 months (inter quartile range, 54.8–129.9 months).

The proportions of all patients who underwent each surgery were 6.2% (95% CI, 6.1%–6.3%) for bilateral mastectomy, 55.0% (95%, 54.8%–55.3%) for breast-conserving surgery with radiation; and 38.8% (95% CI, 38.6%–39.0%) for unilateral mastectomy (Table 1 and eTable in the Supplement). Among all patients, the rate of bilateral mastectomy increased from 2.0% (95% CI, 1.7%–2.2%) in 1998 to 12.3% (95% CI, 11.8%–12.9%) in 2011, an annual increase of 14.3% (95% CI, 13.1%–15.5%)(Table 2 and eTable). The increase in bilateral mastectomy rate was greatest among women younger than 40 years: the rate increased from 3.6% (95% CI, 2.3%–5.0%) in 1998 to 33.0% (95% CI, 29.8%–36.5%) in 2011, increasing by 17.6% (95% CI, 14.9%–20.4%) annually. Use of unilateral mastectomy declined in all age groups (Figure 1).

### Multiple Regression Analysis of Characteristics Associated With Surgical Type

Factors associated with having undergone bilateral mastectomy (vs breast-conserving surgery with radiation) included age younger than 50 years, non-Hispanic white race/ethnicity, larger tumor size, nodal involvement, lobular histology, higher grade or estrogen receptor—progesterone receptor—negative status, care at a hospital predominantly serving patients with lower SES or at an NCI-designated cancer center, having higher neighborhood SES, and recent diagnosis. Factors inversely associated with having undergone bilateral mastectomy (vs breast-conserving surgery with radiation) included age 65 years or older, minority race/ethnicity, receipt of adjuvant therapy, married status, and insurance type other than private (Table 3).

Characteristics associated with having undergone unilateral mastectomy (vs breast-conserving surgery plus radiation) included diagnosis at age other than 50 to 64 years,

Asian, Hispanic, and American Indian race/ethnicity (with notable associations for Filipina and Hispanic women vs non-Hispanic white women), larger tumor size, nodal involvement, lobular histology, higher grade, estrogen receptor—progesterone receptor—negative status, married status, public/Medicaid insurance, or care at a hospital predominantly serving patients of lower SES (Table 3). Factors inversely associated with having unilateral mastectomy (vs breast-conserving surgery with radiation) included black race, receipt of adjuvant therapy, care at an NCI-designated cancer center, higher neighborhood SES, and recent diagnosis.

### Multiple Regression Analysis of Mortality After Surgery

Compared with breast-conserving surgery with radiation, bilateral mastectomy was not associated with a mortality difference (hazard ratio [HR], 1.02 [95% CI, 0.94–1.11]), whereas unilateral mastectomy was associated with higher mortality (HR, 1.35[95% CI, 1.32–1.39]) (Table 4). Other factors associated with overall mortality included age 65 years or older or younger than 40 years, black race, larger tumor size, nodal involvement, higher grade, estrogen receptor–/progesterone receptor–negative status, lower neighborhood SES, unmarried status, having Medicare or public/Medicaid insurance, and receiving care at a hospital predominantly serving patients of lower SES. Higher mortality was associated with unilateral mastectomy in all age groups. Similar mortality between bilateral mastectomy and breast-conserving surgery with radiation was observed in all age groups except women 65 years or older, whose survival was slightly better after breast-conserving surgery with radiation. Findings were similar for breast cancer–specific mortality (Table 5). Compared with unilateral mastectomy, bilateral mastectomy was associated with lower overall mortality (HR, 0.75 [95% CI, 0.70–0.82]) and breast cancer–specific mortality (HR, 0.85 [95% CI, 0.76–0.94]).

## **Propensity Analysis of Marginal Mortality After Surgery**

Figure 2A shows estimated mortality among all patients if surgical procedure were randomly assigned (analysis of average treatment effect). The estimated 10-year mortality rates were 18.8% (95% CI, 18.6%–19.0%) for bilateral mastectomy, 16.8% (95% CI, 16.6%–17.1%) for breast-conserving surgery with radiation, and 20.1% (95% CI, 19.9%–20.4%) for unilateral mastectomy. Figure 2B–D shows estimated mortality from another surgical procedure among patients who had a specific surgical procedure (analysis of average treatment effect for those treated). For patients receiving breast-conserving surgery with radiation, bilateral mastectomy would have resulted in marginally higher mortality, on average, and unilateral mastectomy would have resulted in unchanged mortality and breast-conserving surgery with radiation in lower mortality. For patients receiving bilateral mastectomy, breast-conserving surgery with radiation would have resulted in unchanged mortality and unilateral mastectomy in higher mortality. Proportional hazards regression models showed similar results (Table 6).

# **Discussion**

This observational study comprising 189 734 women with unilateral early-stage breast cancer compared 3 surgical treatments and found a substantial increase in the rate of bilateral mastectomy throughout California from 1998 through 2011. To our knowledge, this is the first side-by-side comparison of all 3 common surgical treatments for early-stage breast cancer. Previous SEER studies have compared 2 treatments at a time: some reported a survival advantage with bilateral vs unilateral mastectomy<sup>21,22</sup> and others reported improved survival after breast-conserving surgery with radiation compared with unilateral mastectomy. <sup>23,24</sup> By comparing all 3 surgical options for a patient with early-stage breast cancer, we found no mortality benefit associated with bilateral mastectomy compared with breast-conserving surgery, and higher mortality associated uniquely with unilateral mastectomy.

For the surgical treatment of early-stage breast cancer, available randomized trial data are limited to those showing no survival difference between unilateral mastectomy and breastconserving surgery. 1,2 There is no randomized trial evidence to inform whether bilateral mastectomy improves survival, and it is unlikely that such a trial will ever be performed. Thus, conclusions about surgical treatments must rely on observational studies that compare the effectiveness of different procedures in practice<sup>21,22,25,26</sup>; however, a recent metaanalysis judged the existing data inadequate to enable conclusions about the effect of bilateral mastectomy on survival.<sup>27</sup> Patient selection attributable to unmeasured factors probably explains much of the higher mortality that we observed with unilateral mastectomy relative to the other 2 surgical procedures. In prior SEER-based studies, both we<sup>24</sup> and Agarwal et al<sup>23</sup> reported worse survival associated with unilateral mastectomy vs breastconserving surgery with radiation, results that persisted after propensity analysis. We agree with previous suggestions that patients with tumor features suggesting poor prognosis, such as lymphovascular invasion or extranodal extension, which SEER does not record and for which we cannot control, are more likely to undergo unilateral mastectomy than breast conservation and also to experience worse survival. 23,24 The current study offers another potential explanation, namely confounding related to sociodemographic differences between women who underwent bilateral mastectomy and women who underwent unilateral mastectomy.

Women who underwent bilateral mastectomy were more likely to be non-Hispanic white and privately insured, to live in high SES neighborhoods, and to be treated in NCI-designated cancer centers. By contrast, women who underwent unilateral mastectomy were more likely to be Asian, Hispanic, or non-Hispanic American Indian/other/unknown; to have public/ Medicaid insurance, and to be treated in hospitals serving patients of lower SES; they were less likely to live in high SES neighborhoods or to be treated in NCI-designated cancer centers. Cancer registry data lack details about comorbidities and specific regimens of endocrine, radiation, and chemotherapy. However, prior studies enriched for clinical data, including our own within the Kaiser Permanente Northern California health care system, reported treatment-limiting comorbidities (for example, diabetes and myocardial infarction) and reduced treatment intensity among the same racial/ethnicminority, low SES patients who most frequently under went unilateral mastectomy in our current study. <sup>28–30</sup> In addition to

signifying unmeasured poor prognostic factors, <sup>21,22</sup> unilateral mastectomy might correlate with subtle disparities in effective access (for example, diabetic neuropathy that limits chemotherapy dosing; lack of transportation to the postsurgical radiation treatments required for breast conservation) that we could not identify using registry data and that may mediate higher mortality. By contrast, patterns of bilateral mastectomy use suggest that affluent non-Hispanic white women, women of high SES, or both seek more aggressive preventive care, consistent with reported associations between greater use of expensive diagnostic tests (such as breast MRI and genetic testing) and bilateral mastectomy within this patient subgroup. <sup>4,31</sup>

The increase in bilateral mastectomy use despite the absence of supporting evidence has puzzled clinicians and health policy makers. Proposed explanations include the increasing use of highly sensitive breast magnetic resonance imaging, with increases in anxietyproducing recall and biopsy rates that may drive patients to undergo preventive surgery, 6,31,32 and the dissemination of genetic testing, which facilitates identification of high-risk patients who benefit from bilateral mastectomy. <sup>7,8,33</sup> Although fear of cancer recurrence may prompt the decision for bilateral mastectomy, such fear usually exceeds the estimated risk. 34,35 Other studies found recurrence fears less influential than aesthetic considerations, notably those that arise with new reconstruction approaches that achieve cosmetic symmetry through bilateral tissue flap placement.<sup>6,36</sup> Because cosmesis may be inferior if both breasts are not reconstructed simultaneously, these new approaches encourage use of immediate bilateral mastectomy. We found that bilateral mastectomy use over time increased most among patients younger than 40 years at diagnosis, which may be attributable to their relatively high probability of carrying genetic mutations (an evidencebased indication for bilateral mastectomy)<sup>37</sup> or to the greater likelihood that they have young children and may therefore seek maximal intervention in hope of extending their lives (an emotional rather than evidence-based decision). 34,35,38 Although some studies reported patient satisfaction after bilateral mastectomy,<sup>39</sup> others observed deleterious effects on body image, sexual function, and quality of life<sup>12</sup>; moreover, repeat operations and complications (including flap failure, necrosis, and infection) are substantially more common with bilateral mastectomy than with other surgical procedures. 10,11

In a time of increasing concern about overtreatment, <sup>40</sup> the risk-benefit ratio of bilateral mastectomy warrants careful consideration and raises the larger question of how physicians and society should respond to a patient's preference for a morbid, costly intervention of dubious effectiveness.

Our study used a population-based statewide data set, multiple regression analysis, and propensity scores. However, given its observational design, it cannot prove causation and may be subject to selection bias and uncontrolled confounding. As discussed above, unmeasured patient selection factors related to cancer prognosis and access to care may explain the higher mortality observed with unilateral mastectomy. Other limitations include the lack of SEER data on diagnostic testing (eg, magnetic resonance imaging, genetic testing for *BRCA1/2* and other inherited mutations, tumor analysis for *ERBB2* amplification, and broader genomic profiling), details of systemic treatments, family cancer history, and comorbidities. Additional information gaps include patient preferences and physician recommendations, which influence surgical decisions.<sup>38</sup> Future research with more

comprehensive data sets that integrate detailed clinical, treatment, and patient-reported information will be essential to advance understanding of breast surgery use and to enhance the quality of cancer care.

### Conclusions

Among all women diagnosed with early-stage breast cancer in California, the percentage undergoing bilateral mastectomy increased substantially between 1998 and 2011, despite a lack of evidence supporting this approach. Bilateral mastectomy was not associated with lower mortality than breast-conserving surgery plus radiation, but unilateral mastectomy was associated with higher mortality than the other options. These results may inform decision-making about the surgical treatment of breast cancer.

# **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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# References

- Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002; 347(16):1233–1241. [PubMed: 12393820]
- Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002; 347(16):1227–1232. [PubMed: 12393819]
- 3. Gomez SL, Lichtensztajn D, Kurian AW, et al. Increasing mastectomy rates for early-stage breast cancer? J Clin Oncol. 2010; 28(10):e155–e157. [PubMed: 20159812]
- 4. Katipamula R, Degnim AC, Hoskin T, et al. Trends in mastectomy rates at the Mayo Clinic Rochester. J Clin Oncol. 2009; 27(25):4082–4088. [PubMed: 19636020]
- 5. Tuttle TM, Habermann EB, Grund EH, et al. Increasing use of contralateral prophylactic mastectomy for breast cancer patients. J Clin Oncol. 2007; 25(33):5203–5209. [PubMed: 17954711]
- King TA, Sakr R, Patil S, et al. Clinical management factors contribute to the decision for contralateral prophylactic mastectomy. J Clin Oncol. 2011; 29(16):2158–2164. [PubMed: 21464413]
- Heemskerk-Gerritsen BA, Menke-Pluijmers MB, Jager A, et al. Substantial breast cancer risk reduction and potential survival benefit after bilateral mastectomy when compared with surveillance in healthy *BRCA1* and *BRCA2* mutation carriers. Ann Oncol. 2013; 24(8):2029–2035. [PubMed: 23576707]
- 8. Kurian AW, Sigal BM, Plevritis SK. Survival analysis of cancer risk reduction strategies for *BRCA1/2* mutation carriers. J Clin Oncol. 2010; 28(2):222–231. [PubMed: 19996031]

 Hartmann LC, Sellers TA, Schaid DJ, et al. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. J Natl Cancer Inst. 2001; 93(21):1633–1637. [PubMed: 11698567]

- Barton MB, West CN, Liu IL, et al. Complications following bilateral prophylactic mastectomy. J Natl Cancer Inst Monogr. 2005; (35):61–66. [PubMed: 16287887]
- 11. Miller ME, Czechura T, Martz B, et al. Operative risks associated with contralateral prophylactic mastectomy. Ann Surg Oncol. 2013; 20(13):4113–4120. [PubMed: 23868655]
- Bresser PJ, Seynaeve C, Van Gool AR, et al. Satisfaction with prophylactic mastectomy and breast reconstruction in genetically predisposed women. Plast Reconstr Surg. 2006; 117(6):1675–1684.
   [PubMed: 16651934]
- Frost MH, Schaid DJ, Sellers TA, et al. Long-term satisfaction and psychological and social function following bilateral prophylactic mastectomy. JAMA. 2000; 284(3):319–324. [PubMed: 10891963]
- [Accessed June 12, 2014] Procedures for Conducting Data Linkages With the California Cancer Registry. http://www.ccrcal.org/Data\_and\_Statistics/Cancer\_Data\_for\_Research.shtml
- Yost K, Perkins C, Cohen R, et al. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes Control. 2001; 12(8):703–711. [PubMed: 11562110]
- 16. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000; 19(3):335–351. [PubMed: 10649300]
- 17. Austin PC. The use of propensity score methods with survival or time-to-event outcomes. Stat Med. 2014; 33(7):1242–1258. [PubMed: 24122911]
- McCaffrey DF, Griffin BA, Almirall D, et al. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med. 2013; 32(19):3388–3414. [PubMed: 23508673]
- 19. Lumley, T. Complex Surveys: A Guide to Analysis Using R. Hoboken, NJ: John Wiley & Sons; 2010.
- 20. Carlson RW, Allred DC, Anderson BO, et al. National Comprehensive Cancer Network. Invasive breast cancer. J Natl Compr Canc Netw. 2011; 9(2):136–222. [PubMed: 21310842]
- Bedrosian I, Hu CY, Chang GJ. Population-based study of contralateral prophylactic mastectomy and survival outcomes of breast cancer patients. J Natl Cancer Inst. 2010; 102(6):401–409. [PubMed: 20185801]
- Kauffmann, R., Nelson, R., Smith, D., et al. Improved survival with contralateral prophylactic mastectomy. Abstract presented at: Society of Surgical Oncology Cancer Symposium; March 13– 15, 2014; Phoenix, AZ.
- Agarwal S, Pappas L, Neumayer L, et al. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. JAMA Surg. 2014; 149(3):267–274.
   [PubMed: 24429935]
- 24. Hwang ES, Lichtensztajn DY, Gomez SL, et al. Survival after lumpectomy and mastectomy for early stage invasive breast cancer. Cancer. 2013; 119(7):1402–1411. [PubMed: 23359049]
- 25. Herrinton LJ, Barlow WE, Yu O, et al. Efficacy of prophylactic mastectomy in women with unilateral breast cancer. J Clin Oncol. 2005; 23(19):4275–4286. [PubMed: 15795415]
- 26. Yao K, Winchester DJ, Czechura T, Huo D. Contralateral prophylactic mastectomy and survival. Breast Cancer Res Treat. 2013; 142(3):465–476. [PubMed: 24218052]
- Lostumbo L, Carbine NE, Wallace J. Prophylactic mastectomy for the prevention of breast cancer.
   Cochrane Database Syst Rev. 2010; (11):CD002748. [PubMed: 21069671]
- 28. Griggs JJ, Culakova E, Sorbero ME, et al. Social and racial differences in selection of breast cancer adjuvant chemotherapy regimens. J Clin Oncol. 2007; 25(18):2522–2527. [PubMed: 17577029]
- 29. Kurian AW, Lichtensztajn DY, Keegan TH, et al. Patterns and predictors of breast cancer chemotherapy use in Kaiser Permanente Northern California, 2004–2007. Breast Cancer Res Treat. 2013; 137(1):247–260. [PubMed: 23139057]
- Wu AH, Gomez SL, Vigen C, et al. The California Breast Cancer Survivorship Consortium (CBCSC): prognostic factors associated with racial/ethnic differences in breast cancer survival. Cancer Causes Control. 2013; 24(10):1821–1836. [PubMed: 23864487]

31. Kurian AW, Mitani A, Desai M, et al. Breast cancer treatment across health care systems. Cancer. 2014; 120(1):103–111. [PubMed: 24101577]

- 32. Tuttle TM. Magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol. 2009; 16(6):1461–1462. [PubMed: 19290489]
- 33. Domchek SM, Friebel TM, Singer CF, et al. Association of risk-reducing surgery in *BRCA1* or *BRCA2* mutation carriers with cancer risk and mortality. JAMA. 2010; 304(9):967–975. [PubMed: 20810374]
- 34. Abbott A, Rueth N, Pappas-Varco S, et al. Perceptions of contralateral breast cancer. Ann Surg Oncol. 2011; 18(11):3129–3136. [PubMed: 21947590]
- 35. Rosenberg SM, Tracy MS, Meyer ME, et al. Perceptions, knowledge, and satisfaction with contralateral prophylactic mastectomy among young women with breast cancer. Ann Intern Med. 2013; 159(6):373–381. [PubMed: 24042365]
- 36. Howard-McNatt M, Schroll RW, Hurt GJ, Levine EA. Contralateral prophylactic mastectomy in breast cancer patients who test negative for *BRCA* mutations. Am J Surg. 2011; 202(3):298–302. [PubMed: 21871984]
- 37. Daly, M. [Accessed June 12, 2014] Genetic/Familial High-Risk Assessment: Breast and Ovarian. NCCN Clinical Practice Guidelines in Oncology. http://www.nccn.org
- 38. Hawley ST, Jagsi R, Morrow M, et al. Social and clinical determinants of contralateral prophylactic mastectomy [published online May 21, 2014]. JAMA Surg.
- 39. Frost MH, Slezak JM, Tran NV, et al. Satisfaction after contralateral prophylactic mastectomy. J Clin Oncol. 2005; 23(31):7849–7856. [PubMed: 16204003]
- Schnipper LE, Smith TJ, Raghavan D, et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs. J Clin Oncol. 2012; 30(14):1715–1724.
   [PubMed: 22493340]

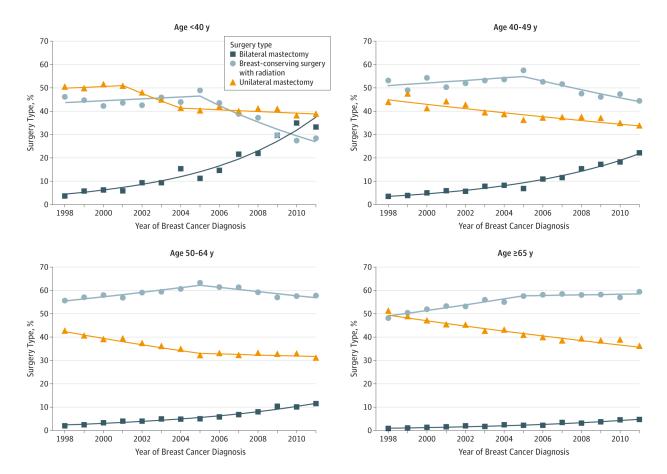


Figure 1.
Joinpoint Analysis Showing Time Trends in Use of Bilateral Mastectomy, Breast-Conserving Surgery With Radiation, and Unilateral Mastectomy, According to Patient Age in Years at Breast Cancer Diagnosis
Data points indicate observed data.

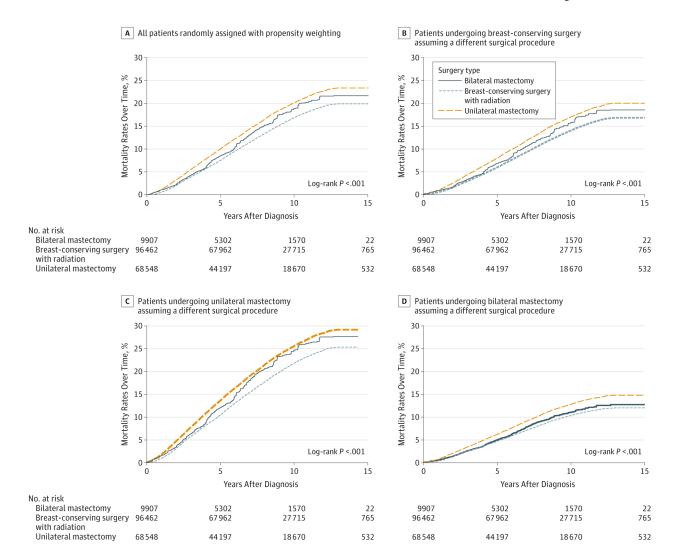


Figure 2.

Propensity-Weighted Kaplan-Meier Plots of Estimated Mortality Among All Patients if
Surgical Procedure Had Been Randomly Assigned and of Estimated Mortality if a Different
Surgical Procedure Had Been Performed Among Patients Who Had Undergone a Specific
Surgical Procedure

A, Estimated mortality among all patients if surgical procedure were randomly assigned (analysis of average treatment effect). B–D, Estimated mortality from another surgical procedure among patients who had a specific surgical procedure (analysis of average treatment effect for those treated). B, For patients receiving breast-conserving surgery with radiation, bilateral mastectomy would have resulted in marginally higher mortality, on average, and unilateral mastectomy in higher mortality. C, For patients receiving unilateral mastectomy, bilateral mastectomy would have resulted in unchanged mortality and breast-conserving surgery with radiation in lower mortality. D, For patients receiving bilateral mastectomy, breast-conserving surgery with radiation would have resulted in unchanged mortality and unilateral mastectomy in higher mortality.

Table 1

Patient and Tumor Characteristics According to Surgery Type: Bilateral Mastectomy, Breast-Conserving Surgery With Radiation, and Unilateral Mastectomy, Stages 0-III Breast Cancer, 1998-2011, California

	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	Row % (95% CI)	No.	Row % (95% CI)	Š.	Row % (95% CI)	Total
All patients	11 692	6.2 (6.1–6.3)	104 420	55.0 (54.8–55.3)	73 622	38.8 (38.6–39.0)	189 734
Race/ethnicity							
Non-Hispanic white	8758	6.9 (6.8–7.1)	73 310	57.9 (57.6–58.2)	44 557	35.2 (34.9–35.5)	126 625
Non-Hispanic black	416	4.2 (3.8–4.6)	5483	55.1 (54.1–56.0)	4057	40.7 (39.8–41.7)	9366
Hispanic	1450	5.0 (4.8–5.3)	14 279	49.4 (48.8–50.0)	13 172	45.6 (45.0–46.2)	28 901
Chinese	172	3.3 (2.8–3.7)	2520	47.9 (46.5–49.2)	2570	48.8 (47.5–50.2)	5262
Japanese	100	4.2 (3.4–5.0)	1317	54.7 (52.7–56.7)	686	41.1 (39.1–43.1)	2406
Filipina	268	4.0 (3.5–4.4)	2922	43.2 (42.0–44.4)	3574	52.8 (51.6–54.0)	6764
Other Asian/Pacific Islander	440	5.3 (4.8–5.8)	3765	45.4 (44.4–46.5)	4079	49.2 (48.2–50.3)	8284
Non-Hispanic American Indian/other/unknown	88	5.7 (4.6–6.9)	824	53.6 (51.2–56.1)	624	40.6 (38.2–43.1)	1536
Age at diagnosis, y							
<40	1586	15.7 (15.0–16.4)	4092	40.4 (39.5–41.4)	4448	43.9 (43.0–44.9)	10 126
40-49	3898	10.3 (10.0–10.6)	19 175	50.8 (50.3–51.4)	14 636	38.8 (38.3–39.3)	37 709
50-64	4549	6.1 (6.0–6.3)	43 709	58.9 (58.6–59.3)	25 922	34.9 (34.6–35.3)	74 180
99	1659	2.4 (2.3–2.6)	37 444	55.3 (54.9–55.7)	28 616	42.3 (41.9–42.6)	67 719
Marital status							
Not married	3698	5.1 (4.9–5.3)	38 936	53.6 (53.3–54.0)	29 954	41.3 (40.9–41.6)	72 588

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	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	Row % (95% CI)	No.	Row % (95% CI)	No.	Row % (95% CI)	Total
Married	7753	6.9 (6.7–7.0)	63 433	56.1 (55.8–56.4)	41 884	37.0 (36.8–37.3)	113 070
Unknown	241	5.9 (5.2–6.6)	2051	50.3 (48.8–51.9)	1784	43.8 (42.2–45.3)	4076
Neighborhood SES quintile <sup>a</sup>							
I (lowest)	795	3.9 (3.7–4.2)	9339	46.2 (45.5–46.8)	10 101	49.9 (49.2–50.6)	20 235
2	1480	4.8 (4.6–5.0)	15 621	50.6 (50.1–51.2)	13 752	44.6 (44.0–45.1)	30 853
3	2164	5.6 (5.4–5.8)	20 904	54.0 (53.5–54.5)	15 665	40.4 (40.0–40.9)	38 733
4	2899	6.3 (6.1–6.6)	26 008	56.9 (56.5–57.4)	16 790	36.7 (36.3–37.2)	45 697
ĸ	4354	8.0 (7.8–8.3)	32 548	60.0 (59.6–60.4)	17 314	31.9 (31.5–32.3)	54 216
Insurance status							
Private	9477	7.7 (7.6–7.9)	68 395	55.7 (55.4–56.0)	44 894	36.6 (36.3–36.8)	122 766
Medicare	782	3.2 (3.0–3.4)	13 722	56.3 (55.7–56.9)	9876	40.5 (39.9–41.1)	24 380
Military	66	6.1 (4.9–7.2)	835	51.3 (48.8–53.7)	969	42.7 (40.3–45.1)	1629
Not insured or self-pay	80	5.4 (4.2–6.5)	693	46.5 (43.9–49.0)	718	48.2 (45.6–50.7)	1491
Public or Medicaid	1072	3.3 (3.1–3.5)	15 762	48.3 (47.8–48.9)	15 768	48.4 (47.8–48.9)	32 602
Unknown	182	2.7 (2.3–3.0)	5013	73.0 (72.0–74.1)	1671	24.3 (23.3–25.4)	9989
American Joint Committee on Cancer stage							
0	1779	7.6 (7.3–8.0)	14 697	63.0 (62.3–63.6)	6864	29.4 (28.8–30.0)	23 340
I	4376	5.0 (4.9–5.2)	57 946	66.8 (66.5–67.1)	24 436	28.2 (27.9–28.5)	86 758
П	4641	6.7 (6.5–6.8)	29 397	42.2 (41.8–42.5)	35 669	51.2 (50.8–51.5)	202 69
Ш	968	9.0 (8.5–9.6)	2380	24.0 (23.1–24.8)	6653	67.0 (66.1–67.9)	9926

	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	Row % (95% CI)	No.	Row % (95% CI)	No.	Row % (95% CI)	Total
Tumor size, cm							
⊽	2366	5.8 (5.6–6.0)	28 022	68.9 (68.4–69.3)	10 310	25.3 (24.9–25.8)	40 698
1–1.9	3933	5.3 (5.2–5.5)	46 936	63.5 (63.2–63.8)	23 047	31.2 (30.8–31.5)	73 916
2–2.9	2786	6.6 (6.3–6.8)	20 044	47.3 (46.9–47.8)	19 507	46.1 (45.6–46.6)	42 337
3–3.9	1419	7.4 (7.0–7.8)	6395	33.3 (32.6–33.9)	11 400	59.3 (58.6–60.0)	19 214
4-5	1188	8.8 (8.3–9.2)	3023	22.3 (21.6–23.0)	9358	69.0 (68.2–69.7)	13 569
Grade							
I	1962	4.9 (4.7–5.1)	26 134	65.7 (65.2–66.1)	11 694	29.4 (28.9–29.8)	39 790
П	4610	6.0 (5.8–6.2)	42 862	55.9 (55.5–56.2)	29 219	38.1 (37.8–38.4)	76 691
Ш	4421	7.0 (6.8–7.2)	30 525	48.4 (48.0–48.8)	28 159	44.6 (44.2–45.0)	63 105
Unknown	669	6.9 (6.4–7.4)	4899	48.3 (47.3–49.2)	4550	44.8 (43.9–45.8)	10 148
Histology							
Ductal	90/6	6.0 (5.9–6.1)	90 011	55.5 (55.3–55.8)	62 336	38.5 (38.2–38.7)	162 053
Lobular or lobular component	1290	9.6 (9.1–10.1)	0209	45.0 (44.1–45.8)	6134	45.5 (44.6–46.3)	13 494
Other	969	4.9 (4.6–5.3)	8339	58.8 (58.0–59.6)	5152	36.3 (35.5–37.1)	14 187
ER/PR status							
Negative (ER- and PR-negative)	1974	6.9 (6.6–7.2)	13 914	48.4 (47.8–49.0)	12 870	44.8 (44.2–45.3)	28 758
Positive (ER- or PR-positive)	8536	6.2 (6.0–6.3)	79 457	57.5 (57.2–57.8)	50 213	36.3 (36.1–36.6)	138 206
Unknown or borderline	1182	5.2 (4.9–5.5)	11 049	48.5 (47.9–49.2)	10 539	46.3 (45.6–46.9)	22 770
Lymph node involvement							

	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	No. Row % (95% CI)	No.	No. Row % (95% CI)	No.	No. Row % (95% CI)	Total
Negative	7824	7824 5.7 (5.6–5.8)	84 655	61.7 (61.5–62.0)	44 667	44 667 32.6 (32.3–32.8) 137 146	137 146
Positive	3868	7.4 (7.1–7.6)	19 765	37.6 (37.2–38.0)	28 955	28 955 55.1 (54.6–55.5)	52 588

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; SES, socioeconomic status.

 $<sup>^{</sup>a}$ Distribution based on statewide quintiles.

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Table 2

Diagnosis and Treatment Characteristics According to Surgery Type: Bilateral Mastectomy, Breast-Conserving Surgery With Radiation, and Unilateral Mastectomy, Stages 0-III Breast Cancer, 1998-2011, California

	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	Row % (95% CI)	No.	Row % (95% CI)	No.	Row % (95% CI)	Total
Year of cancer diagnosis							
8661	249	2.0 (1.7–2.2)	6453	51.7 (50.8–52.5)	5790	46.3 (45.5–47.2)	12 492
6661	298	2.4 (2.1–2.6)	9959	52.3 (51.4–53.1)	5702	45.4 (44.5–46.2)	12 566
2000	400	3.0 (2.7–3.3)	7226	54.1 (53.3–54.9)	5730	42.9 (42.1–43.7)	13 356
2001	483	3.5 (3.2–3.9)	7286	53.5 (52.7–54.4)	5842	42.9 (42.1–43.8)	13 611
2002	509	3.8 (3.5–4.1)	7341	54.6 (53.8–55.5)	5591	41.6 (40.8–42.4)	13 441
2003	909	4.6 (4.3–5.0)	7310	56.1 (55.3–57.0)	5107	39.2 (38.4–40.1)	13 022
2004	704	5.3 (4.9–5.7)	7468	56.2 (55.4–57.1)	5111	38.5 (37.7–39.3)	13 283
2005	642	4.7 (4.3–5.0)	8117	59.3 (58.5–60.2)	4920	36.0 (35.2–36.8)	13 679
2006	821	6.1 (5.7–6.5)	7746	57.5 (56.7–58.3)	4905	36.4 (35.6–37.2)	13 472
2007	1017	7.2 (6.8–7.7)	8053	57.3 (56.5–58.1)	4979	35.4 (34.6–36.2)	14 049
2008	1209	8.5 (8.0–9.0)	7852	55.3 (54.4–56.1)	5148	36.2 (35.4–37.0)	14 209
2009	1437	10.3 (9.8–10.8)	7541	54.0 (53.2–54.8)	4987	35.7 (34.9–36.5)	13 965
2010	1550	10.9 (10.4–11.4)	1891	53.9 (53.1–54.7)	5021	35.2 (34.4–36.0)	14 258
2011	1768	12.3 (11.8–12.9)	7774	54.2 (53.4–55.1)	4789	33.4 (32.6–34.2)	14 331
Received care at an NCI- designated cancer center							
No	10 860	6.0 (5.9–6.1)	859 86	54.8 (54.6–55.0)	70 559	39.2 (39.0–39.4)	180 077

	Bilate	Bilateral Mastectomy	Breast-Conserving	Breast-Conserving Surgery With Radiation	Unilat	Unilateral Mastectomy	
Variable	No.	Row % (95% CI)	No.	Row % (95% CI)	No.	Row % (95% CI)	Total
Yes	832	8.6 (8.1–9.2)	5762	59.7 (58.7–60.6)	3063	31.7 (30.8–32.6)	1657
Patient SES quintile distribution of reporting hospital $^{\it a}$							
>50% of patients in quintiles 1 (lowest)-2	1587	4.7 (4.5–4.9)	15 773	46.9 (46.3–47.4)	16 286	48.4 (47.9–48.9)	33 646
>50% of patients in quintiles 4–5	7044	7.2 (7.1–7.4)	57 514	59.1 (58.8–59.4)	32 701	33.6 (33.3–33.9)	97 259
Mixed SES distribution	3061	5.2 (5.0–5.4)	31 133	52.9 (52.5–53.3)	24 635	41.9 (41.5–42.3)	58 829
Radiation therapy							
No	6986	13.8 (13.5–14.0)	0	NA	61 811	86.2 (86.0–86.5)	71 680
Yes	1823	1.5 (1.5–1.6)	104 420	88.5 (88.3–88.6)	11 811	10.0 (9.8–10.2)	118 054
Chemotherapy							
No	6392	5.2 (5.1–5.4)	71 382	58.5 (58.2–58.8)	44 296	36.3 (36.0–36.6)	122 070
Yes	5300	7.8 (7.6–8.0)	33 038	48.8 (48.4–49.2)	29 326	43.3 (43.0–43.7)	67 664
Chemotherapy timing							
After surgery	3753	6.5 (6.3–6.7)	29 123	50.7 (50.3–51.1)	24 583	42.8 (42.4–43.2)	57 459
Before surgery	1490	17.9 (17.1–18.7)	2874	34.5 (33.5–35.5)	3963	47.6 (46.5–48.7)	8327
No chemotherapy	6392	5.2 (5.1–5.4)	71 382	58.5 (58.2–58.8)	44 296	36.3 (36.0–36.6)	122 070
Unknown	57	3.0 (2.3–3.8)	1041	55.4 (53.2–57.7)	780	41.5 (39.3–43.8)	1878
Adjuvant treatment, chemotherapy, and/or radiation therapy							
No	6143	5.1 (5.0–5.3)	71 382	59.8 (59.5–60.1)	41 892	35.1 (34.8–35.4)	119 417
Yes	5549	7.9 (7.7–8.1)	33 038	47.0 (46.6–47.4)	31 730	45.1 (44.8–45.5)	70 317
Breast reconstructive surgery							

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	Bilate	Bilateral Mastectomy I	Breast-Conserving	Breast-Conserving Surgery With Radiation Unilateral Mastectomy	Unilat	eral Mastectomy	
Variable	No.	No. Row % (95% CI)	No.	No. Row % (95% CI)	No.	No. Row % (95% CI) Total	Total
No	6428	6428 3.7 (3.6–3.8)	104 229	59.8 (59.6–60.1)	63 529	63 529 36.5 (36.2–36.7) 174 186	174 186
Yes	5264	5264 33.9 (33.1–34.6)	191	1.2 (1.1–1.4)	10 093	10 093 64.9 (64.2–65.7) 15 548	15 548
Vital status							
Dead	903	2.8 (2.6–3.0)	13 571	42.5 (41.9–43.0)	17 489	17 489 54.7 (54.2–55.3)	31 963
Alive	10 789	6.8 (6.7–7.0)	90 849	57.6 (57.3–57.8)	56 133	56 133 35.6 (35.3–35.8) 157 771	157 771

Abbreviations: NA, not available; NCI, National Cancer Institute; SES, socioeconomic status.

 $<sup>^{</sup>a}$ Distribution based on statewide quintiles.

 $\label{eq:Table 3} \label{eq:Table 3}$  Multiple Regression Odds Ratios for Associations With Receipt of Bilateral Mastectomy or Unilateral Mastectomy vs Breast-Conserving Surgery With Radiation as the Reference Group  $^a$ 

	Odds Ratio	o (95% CI)
Variable	Bilateral Mastectomy vs Breast- Conserving Surgery With Radiation	Unilateral Mastectomy vs Breast- Conserving Surgery With Radiation
Race/ethnicity		
Non-Hispanic white	1 [Reference]	1 [Reference]
Chinese	0.41 (0.35–0.48)	1.95 (1.84–2.08)
Filipina	0.61 (0.54–0.70)	2.00 (1.90–2.11)
Hispanic	0.63 (0.59–0.67)	1.16 (1.13–1.20)
Japanese	0.63 (0.51–0.77)	1.40 (1.28–1.53)
Non-Hispanic American Indian/other/unknown	0.76 (0.61–0.96)	1.23 (1.10–1.38)
Non-Hispanic black	0.53 (0.47–0.59)	0.89 (0.85-0.94)
Other Asian/Pacific Islander	0.64 (0.58–0.71)	1.88 (1.79–1.97)
Age at diagnosis, y		
<40	3.81 (3.55–4.08)	1.31 (1.25–1.38)
40–49	2.00 (1.91–2.10)	1.15 (1.12–1.18)
50–64	1 [Reference]	1 [Reference]
65	0.45 (0.42–0.48)	1.34 (1.30–1.38)
Tumor size		
Per centimeter	1.36 (1.34–1.39)	1.61 (1.60–1.63)
Lymph node involvement		
Negative	1 [Reference]	1 [Reference]
Positive	1.66 (1.58–1.75)	2.16 (2.10–2.22)
Histology		
Ductal	1 [Reference]	1 [Reference]
Lobular or with lobular component	2.19 (2.05–2.35)	1.36 (1.31–1.42)
Other	0.89 (0.82–0.97)	0.96 (0.92–1.00)
Grade		
I	1 [Reference]	1 [Reference]
II	1.17 (1.11–1.24)	1.18 (1.15–1.22)
III	1.30 (1.22–1.38)	1.24 (1.20–1.28)
Unknown	1.67 (1.52–1.84)	1.45 (1.38–1.52)
ER/PR status		
Positive	1 [Reference]	1 [Reference]
Negative	1.12 (1.05–1.19)	1.17 (1.13–1.21)
Unknown or borderline	1.53 (1.43–1.64)	1.53 (1.48–1.58)
Adjuvant treatment, chemotherapy, and/or radiation		
No	1 [Reference]	1 [Reference]

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Odds Ratio (95% CI) Bilateral Mastectomy vs Breast-Unilateral Mastectomy vs Breast-Variable Conserving Surgery With Radiation Conserving Surgery With Radiation 0.91 (0.86-0.95) 0.86 (0.84-0.89) Yes Neighborhood SES quintile b,c 1 (lowest) 1 [Reference] 1 [Reference] 2 1.10 (1.00-1.21) 0.91 (0.88-0.95) 3 1.18 (1.08-1.29) 0.85 (0.82-0.89) 4 1.22 (1.11-1.33) 0.80 (0.76-0.83) 5 1.41 (1.29–1.55) 0.73 (0.70-0.76) Marital status Not married 1 [Reference] 1 [Reference] 0.95 (0.91-0.99) 1.07 (1.05-1.10) Married Unknown 1.06 (0.92-1.22) 1.37 (1.28-1.47) Insurance status 1 [Reference] 1 [Reference] Private Medicare 0.97 (0.88-1.06) 0.97 (0.93-1.00) 0.84 (0.68-1.04) 1.08 (0.97-1.21) Military Not insured or self-pay 0.78 (0.61-0.99) 1.08 (0.96-1.21) Public or Medicaid 0.66 (0.61-0.71) 1.08 (1.05-1.11) Unknown 0.26 (0.22-0.31) 0.37 (0.35-0.40) Patient SES distribution of reporting hospital  $^{b}$ >50% of patients in quintiles 1-2 1.12 (1.05-1.20) 1.49 (1.44-1.53) >50% of patients in quintiles 4-5 1 [Reference] 1 [Reference] Mixed distribution 1.05 (1.00-1.10) 1.32 (1.28-1.35) Received care at an NCI- designated cancer center No 1 [Reference] 1 [Reference] Yes 1.13 (1.04-1.22) 0.81 (0.77-0.85)

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Abbreviations: ER, estrogen receptor; NCI, National Cancer Institute; PR, progesterone receptor; SES, socioeconomic status.

1 [Reference]

2.73 (2.61-2.86)

1 [Reference]

0.84 (0.82-0.86)

Year of cancer diagnosis
1998–2004

2005-2011

<sup>&</sup>lt;sup>a</sup>Odds ratios based on polytomous logistic regression modeling. Model covariates were age, race/ethnicity, tumor size, grade, ER/PR status, nodal status, histology, receipt of adjuvant treatments including chemotherapy and radiation, neighborhood SES quintile, marital status, insurance status, SES composition of patients at the reporting hospital, care at an NCI-designated cancer center, and year of diagnosis.

Distribution based on statewide quintiles.

<sup>&</sup>lt;sup>C</sup>Pvalue for trend of SES was <.001 for both bilateral mastectomy and unilateral mastectomy compared with breast-conserving surgery with radiation

Table 4

Multiple Regression Hazard Ratios for Associations of Patient and Clinical Characteristics With Overall Mortality, Stages 0–III Breast Cancer, 1998–2010, California<sup>a</sup>

Variable	Deceased Patients	<b>Total Patients</b>	HR (95% CI)
Surgical procedure			
Bilateral mastectomy	635	9907	1.02 (0.94–1.11)
Breast-conserving surgery with radiation	9949	96 462	1 [Reference]
Unilateral mastectomy	13 699	68 548	1.35 (1.32–1.39)
Race/ethnicity			
Chinese	383	4787	0.70 (0.63-0.78)
Filipina	529	6150	0.69 (0.63-0.75)
Hispanic	2982	26 035	0.81 (0.77-0.84)
Japanese	244	2263	0.70 (0.62-0.80)
Non-Hispanic American Indian/other/unknown	150	1378	0.85 (0.72–1.00)
Non-Hispanic black	1701	9112	1.12 (1.06–1.17)
Non-Hispanic white	17 782	117 853	1 [Reference]
Other Asian/Pacific Islander	512	7339	0.67 (0.61–0.73)
Age at diagnosis, y			
<40	1124	9341	1.11 (1.04–1.19)
40–49	2503	34 878	0.82 (0.78-0.86)
50–64	5621	68 104	1 [Reference]
65	15 035	62 594	2.65 (2.56–2.75)
Tumor size			
Per centimeter	NA	NA	1.23 (1.21–1.25)
Lymph node involvement			
Negative	14 327	126 165	1 [Reference]
Positive	9956	48 752	1.46 (1.40–1.51)
Histology			
Ductal	20 561	149 278	1 [Reference]
Lobular or with lobular component	1961	12 403	0.89 (0.84-0.93)
Other	1761	13 236	0.92 (0.87-0.96)
Grade			
I	3825	36 593	1 [Reference]
П	8919	70 377	1.15 (1.11–1.20)
Ш	9828	58 247	1.49 (1.43–1.55)
Unknown	1711	9700	1.23 (1.16–1.30)
ER/PR status			
Negative	4992	26 685	1.48 (1.43–1.53)
Positive	15 375	125 955	1 [Reference]
Unknown or borderline	3916	22 277	1.11 (1.07–1.15)

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HR (95% CI) Variable **Deceased Patients Total Patients** Adjuvant treatment, chemotherapy, and/or radiation 109 699 15 336 1 [Reference] Yes 8947 65 218 0.78 (0.76-0.81) Neighborhood SES quintile b,c 18 484 1 (lowest) 3308 1 [Reference] 2 4758 28 329 0.97 (0.92-1.01) 3 5394 35 740 0.90 (0.86-0.94) 4 5564 42 120 0.85 (0.81-0.89) 5 5259 50 244 0.73 (0.70-0.77) Marital status 11 432 104 647 Married 1 [Reference] 12 438 67 098 1.36 (1.33-1.40) Not married 413 1.18 (1.07-1.30) Unknown 3172 Insurance status 5229 22 445 1.22 (1.18-1.26) Medicare 1.12 (0.96-1.31) Military 158 1487 187 1408 1.10 (0.95-1.27) Not insured or self-pay 11 957 113 347 Private 1 [Reference] Public or Medicaid 1.25 (1.21-1.29) 5892 29 746 Unknown 860 6484 0.92 (0.86-0.99) Patient SES distribution of reporting hospital<sup>b</sup> >50% of patients in quintiles 4-5 10 471 89 573 1 [Reference] >50% of patients in quintiles 1-2 5555 31 015 1.12 (1.08-1.16) 54 329 Mixed distribution 8257 1.07 (1.04-1.11) Received care at an NCI-designated cancer center 23 494 166 025 1 [Reference] 0.82 (0.76-0.88) Yes 789 8892 Year of cancer diagnosis

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Abbreviations: ER, estrogen receptor; HR, hazard ratio; NA, not applicable; NCI, National Cancer Institute; PR, progesterone receptor; SES, socioeconomic status.

NA

NA

0.87 (0.87-0.88)

Per year

<sup>&</sup>lt;sup>a</sup>Mortality analyses excluded women diagnosed after 2010 because of incomplete mortality data for 2011. Model covariates included age, race/ethnicity, tumor size, grade, and ER/PR status, nodal status, histology, receipt of adjuvant treatments including chemotherapy and radiation, neighborhood SES quintile, marital status, insurance status, SES composition of patients at the reporting hospital, care at an NCI-designated cancer center, and year of diagnosis. Models were stratified by American Joint Committee on Cancer stage.

Distribution based on statewide quintiles.

 $<sup>^{</sup>C}P$  value for trend of SES was <.001.

Table 5

Multiple Regression Hazard Ratios for Associations of Patient and Clinical Characteristics With Breast Cancer–Specific Mortality, Stages 0–III Breast Cancer, 1998–2010, California<sup>a</sup>

Variable	<b>Deceased Patients</b>	<b>Total Patients</b>	HR (95% CI)
Surgical procedure			
Bilateral mastectomy	392	9907	1.09 (0.98–1.21)
Breast-conserving surgery with radiation	3620	96 462	1 [Reference]
Unilateral mastectomy	6115	68 548	1.29 (1.23–1.35)
Race/ethnicity			
Chinese	210	4787	0.85 (0.74-0.97)
Filipina	315	6150	0.83 (0.74-0.94)
Hispanic	1703	26 035	0.90 (0.85-0.95)
Japanese	80	2263	0.70 (0.56-0.88)
Non-Hispanic American Indian/other/unknown	73	1378	1.06 (0.84–1.34)
Non-Hispanic black	896	9112	1.22 (1.14–1.32)
Non-Hispanic white	6529	117 853	1 [Reference]
Other Asian/Pacific Islander	321	7339	0.81 (0.72-0.90)
Age at diagnosis, y			
<40	1027	9341	1.32 (1.22–1.41)
40–49	1995	34 878	0.97 (0.92–1.03)
50–64	3311	68 104	1 [Reference]
65	3794	62 594	1.43 (1.35–1.51)
Tumor size			
Per centimeter	NA	NA	1.33 (1.30–1.36)
Lymph node involvement			
Negative	3905	126 165	1 [Reference]
Positive	6222	48 752	1.96 (1.85–2.07)
Histology			
Ductal	8915	149 278	1 [Reference]
Lobular or with lobular component	684	12 403	0.98 (0.90–1.07)
Other	528	13 236	0.78 (0.71–0.85)
Grade			
I	634	36 593	1 [Reference]
II	3071	70 377	1.87 (1.71–2.04)
Ш	5953	58 247	3.12 (2.86–3.41)
Unknown	469	9700	1.82 (1.60–2.06)
ER/PR status			
Negative	3295	26 685	1.80 (1.71–1.88)
Positive	5622	125 955	1 [Reference]
Unknown or borderline	1210	22 277	1.12 (1.05–1.20)

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Variable	<b>Deceased Patients</b>	<b>Total Patients</b>	HR (95% CI)
Adjuvant treatment, chemotherapy, and/or radiation			
No	3742	109 699	1 [Reference]
Yes	6385	65 218	1.10 (1.05–1.16)
Neighborhood SES quintile b,c			
1 (lowest)	1506	18 484	1 [Reference]
2	2007	28 329	0.99 (0.93–1.06)
3	2181	35 740	0.93 (0.87-1.00)
4	2257	42 120	0.89 (0.83-0.96)
5	2176	50 244	0.80 (0.74-0.86)
Marital status			
Married	5559	104 647	1 [Reference]
Not married	4393	67 098	1.13 (1.08–1.18)
Unknown	175	3172	1.08 (0.93–1.26)
Insurance status			
Medicare	1362	22 445	1.23 (1.15–1.31)
Military	84	1487	1.07 (0.86–1.33)
Not insured or self-pay	120	1408	1.09 (0.91–1.31)
Private	5831	113 347	1 [Reference]
Public or Medicaid	2368	29 746	1.30 (1.23–1.37)
Unknown	362	6484	0.80 (0.72-0.89)
Patient SES distribution of reporting hospital b			
>50% of patients in quintiles 4–5	4316	89 573	1 [Reference]
>50% of patients in quintiles 1–2	2456	31 015	1.12 (1.05–1.18)
Mixed distribution	3355	54 329	1.07 (1.02–1.12)
Received care at an NCI-designated cancer center			
No	9731	166 025	1 [Reference]
Yes	396	8892	0.87 (0.78-0.96)
Year of cancer diagnosis			
Per year	Not applicable	Not applicable	0.87 (0.87–0.88)

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Abbreviations: HR, hazard ratio; NA, not applicable; NCI, National Cancer Institute; SES, socioeconomic status.

<sup>&</sup>lt;sup>al</sup>Mortality analyses excluded women diagnosed after 2010 because of incomplete mortality data for 2011. Model covariates included age, race/ethnicity, tumor size, grade, and ER/PR status, nodal status, histology, receipt of adjuvant treatments including chemotherapy and radiation, neighborhood SES quintile, marital status, insurance status, SES composition of patients at the reporting hospital, care at an NCI-designated cancer center, and year of diagnosis. Models were stratified by American Joint Committee on Cancer stage.

 $<sup>^{</sup>b}$ Distribution based on statewide quintiles.

 $<sup>^{</sup>C}P$  value for trend of SES was <.001.

Table 6

Propensity Score Analysis of Overall Mortality, Showing Average Effect of an Alternative Surgical Procedure on Patients Treated With a Specific Surgical Procedure (Average Treatment Effect of Those Treated)

Surgical Treatment and Alternatives	Hazard Ratio for Mortality (95% CI)		
Bilateral mastectomy			
vs unilateral mastectomy	1.23 (1.13–1.33)		
vs breast-conserving surgery with radiation	0.94 (0.86–1.02)		
Breast-conserving surgery with radiation			
vs bilateral mastectomy	1.13 (1.00–1.28)		
vs unilateral mastectomy	1.27 (1.23–1.31)		
Unilateral mastectomy			
vs bilateral mastectomy	0.93 (0.83–1.04)		
vs breast-conserving surgery with radiation	0.81 (0.78-0.84)		