Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Jennifer Lauren Kline Date

Factors predicting receipt of contralateral prophylactic mastectomy for women diagnosed with early stage invasive breast cancer in the United States, 2004-2010

By

Jennifer Lauren Kline
Master of Public Health

Epidemiology

_____

Kevin C. Ward, PhD, MPH
Faculty Thesis Advisor

Factors predicting receipt of contralateral prophylactic mastectomy for women diagnosed with early stage invasive breast cancer in the United States, 2004-2010

By

Jennifer Lauren Kline
B.S., Emory University, 2012

Faculty Thesis Advisor: Kevin C. Ward, PhD, MPH

An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology

2014

Abstract

Factors predicting receipt of contralateral prophylactic mastectomy for women diagnosed with early stage invasive breast cancer in the United States, 2004-2010

By Jennifer Lauren Kline

Objective: The use of contralateral prophylactic mastectomy (CPM) for early stage breast cancers has been increasing over the last decade. Although CPM does not provide increased survival, many women are beginning to choose this therapy over the recommended surgeries, unilateral total mastectomy (UTM) and breast conserving surgery (BCS). Trends and predictors of CPM have been researched before 2004, but not for the most recent years.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER) research-access dataset from 2004 through 2010, predictors of receipt of CPM were compared across three age groups. Multivariate logistic regression models were used to determine associations between patient and diagnostic characteristics and receipt of CPM, across the three age groups.

Results: For women of all ages, the odds of electing CPM over UTM/BCS in 2010 were over 2.5 times the odds of electing CPM in 2004. Women of all ages living in the Midwest, as well as women under 64 in the South and women under 49 in the Northeast, were more likely to elect CPM over UTM/BCS than women living in the West at their time of diagnosis. Women between 60 and 79 in the Northeast were less likely to elect CPM over UTM/BCS than their counterparts in the Western region of the US. White women and married women were the most likely to undergo CPM. In addition, women under the age of 64 living in metropolitan areas were more likely to elect CPM compared to women living in urban areas. Across all age groups, women with increased nodal involvement, larger tumor size, and lobular histologic type were the most likely to elect CPM over the alternative surgeries.

Conclusion: Women with early stage unilateral breast cancer are increasingly electing CPM over UTM and BCS from year to year. Future studies will be able to use this data, along with previous data, to address this growing trend and evaluate the processes in which physicians discuss therapy options with early stage breast cancer patients.

Factors predicting receipt of contralateral prophylactic mastectomy for women diagnosed with early stage invasive breast cancer in the United States, 2004-2010

By

Jennifer Lauren Kline
B.S., Emory University, 2012

Faculty Thesis Advisor: Kevin C. Ward, PhD, MPH

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology

2014

Acknowledgements

I would like to thank my advisor, Dr. Kevin Ward for his guidance and patience throughout this process. I would also like to thank my family and friends for their encouragement and support through this, and my throughout overall education.

Table of Contents

BACKGROUND AND LITERATURE REVIEW

In the United States, breast cancer accounts for 14.1% of all new cancer cases. The American Cancer Society estimates that in 2014 about 232,670 women will be diagnosed with invasive breast cancer and 40,000 women will die from the disease [1]. Breast cancer is the third leading cause of cancer death in the US. Survival depends on many factors, but women who are diagnosed at an older age are more likely to die of the disease compared to younger women. In addition, five year relative survival is lower for women with a more advanced stage at diagnosis [1]. Breast cancer can occur in males and females, but cases in men only represent 1% of all breast cancers in the US [1]. Breast cancer is most frequently diagnosed in women between the ages of 55 and 64 [2]. In 2013, 79% of new cases and 88% of deaths occurred in women who were 50 years or older [1].

The breast is made up of 15 to 20 sections, called lobes, which have smaller sections called lobules. The lobules end in dozens of small bulbs that make milk. The lobes, lobules, and bulbs are connected to one another by thin tubes called ducts. Each breast also contains blood vessels and lymph vessels. The lymph vessels connect the breast to the lymph nodes, which filter substances and help fight infection and disease. Lymph nodes near the breast are located in the axilla (under the arm), above the collarbone, and in the chest. The most common type of breast cancer is ductal carcinoma. It begins in the cells of the ducts. Lobular carcinoma begins in the lobes or lobules and is the type of breast cancer that is more likely than any other kind to be found in both breasts [3].

There are many well-studied factors that are associated with a higher risk of breast cancer. These include a family history of breast cancer, nulliparity or older age at first birth, early menarche, advanced age, mutations in the BRCA1 or BRCA2 genes, and a personal history of breast cancer [3]. Carriers of the BRCA1 and BRCA2 mutations that have a history of breast cancer have an increased risk of contralateral disease as high as 5% per year [3]. Other factors associated with an increased risk of contralateral breast cancer are lobular type histology, multicentric cancer, previous chest radiation, and high breast tissue density [1, 4].

Treatment of breast cancer typically includes surgery with other treatments like radiation therapy, chemotherapy, hormone therapy, or targeted therapy. Breast-conserving surgery (BCS) is a surgery that removes only the cancerous tissue and a rim of normal tissue. It is almost always followed by radiation therapy because it reduces risk of recurrence by 50% [1]. The standard type of radiation for women with breast cancer who have just had BCS is external beam radiation, which requires daily administration over the course of 5 to 6 weeks. A unilateral total mastectomy (UTM) is the removal of the entire breast. According to the American Cancer Society, 57% of women diagnosed with early stage (stages I and II) breast cancer undergo BCS, 36% have UTM, 6% have no surgery, and about 1% do not receive any treatment [1]. Among the women diagnosed with late stage (stages III and IV) breast cancer, 13% undergo BCS, 60% have UTM, 18% have no surgery, and 7% receive no treatment [1].

Prophylactic mastectomy (including contralateral prophylactic mastectomy) and chemoprevention are some of the ways to prevent breast cancer. Prophylactic mastectomy is the removal of one or both breasts before breast cancer occurs. It can

reduce the risk of breast cancer by 90% or more, however, not all women who receive this surgery would have developed cancer [1]. Bilateral prophylactic mastectomy can reduce the risk of breast cancer in women who have a family history of breast or ovarian cancer, deleterious mutation in the BRCA1 or BRCA2 gene, or mutations in other breast cancer-associated genes like TP53 and PTEN [5]. Women who have a high risk of breast cancer and have been diagnosed with cancer in one breast may elect to have the other breast removed as well, in a procedure called contralateral prophylactic mastectomy (CPM). Removal of the contralateral breast reduces risk of cancer in that breast, but does not necessarily translate to longer survival [5]. This procedure is discouraged for women who are not at high risk of developing breast cancer since the risk of these women developing a contralateral breast cancer (CBC) is very low.

In more recent years, women who do not fall into the high-risk category for developing CBC have been opting to undergo CPM [6]. According to a study done by Rosenberg et al. [7], women chose this method of prevention because they wanted to decrease their risk of CBC, improve survival, and gain peace of mind. The study also found that women were overestimating their risk of contralateral breast cancer; women who did not have BRCA mutations estimated that if they had not received CPM, their risk of developing contralateral breast cancer would be 10% over 5 years, whereas the actual risk is between 2 and 4% over 5 years [7]. Misinformation may be a factor influencing decision to choose CPM over UTM or BCS.

In a review of current literature about CPM, Tracy et al. [8] determined that studies consistently found that women undergoing CPM are more likely to be non-Hispanic white, younger in age, more educated, and have a family history of breast or

ovarian cancer. In addition, they are more likely to be of a higher socioeconomic status and be privately insured. The study determined that while diagnostic factors, such as tumor grade, stage, size, and lobular type histology, are associated with CPM, they are not as strong of predictors as the patient's characteristics.

A study by Bedrosian et al. [9] used SEER data to determine if CPM conferred a significant survival benefit to women with unilateral breast cancer between 1998 and 2003. The study found that improved survival by CPM was associated with an age less than 50 years and early stage (I or II) ER-negative tumors. They determined that this effect was related to ER-negative cases having a higher baseline risk of contralateral breast cancer. Another study by King et al. [10] determined that the increase in CPM is not associated with the increased recognition of patients at high risk for contralateral breast cancer. Increased rates of CPM were found to be associated with treatment factors like immediate reconstruction, preoperative MRI, and unsuccessful attempts at breast conservation.

In 2007, the Society of Surgical Oncology (SSO) revised their position statement on prophylactic mastectomy. The purpose of the position statement was to guide insurance programs in determining coverage and to help patients obtain reimbursement [11]. SSO considers contralateral prophylactic mastectomy to be appropriate for a patient who has a high risk of contralateral breast cancer, for patients in whom surveillance of the contralateral breast would be difficult (including patients with dense breast tissue), or for women looking to have improved symmetry after reconstruction [11]. SSO recommends that a discussion be held with individuals diagnosed with breast cancer to assess their risk of developing a second cancer, to educate them on the lack of impact

CPM has on mortality from the index cancer, and to determine if endocrine therapy could be a significant benefit in reducing risk of contralateral cancer [11]. Instead of undergoing risk-reducing surgery, women can choose to undergo enhanced screening so that if a contralateral primary occurs, there is an increased chance that the cancer will be detected at an early stage and be treated successfully [5].

The increased rate of contralateral prophylactic mastectomy in the past decade has led researchers to become interested in understanding why women are choosing this surgery over the recommended therapies for early stage breast cancer, like unilateral total mastectomy and breast conserving surgery. The aim of this study is to provide updated data on the utilization and predictors of contralateral prophylactic mastectomy in the hopes that future studies will address the growing trend of potential over-treatment of early stage breast cancer and work to better improve communication with patients regarding the benefits and risks of their therapeutic options.

METHODS

Data Source

Information on breast cancer cases was retrieved from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database, which collects demographic and clinical data on cancer patients. SEER is a research-access and de-identified dataset that is available for use after signing a Data Use Agreement from the National Cancer Institute. This analysis used data from 18 SEER registries, including San Francisco-Oakland, Connecticut, Metropolitan Detroit, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Metropolitan Atlanta, San Jose-Monterey, Los Angeles, Alaska Natives, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, and Greater Georgia [12]. Together, these registries cover approximately 27.8% of the U.S. population [13].

Study Subjects

Data on breast cancer cases were extracted from the SEER database using SEER*Stat (version 8.1.5) in a Case Listing Session. In the 'Selection' tab, the boxes for 'Malignant Behavior' and 'Known Age' were selected. In addition, cases were selected using the following criteria:

a. {Site and Morphology.Site recode ICD-O-3/WHO 2008}= 'Breast'
b. {Race, Sex, Year Dx, Registry, County.Sex}= 'Female'
c. {Race, Sex, Year Dx, Registry, County.Year of diagnosis}= '2004', '2005', '2006', '2007', '2008', '2009', '2010'

d. {Age at Diagnosis.Age recode with <1 year olds}= ’20-24 years’, ’25-29 years’, ’30-34 years’, ’35-39 years’, ‘40-44 years’, ’45-49 years’, ’50-54 years’, ’55-59 years’, ’60-64 years’, ’65-69 years’, ’70-74 years’, ’75-79 years’
e. {Extent of Disease – CS.Laterality (1973+)}= ‘Right – origin of primary’, ‘Left – origin of primary’
f. {Stage – AJCC.Derived AJCC Stage Group, 6th ed (2004+)}= ‘I’, ‘INOS’, ‘IA’, ‘IA1’, ‘IA2’, ‘IB’, ‘IB1’, ‘IB2’, ‘IC’, ‘IS’, ‘IEA’, ‘IEB’, ‘IE’, ‘ISA’, ‘ISB’, ‘II’, ‘IINOS’, ‘IIA’, ‘IIB’, ‘IIC’, ‘IIEA’, ‘IIEB’, ‘IIE’, ‘IISA’, ‘IISB’, “IIS’, ‘IIESA’, ‘IIESB’, ‘IIES’, ‘III’, ‘IIINOS’, ‘IIIA’

The above selection criteria results in a dataset of invasive, female breast cancer cases diagnosed with unilateral, stage I-IIIA cancer between the ages of 20 and 79 during the calendar years 2004 through 2010. These data were exported into SAS software, version 9.3 (SAS Institute Inc., Cary, NC) and the following criteria were used to select eligible cases of breast cancer:

a. Case selection:
    a. Cases with 1 primary
    b. Cases with first primary (if multiple primaries recorded for an individual)
b. Case exclusion:
    a. Cases with unknown marital status
    b. Cases with nodal stage ‘NX’
    c. Cases with tumor stage ‘TX’, ‘Tis’, ‘T0’, ‘T4a’, ‘T4b’, ‘T4c’, ‘T4d’
    d. Cases that did not undergo UTM, CPM, or BCS (RX Summ—Surg Prim Site (1998+)= 00, 19, 76, 90, 99)

Analysis

Variables

The outcome of interest was receipt of contralateral prophylactic mastectomy (CPM) as opposed to unilateral total mastectomy (UTM) or breast conservation therapy (BCS). Therapy codes were combined into the following 3 categories: BCS (codes 20, 21, 22, 23, 24), UTM (codes 30, 40, 41, 43, 44, 45, 46, 50, 51, 53, 54, 55, 56, 61, 64, 65, 66, 67, 71), and CPM (codes 42, 47, 48, 49, 52, 57, 58, 59, 62, 63, 68, 69, 72, 73, 74, 75) [14]. Surgery codes for mastectomy without specified laterality (codes 60, 70, 80) were categorized as UTM. The BCS and UTM groups were combined for the analysis as the primary focus was on factors predicting CPM.

The 18 SEER registries were grouped into the U.S. Census Bureau's 4 geographic regions: West (Alaska Natives, Seattle (Puget Sound), Los Angeles, San Francisco-Oakland SMSA, California excluding SF/SJM/LA, San Jose-Monterey, Hawaii, Utah, and New Mexico), Northeast (Connecticut, New Jersey), Midwest (Metropolitan Detroit, Iowa), and South (Metropolitan Atlanta, Greater Georgia, Rural Georgia, Kentucky, Louisiana) [15]. Age was categorized into three groups: 20-49 year olds, 50-64 year olds, and 65-79 year olds. Marital status at the time of diagnosis was categorized into two groups: married (Marital status at diagnosis='Married (including common law)') and not married (Marital status at diagnosis='Divorced', 'Separated', 'Single (never married)', 'Unmarried or Domestic Partner', 'Widowed').

The rural/urban/metropolitan status of each case was derived from the Rural/Urban Continuum Code 2003 variable from SEER. The rural-urban status of each case is determined by county of residence at the time of diagnosis, and is grouped into 9

categories. For the analysis, these categories were collapsed into 4 groups: rural (includes completely rural counties with an urban population < 2,500 adjacent to a metropolitan area and completely rural counties with an urban population < 2,500 not adjacent to a metropolitan area), urban (includes counties with an urban population of 2,500 to 19,999 adjacent to a metropolitan area, counties with an urban population of 2,500 to 19,999 not adjacent to a metropolitan area, counties with an urban population of ≥ 20,000 adjacent to a metropolitan area, and counties with an urban population of ≥ 20,000 not adjacent to a metropolitan area), metropolitan (includes counties in metropolitan area with a population ≥ 1 million, counties in a metropolitan area with a population of 250,000 to 1 million, and counties in a metropolitan area with a population < 250,000), and other/unknown (includes all Alaska cases, as well as counties with unknown rural/urban/metro status, and no match).

ICD-O-3 histology and behavior codes were combined into the following breast cancer histologic categories: lobular (8520, 8524), ductal (8022, 8035, 8500, 8501, 8502, 8503, 8504, 8507, 8508, 8521, 8523), mixed ductal and lobular (8522), and other [14]. AJCC regional node involvement (N) was categorized into 3 groups: N0 (includes N0, N0(i+), N0(i-), N0(mol+), N0(mol-)), N1 (includes N1, N1NOS, N1a, N1b, N1c, N1mi), and N2 (includes N2NOS, N2a, N2b) while AJCC tumor size/extension (T) was also categorized into 3 groups: T1 (includes T1NOS, T1a, T1b, T1c, T1mic), T2, and T3. Radiation was dichotomized into those who either received radiation of some form (beam radiation, combination of beam with implants or isotopes, NOS method or source, radioactive implants, radioisotopes) or did not (Recommended, unknown if administered,

refused, unknown). Other variables of interest included the SEER grade ('Grade') and race ('Race recode (W, B, AI, API)') variables.

Statistical Analysis

Frequencies for descriptive statistics were produced and chi-square tests were carried out to compare the distributions of categorical variables between therapy options. Unadjusted odds ratios and 95% confidence intervals were obtained using logistic regression models that included only one variable of interest as a predictor. Adjusted odds ratios were computed by including all predictors of interest in the model. Tumor stage was not included in the model due to the inclusion of the nodal involvement and tumor size variables, which are the components that determine stage. Laterality was not included in the model because of its insignificant association with surgery decision.

Interaction between variables of interest was assessed, including interaction between age and region, age and marital status, and age and race. A log likelihood ratio test was first completed which compared the full model including all interaction terms to the reduced model with no interaction terms. Following a statistically significant result, a backward selection method was used, which assessed and dropped insignificant interaction terms (α=0.05) from the model. After considering the results of both tests that assessed interaction, the interaction term for age and race was dropped from the model. The interaction terms for age and marital status and age and region were kept in the model.

Precision was not assessed due to the significance of all variables in the model. The final model included all variables, including the two interaction terms. Results are

presented stratified by age because of its presence in both interaction terms (age and marital status, and age and region).

RESULTS

The total study population included 211,563 breast cancer patients; of those 7.9% underwent contralateral prophylactic mastectomy (N=16,641), 30.83% underwent unilateral total mastectomy (N=65,215), and 61.31% underwent breast conserving surgery (N=129,707). Tables 1 and 2 provide a breakdown of all three surgical choices by patient and diagnostic characteristics; however, the UTM and BCS groups were combined for primary analysis. Statistically significant differences between the two main treatment groups were observed with regard to marital status at time of diagnosis, age, region of the US, race, year of diagnosis, rural/urban location (Table 3) as well as nodal involvement, tumor size, tumor grade, histology, radiation, and tumor stage (Table 4). Looking across the entire study cohort, most cases (70.08%) had no nodal involvement (AJCC Stage 'N0'), a tumor size less than or equal to 20 mm in dimension (AJCC Stage 'T1'), and were diagnosed with a ductal histology type, and a tumor grade of II. Approximately 81% of the women were White, 10% Black, 8% Asian or Pacific Islander, and 0.5% American Indian or Alaska Native. Most women came from a county located in a metropolitan area (89.28%).

By treatment type, about 70% of women who chose CPM were married, compared to 62.35% of women who chose UTM or BCS. Most women electing CPM were between the ages of 20 and 49 (52.23%) while most women electing UTM or BCS were between the ages of 50 and 64 (42.82%). American Indians/Alaska Natives made about 0.5% of each therapy category. White women represented almost 88% of CPM cases, Black women represented about 6%, and Asian/Pacific Islander women made up about 5% of CPM cases. UTM/BCS patients were made up of about 80% White, 10%

Black, and 8% Asian/Pacific Islander women. A larger proportion of women electing CPM were from the Southern and Midwestern regions of the US. While significant differences existed by urban/rural classification, differences were very small with most women in both groups residing in Metropolitan areas at the time of their diagnosis. About 8% of women electing CPM in the study were diagnosed in 2004, and almost 21% in 2010. Among women electing UTM/BCS, about 14% were diagnosed in 2004, and almost 14.5% in 2010.

More of the cases with less nodal involvement and smaller tumor size elected UTM or BCS. The CPM cohort, on the other hand, comprised women with a greater percentage of lobular histology, higher grade, and later stage disease. Almost 76% of CPM patients had ductal histologic type, and about 12% had lobular type. Among those who opted for UTM or BCS, almost 80% had ductal histologic type and 7.5% had lobular type. Approximately 42% of women who opted for CPM had stage I cancer, 28.68% had stage IIA, 16.68% had stage IIB, and 13.05% had stage IIIA. About 54% of UTM/BCS patients were stage I, 26.97% stage IIA, 11.72% stage IIB, and 7.71% stage IIIA. As expected due to standard of care recommendations for women undergoing BCS, only 20.86% of women who underwent CPM received radiation therapy compared to 57.28% of women who underwent UTM/BCS.

Table 5 shows the significance of association of each patient and diagnostic characteristic with surgery type, controlling for all other predictors. The analysis was stratified by age due to the effect modification described previously with marital status and region. The odds of electing CPM over UTM or BCS was increased for married women across all age groups. The odds of electing CPM over UTM/BCS were highest

among married women ages 20-49 (OR=1.32, 95% CI: 1.25, 1.40), next among married women ages 65-79 (OR=1.24, 95% CI: 1.12, 1.37), then among married women ages 50-64 (OR=1.18, 95% CI: 1.11, 1.25), compared to unmarried women in the same age categories. Asian/Pacific Islander and Black women were less likely to choose CPM over UTM/BCS compared to their White counterparts. For a woman between 20 and 49, the odds of electing CPM over UTM/BCS in 2010 was 2.82 times the odds of a woman the same age electing CPM in 2004, controlling for everything else in the model (95% CI: 1.56, 3.12). Women between 50 and 64 were 2.50 times more likely to elect CPM over UTM/BCS in 2010 than in 2004 (95% CI: 1.24, 2.80). For women between 65 and 79, the odds of electing CPM over UTM/BCS in 2010 were 2.90 times higher than in 2004 (95% CI: 2.34, 3.57).

Women between the ages of 20 and 49, as well as between 50 and 64 living in metropolitan areas were significantly more likely to choose CPM over UTM/BCS compared to women of the same age living in urban areas (ORs=1.28, 1.31, respectively). Women of all ages living in the Midwest, as well as women under 64 in the South and women under 49 in the Northeast, were more likely to elect CPM over UTM/BCS than women living in the West at their time of diagnosis. Women between 60 and 79 in the Northeast were less likely to elect CPM over UTM/BCS than their counterparts in the Western region of the US.

In all age groups, women with increased nodal involvement and larger tumor size were more likely to opt for CPM. Women between the ages of 20 and 49 with grade II or III cancer, as well as women between the ages of 65 and 79 with grade III cancer, were more likely to choose CPM than women of the same ages with grade I cancer. As

expected due to risk profile, women with lobular or mixed ductal and lobular histologic types were also the most likely to undergo CPM. For a woman between the ages of 20 and 49 with a lobular histologic type, the odds of choosing CPM over UTM/BCS was 1.65 times the odds of a woman of the same age who had a ductal histologic type (95% CI: 1.50, 1.83). Similarly, for women aged 50-64, this odds ratio was 2.11 (95% CI: 1.93, 2.30) and 1.76 (95% CI: 1.62, 2.05) for women aged 65-79.

DISCUSSION

The results of this study suggest that early stage breast cancer patients with certain personal and diagnostic characteristics may be more likely to elect contralateral prophylactic mastectomy over unilateral total mastectomy or breast conserving surgery. The biggest predictors were found to be increased nodal involvement, larger tumor size, and lobular histologic type; the biggest patient characteristic predictors included residency in a Metropolitan area, as well as having a White race. However, some characteristics with increased odds were age-specific. Marital status had the biggest effect of choosing CPM over UTM/BCS for younger women, although marital status for all age groups increased the odds of choosing CPM. In addition to marital status, region of the United States also had a different effect across age groups. Women over the age of 50 in the Northeast were less likely to opt for CPM compared to women in the Western region. In addition to these predictors, this study confirms that the odds that a woman with early stage breast cancer selects CPM over UTM or BCS are continuing to increase from year to year. The findings of this study are consistent with several of those described by Tracy et al. [8]. Both studies found that women who undergo CPM are more likely to be white and have a lobular histologic type.

A major strength of this study is that the data were drawn from SEER, a large population-based dataset that covers 27.8% of the US population [2]. It includes breast cancer cases from several large cities in different regions of the US, and also from different urban, rural, and metropolitan areas. In addition to the strengths of SEER, this study is the first to investigate predictive factors for choosing CPM for women with early

stage invasive breast cancer nation-wide for the years 2004 through 2010. This had previously only been done for the years before 2004.

Limitations to this study include the absence of data on factors associated to increased risk of CBC, including BRCA1 and BRCA2 mutation status and family history of breast and ovarian cancer. A reason for deciding on UTM or CPM could be because of the inability of a case to commit to radiation therapy, which requires radiation every day for several weeks. A study by Schroen et al. [16] looked at patient distance to radiation therapy on mastectomy decision in early stage breast cancer patients diagnosed between 1996 and 2000 in Virginia. They found that over the study period, mastectomy rates decreased from 48% to 43% in Virginia, including in 15-mile areas surrounding new radiation facilities in urban settings, and surrounding a new radiation therapy facility in a rural setting. This study shows that increased access to radiation therapy facilities may impact a woman's choice when choosing between BCS and UTM or CPM.

CONCLUSION

Although there is a very small difference in survival rates of those undergoing CPM, BCS, and UTM, there has been an increase in women choosing CPM. This study presents age-specific predictors for the choice between CPM and the recommended therapies. Despite the findings of this analysis, it is still difficult to determine the true factors that cause a woman to choose CPM. Younger women may prefer CPM because they are more concerned with the cosmetic outcome, including symmetry after reconstruction of the breasts. Women with lobular histologic types may choose CPM because they are at a higher risk for CBC and they are seeking a preventative measure. Many women may depend on their physicians or surgeons when making a decision. Also, some may be misinformed of the risk of CBC occurring, especially those who are not at high risk.

This data can be used along with previous years' research to evaluate the processes in which physicians discuss therapy options with early stage breast cancer patients. This study, along with future studies, has the potential to serve as a basis for which communication with patients regarding benefits and risks of CPM, as well as effective alternatives, can be improved.

REFERENCES

1. *American Cancer Society. Cancer Facts and Figures 2014. Atlanta, Ga: American Cancer Society; 2014.*
2. *Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2010/, based on November 2012 SEER data submission, posted to the SEER web site, April 2013.*
3. *National Cancer Institute*. April 8, 2014]; Available from: http://www.cancer.gov/.
4. Tuttle, T.M., et al., *Increasing use of contralateral prophylactic mastectomy for breast cancer patients: a trend toward more aggressive surgical treatment.* J Clin Oncol, 2007. **25**(33): p. 5203-9.
5. *Surgery to Reduce the Risk of Breast Cancer*. [cited 2014 4/8/2014].
6. Jin, J., *Women with breast cancer who opt for contralateral prophylactic mastectomy may overestimate future risk.* JAMA, 2013. **310**(15): p. 1548.
7. Rosenberg, S.M., et al., *Perceptions, knowledge, and satisfaction with contralateral prophylactic mastectomy among young women with breast cancer: a cross-sectional survey.* Ann Intern Med, 2013. **159**(6): p. 373-81.
8. Tracy, M.S., et al., *Contralateral prophylactic mastectomy in women with breast cancer: trends, predictors, and areas for future research.* Breast Cancer Res Treat, 2013. **140**(3): p. 447-52.
9. Bedrosian, I., C.Y. Hu, and G.J. Chang, *Population-based study of contralateral prophylactic mastectomy and survival outcomes of breast cancer patients.* J Natl Cancer Inst, 2010. **102**(6): p. 401-9.
10. King, T.A., et al., *Clinical management factors contribute to the decision for contralateral prophylactic mastectomy.* J Clin Oncol, 2011. **29**(16): p. 2158-64.
11. Giuliano, A.E., et al., *Society of Surgical Oncology: position statement on prophylactic mastectomy. Approved by the Society of Surgical Oncology Executive Council, March 2007.* Ann Surg Oncol, 2007. **14**(9): p. 2425-7.
12. *Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2012 Sub (1973-2010 varying) - Linked To County Attributes - Total U.S., 1969-2010 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2013, based on the November 2012 submission.*
13. SEER Program (National Cancer Institute (U.S.)) and National Cancer Institute (U.S.), *SEER, Surveillance, Epidemiology, and End Results Program*. NIH publication. 8 pages.
14. *Adamo MB, Johnson CH, Ruhl JL, Dickie, LA, (eds.). 2013 SEER Program Coding and Staging Manual. National Cancer Institute, NIH Publication number 13-5581, Bethesda, MD.*

15. *Census Regions and Divisions of the United States. U.S. Department of Commerce Economics and Statistics Administration U.S. Census Bureau: Geography Division.*
16. Schroen, A.T., et al., *Impact of patient distance to radiation therapy on mastectomy use in early-stage breast cancer patients.* J Clin Oncol, 2005. **23**(28): p. 7074-80.

TABLES

Table 1. Patient characteristics of breast cancer cases by surgery type (CPM vs. UTM vs. BCS), 2004-2010

	Total (N=211,563)		**CPM (N=16,641)**		**UTM (N=65,215)**		**BCS (N=129,707)**	
	n	%	n	%	n	%	n	%
Married								
Yes	133,185	62.95	11,649	70.00	39,633	60.77	81,903	63.14
No	78,378	37.05	4,992	30.00	25,582	39.23	47,804	36.86
Age								
20-49	59,798	28.26	8,692	52.23	19,450	29.82	31,656	24.41
50-64	89,637	42.37	6,180	37.14	26,034	39.92	57,423	44.27
65-79	62,128	29.37	1,769	10.63	19,731	30.26	40,628	31.32
Region								
Midwest	18,383	8.69	1,848	11.11	5,628	8.63	10,907	8.41
Northeast	34,305	16.22	2,551	15.33	8,873	13.61	22,881	17.64
South	45,237	21.38	4,146	24.91	16,017	24.56	25,074	19.33
West	113,638	53.71	8,096	48.65	34,697	53.20	70,845	54.62
Race								
American Indian/AK Native	998	0.47	81	0.49	357	0.55	560	0.43
Asian/Pacific Islander	17,134	8.10	818	4.92	6,883	10.55	9,433	7.27
Black	21,214	10.03	1,028	6.18	7,632	11.70	12,554	9.68
White	171,132	80.89	14,633	87.93	49,994	76.66	106,505	82.11
Unknown	1,085	0.51	81	0.49	349	0.54	655	0.50
Year of Diagnosis								
2004	28,374	13.41	1,383	8.31	9,473	14.53	17,518	13.51
2005	28,242	13.35	1,460	8.77	8,848	13.57	17,934	13.83
2006	29,111	13.76	1,811	10.88	9,013	13.82	18,287	14.10
2007	30,540	14.44	2,363	14.20	9,488	14.55	18,689	14.41
2008	31,348	14.82	2,889	17.36	9,546	14.64	18,913	14.58
2009	32,318	15.28	3,273	19.67	9,635	14.77	19,410	14.96
2010	31,630	14.95	3,462	20.80	9,212	14.13	18,956	14.61
County Location								
Metro	188,875	89.28	14,889	89.47	56,961	87.34	117,025	90.22
Rural	2,477	1.17	220	1.32	971	1.49	1,286	0.99
Urban	19,987	9.45	1,524	9.16	7,185	11.02	11,278	8.69
Unknown	224	0.11	8	0.05	98	0.15	118	0.09

Table 2. Diagnostic characteristics of breast cancer cases by surgery type (CPM vs. UTM vs. BCS), 2004-2010

	Total (N=211,563)		**CPM (N=16,641)**		**UTM (N=65,215)**		**BCS (N=129,707)**	
	n	%	n	%	n	%	n	%
N								
N0	148,266	70.08	10,006	60.13	37,116	56.91	101,144	77.98
N1	50,075	23.67	5,181	31.13	20,630	31.63	24,264	18.71
N2	13,222	6.25	1,454	8.74	7,469	11.45	4,299	3.31
T								
T1	138,952	65.68	9,353	56.20	32,417	49.71	97,182	74.92
T2	62,979	29.77	5,801	34.86	26,648	40.86	30,530	23.54
T3	9,632	4.55	1,487	8.94	6,150	9.43	1,995	1.54
Grade								
I	45,575	21.54	2,752	16.54	10,311	15.81	32,512	25.07
II	85,266	40.30	6,664	40.05	25,971	39.82	52,631	40.58
III	69,174	32.70	6,243	37.52	24,786	38.01	38,145	29.41
IV	2,022	0.96	163	0.98	832	1.28	1,027	0.79
Unknown	9,526	4.50	819	4.92	3,315	5.08	5,392	4.16
Histology								
Ductal & Lobular	14,555	6.88	1,304	7.84	4,974	7.63	8,277	6.38
Ductal	167,100	78.98	12,621	75.84	50,162	76.92	104,317	80.43
Lobular	16,538	7.82	2,004	12.04	6,081	9.32	8,453	6.52
Other	13,370	6.32	712	4.28	3,998	6.13	8,660	6.68
Laterality								
Left	107,314	50.72	8,360	50.24	33,213	50.93	65,741	50.68
Right	104,249	49.28	8,281	49.76	32,002	49.07	63,966	49.32
Radiation								
Yes	115,126	54.42	3,471	20.86	13,827	21.20	97,828	75.42
No	96,437	45.58	13,170	79.14	51,388	78.80	31,879	24.58
Stage								
I	111,384	52.65	6,921	41.59	23,271	35.68	81,192	62.60
IIA	57,347	27.11	4,772	28.68	19,532	29.95	33,043	25.48
IIB	25,626	12.11	2,776	16.68	12,323	18.90	10,527	8.12
IIIA	17,206	8.13	2,172	13.05	10,089	15.47	4,945	3.81

Table 3. Chi-square tests for the association of patient characteristics and surgery type (CPM vs. UTM/BCS), 2004-2010

	Total (N=211,563)		**CPM (N=16,641)**		**UTM/BCS (N=194,922)**		
	n	%	n	%	n	%	*p*
Married							<0.0001
Yes	133,185	62.95	11,649	70.00	121,536	62.35	
No	78,378	37.05	4,992	30.00	73,386	37.65	
Age							<0.0001
20-49	59,798	28.26	8,692	52.23	51,106	26.22	
50-64	89,637	42.37	6,180	37.14	83,457	42.82	
65-79	62,128	29.37	1,769	10.63	60,359	30.97	
Region							<0.0001
Midwest	18,383	8.69	1,848	11.11	16,535	8.48	
Northeast	34,305	16.22	2,551	15.33	31,754	16.29	
South	45,237	21.38	4,146	24.91	41,091	21.08	
West	113,638	53.71	8,096	48.65	105,542	54.15	
Race							<0.0001
American Indian/AK Native	998	0.47	81	0.49	917	0.47	
Asian/Pacific Islander	17,134	8.10	818	4.92	16,316	8.37	
Black	21,214	10.03	1,028	6.18	20,186	10.36	
White	171,132	80.89	14,633	87.93	156,499	80.29	
Unknown	1,085	0.51	81	0.49	1,004	0.52	
Year of Diagnosis							<0.0001
2004	28,374	13.41	1,383	8.31	26,991	13.85	
2005	28,242	13.35	1,460	8.77	26,782	13.74	
2006	29,111	13.76	1,811	10.88	27,300	14.01	
2007	30,540	14.44	2,363	14.20	28,177	14.46	
2008	31,348	14.82	2,889	17.36	28,459	14.60	
2009	32,318	15.28	3,273	19.67	29,045	14.90	
2010	31,630	14.95	3,462	20.80	28,168	14.45	
County Location							0.0123
Metropolitan	188,875	89.28	14,889	89.47	173,986	89.26	
Rural	2,477	1.17	220	1.32	2,257	1.16	
Urban	19,987	9.45	1,524	9.16	18,463	9.47	
Unknown	224	0.11	8	0.05	216	0.11	

Table 4. Chi-square tests for the association of diagnostic characteristics and surgery type (CPM vs. UTM/BCS), 2004-2010

	Total (N=211,563)		**CPM (N=16,641)**		**UTM/BCS (N=194,922)**		
	n	%	n	%	n	%	*p*
N							<0.0001
N0	148,266	70.08	10,006	60.13	138,260	70.93	
N1	50,075	23.67	5,181	31.13	44,894	23.03	
N2	13,222	6.25	1,454	8.74	11,768	6.04	
T							<0.0001
T1	138,952	65.68	9,353	56.20	129,599	66.49	
T2	62,979	29.77	5,801	34.86	57,178	29.33	
T3	9,632	4.55	1,487	8.94	8,145	4.18	
Grade							<0.0001
I	45,575	21.54	2,752	16.54	42,823	21.97	
II	85,266	40.30	6,664	40.05	78,602	40.32	
III	69,174	32.70	6,243	37.52	62,931	32.29	
IV	2,022	0.96	163	0.98	1,859	0.95	
Unknown	9,526	4.50	819	4.92	8,707	4.47	
Histology							<0.0001
Ductal & Lobular	14,555	6.88	1,304	7.84	13,251	6.80	
Ductal	167,100	78.98	12,621	75.84	154,479	79.25	
Lobular	16,538	7.82	2,004	12.04	14,534	7.46	
Other	13,370	6.32	712	4.28	12,658	6.49	
Laterality							0.1905
Left	107,314	50.72	8,360	50.24	98,954	50.77	
Right	104,249	49.28	8,281	49.76	95,968	49.23	
Radiation							<0.0001
Yes	115,126	54.42	3,471	20.86	111,655	57.28	
No	96,437	45.58	13,170	79.14	83,267	42.72	
Stage							<0.0001
I	111,384	52.65	6,921	41.59	104,463	53.59	
IIA	57,347	27.11	4,772	28.68	52,575	26.97	
IIB	25,626	12.11	2,776	16.68	22,850	11.72	
IIIA	17,206	8.13	2,172	13.05	15,034	7.71	

Table 5. Adjusted odds ratios for receipt of CPM compared to UTM/BCS, by age group

	Ages 20-49			Ages 50-64			Ages 65-79		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Married									
No	1.00			1.00			1.00		
Yes	1.32	1.25, 1.40	<.0001	1.18	1.11, 1.25	<.0001	1.24	1.12, 1.37	<.0001
Region									
West	1.00			1.00			1.00		
Midwest	2.00	1.83, 2.18	<.0001	1.89	1.72, 2.08	<.0001	1.37	1.16, 1.61	0.0001
Northeast	1.09	1.02, 1.17	0.0118	0.88	0.81, 0.96	0.0037	0.44	0.36, 0.54	<.0001
South	1.65	1.54, 1.76	<.0001	1.52	1.41, 1.63	<.0001	1.06	0.92, 1.20	0.4090
Race									
White	1.00			1.00			1.00		
American Indian/AK Native	1.12	0.79, 1.59	0.5234	1.03	0.68, 1.56	0.9987	0.53	0.17, 1.64	0.2710
Asian/Pacific Islander	0.49	0.45, 0.54	<.0001	0.42	0.36, 0.48	<.0001	0.39	0.29, 0.52	<.0001
Black	0.43	0.39, 0.48	<.0001	0.33	0.29, 0.38	<.0001	0.42	0.33, 0.53	<.0001
Unknown	0.65	0.46, 0.90	0.0097	0.75	0.51, 1.11	0.1471	0.21	0.05, 0.83	0.0267
Year of Diagnosis									
2004	1.00			1.00			1.00		
2005	1.08	0.96, 1.20	0.1981	1.12	0.98, 1.28	0.0848	1.15	0.89, 1.48	0.2878
2006	1.43	1.29, 1.59	<.0001	1.21	1.06, 1.37	0.0044	1.26	0.99, 1.61	0.0589
2007	1.73	1.56, 1.91	<.0001	1.69	1.50, 1.91	<.0001	1.96	1.57, 2.46	<.0001
2008	2.29	2.08, 2.52	<.0001	2.04	1.81, 2.29	<.0001	2.25	1.81, 2.80	<.0001
2009	2.42	2.19, 2.67	<.0001	2.31	2.06, 2.59	<.0001	2.35	1.90, 2.92	<.0001
2010	2.82	1.56, 3.12	<.0001	2.50	1.24, 2.80	<.0001	2.90	2.34, 3.57	<.0001
County Location									
Urban	1.00			1.00			1.00		
Metropolitan	1.28	1.17, 1.41	<.0001	1.31	1.19, 1.45	<.0001	1.04	0.90, 1.22	0.5840
Rural	1.11	0.87, 1.42	0.3896	0.97	0.75, 1.25	0.7910	0.86	0.57, 1.29	0.4612
Unknown	0.21	0.05, 0.91	0.0367	0.65	0.22, 1.93	0.4373	2.34	0.39, 14.1	0.3546

(Table 5 continued)

	Ages 20-49			Ages 50-64			Ages 65-79		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
N									
N0	1.00			1.00			1.00		
N1	1.28	1.20, 1.35	<.0001	1.18	1.11, 1.26	<.0001	1.23	1.09, 1.39	0.0008
N2	1.44	1.31, 1.58	<.0001	1.64	1.47, 1.82	<.0001	1.50	1.22, 1.84	0.0001
T									
T1	1.00			1.00			1.00		
T2	1.01	0.96, 1.07	0.6806	1.03	0.97, 1.10	0.2992	1.18	1.05, 1.32	0.0060
T3	1.99	1.81, 2.19	<.0001	2.12	1.89, 2.38	<.0001	2.47	2.00, 3.04	<.0001
Grade									
I	1.00			1.00			1.00		
II	1.12	1.03, 1.20	0.0051	1.05	0.97, 1.13	0.2389	1.13	0.99, 1.29	0.0642
III	1.19	1.10, 1.28	<.0001	1.08	0.99, 1.17	0.0757	1.24	1.07, 1.44	0.0041
IV	1.13	0.89, 1.43	0.3233	1.14	0.85, 1.51	0.3814	1.02	0.58, 1.81	0.9373
Histology									
Ductal	1.00			1.00			1.00		
Lobular	1.65	1.50, 1.83	<.0001	2.11	1.93, 2.30	<.0001	1.76	1.52, 2.05	<.0001
Ductal & Lobular	1.20	1.09, 1.33	0.0002	1.40	1.27, 1.55	<.0001	1.23	1.02, 1.49	0.0280
Other	0.78	0.69, 0.89	0.0001	0.81	0.70, 0.93	0.0037	0.71	0.56, 0.91	0.0068
Radiation									
No	1.00			1.00			1.00		
Yes	0.23	0.21, 0.24	<.0001	0.15	0.13, 0.15	<.0001	0.14	0.12, 0.16	<.0001