DEMOGRAPHIC DISPARITIES IN THE MANAGEMENT OF LOBULAR CARCINOMA IN SITU OF THE BREAST

A Thesis Submitted to the Temple University Graduate Board

In Partial Fulfillment
of the Requirements for the Degree
MASTER OF SCIENCE

---

by
Ambria S. Moten, MD
May 2018

Thesis Approvals:
Resa M. Jones, MPH, PhD, Thesis Advisor
Chair and Associate Professor, Department of Epidemiology and Biostatistics
College of Public Health
Temple University

Donna Coffman, PhD, Committee Member
Assistant Professor, Department of Epidemiology and Biostatistics
College of Public Health
Temple University

ABSTRACT

Background: Lobular carcinoma in situ (LCIS) of the breast has been shown to be a marker for an increased risk of breast cancer, rather than an actual carcinoma. There are several recommended options for the management of LCIS: observation alone, chemoprevention using Tamoxifen, and prophylactic mastectomy. It is unclear how demographic factors such as age, race and insurance type are associated with the type of management received; specifically, whether surgery was received and the type of surgery received. Therefore, the aim of this study was to identify whether demographic disparities exist in the management of LCIS and to quantify the risk associated with such disparities. Specifically, we sought to assess whether race-related differences exist in whether a person with LCIS received no surgery, partial mastectomy or complete mastectomy. Of secondary interest was to assess whether age and insurance-related differences exist in whether a person with LCIS received no surgery, partial mastectomy or complete mastectomy.

Methods: The Surveillance, Epidemiology and End Results (SEER) database was used to obtain information on patients diagnosed with LCIS between 2005 and 2014. Patients were stratified by race, and racial differences in variables related to clinical features and treatment were assessed. Descriptive statistics were calculated; Chi-square tests compared categorical variables and one-way ANOVA compared group means for continuous variables. To assess whether age was an effect modifier of the association between race and type of treatment received, a

multinomial logistic regression model was run including the interaction or product term of race*age. Similarly, to assess whether insurance type was an effect modifier of the association between race and type of treatment received, a multinomial logistic regression model was run including the interaction or product term of race*insurance type. Age was considered an effect modifier, and thus multinomial logistic regression was performed with the study sample stratified by age category. To assess whether a variable was a confounder of the association between race and treatment type, stratified multinomial logistic regression was performed with each variable in question independently added as a covariate to the stratified analyses. The crude odds ratio was compared to the odds ratio adjusted for the variable in question. If the odds ratios differed by more than 10%, the variable in question was considered a confounder. No variable acted as a confounder. Thus, no covariates were added to the model for adjustment. In the final model, multinomial logistic regression with stratification by age category was performed to assess the association between race and treatment type (i.e., no surgery, partial mastectomy, or complete mastectomy), and calculate relative risk ratios (RRR) that reflected the likelihood of receiving a particular treatment for each racial group. Although insurance type did not appear to act as an effect modifier or confounder, another stratified multinomial logistic regression model was run that included insurance type as a covariate in order to assess whether insurance type had any impact at all on the association between race and treatment type. A p-value of < 0.05 was used to

determine significance for all statistical tests, and 95% confidence intervals were used for logistic models.

Results: The study sample (N=16,646) was 75.6% non-Hispanic white, 8.0% non-Hispanic Black, 9.3% Hispanic, 5.1% non-Hispanic Asian, and 2.1% other/unknown. White patients were older (mean age 55.4 years versus 54.9 years for Blacks, 52.0 years for Hispanics, and 51.4 years for Asians; $p < 0.001$). A greater proportion of whites and Asians were insured than Blacks and Hispanics (73.9% for whites and 77.0% for Asians versus 66.5% for Blacks, and 66.0% for Hispanics; $p < 0.001$). The predominant treatment type was partial mastectomy for all races. However, a greater proportion of whites underwent complete mastectomy compared to other races (22.8% versus 15.5% for Blacks, 19.3% for Hispanics, and 16.9% for Asians; $p < 0.001$). Among patients 65 – 74 years, Blacks were less likely to undergo partial mastectomy than no surgery compared to whites (RRR = 0.61, 95% CI 0.40 – 0.95). Moreover, Blacks in all but the youngest age group were less likely to undergo complete mastectomy than no surgery compared to whites (RRR range: 0.35 – 0.48). There were no significant differences in the type of treatment received among Hispanics. In all age groups, patients of other/unknown race were significantly less likely to undergo partial (RRR range: 0.02 –0.14) or complete mastectomy (RRR range: 0.19 – 0.28) than no surgery compared to whites. There were less consistent findings for other race and age strata. Asians were more likely to undergo partial mastectomy than no surgery compared to whites if they were

aged 45 – 54 years (RRR = 1.57, 95% CI 1.03 – 2.41). But Asians were less likely to undergo complete mastectomy than no surgery compared to whites if they were aged 55 – 64 years (RRR = 0.48, 95% CI 0.26 – 0.92). In the additional stratified multinomial logistic regression model that included insurance type as a covariate, racial differences in treatment were also noted and results were similar to those reported above for the unadjusted model.

Conclusion: A larger proportion of white women had complete mastectomy compared to all other racial groups. While there were significant racial differences in socioeconomic variables in descriptive analyses, they did not confound the relationship between race and treatment of patients with LCIS. Racial differences in treatment were most significant among patients who were Black or of other/unknown race and the association was modified by age. Further research into factors affecting the decision to proceed with surveillance or surgery, as well as reasons behind the disparity in treatment among certain racial groups is warranted.

TABLE OF CONTENTS

Page

LIST OF TABLES

Table Page

CHAPTER 1

INTRODUCTION

Lobular carcinoma in situ (LCIS) is a lesion of the breast that is characterized by the growth of neoplastic cells within breast lobules, the glands in the breast that produce milk (E. M. Ward et al., 2015). These neoplastic cells do not invade through the walls of the breast lobules, which is why this lesion is referred to as "in situ". LCIS does not typically present as a breast mass, and it has no radiographic features that make it identifiable on a mammogram (Oppong & King, 2011). Thus, it is usually found during histologic examination of a breast biopsy performed for some other reason (Oppong & King, 2011; E. M. Ward et al., 2015).

Between 1999 and 2004, the incidence of LCIS was approximately 3.4 per 100,000 women in the United States (Eheman et al., 2009). This increased slightly to 3.9 per 100,000 between 2007 and 2011 (E. M. Ward et al., 2015). LCIS is diagnosed at a frequency much lower than other breast lesions. For instance, the most common type of breast cancer, invasive ductal carcinoma, has an age-adjusted incidence of 86.3 per 100,000 (Eheman et al., 2009). LCIS occurs most often among women aged 50 – 59 years, for whom the age-adjusted incidence is between 10.2 – 11.2 per 100,000, followed by women aged 60 – 69 years, for whom the age-adjusted incidence is 8.3 – 8.6 per 100,000 (Eheman et al., 2009; E. M. Ward et al., 2015). Moreover, LCIS occurs more frequently in white women compared to

women of other races (Eheman et al., 2009; Han, Talbott, & Donovan, 2011; E. M. Ward et al., 2015). The reported age-adjusted incidence of LCIS between 1999 and 2004 was 3.6 per 100,000 in whites compared to 1.9 per 100,000 in Blacks, 1.0 per 100,000 in Asians, and 1.2 per 100,000 in American Indians (Eheman et al., 2009). More recent data on LCIS incidence continued to demonstrate racial differences (E. M. Ward et al., 2015). Between 2007 and 2011, the incidence was 4.4 per 100,000 in whites, 2.6 per 100,000 in Blacks, 2.1 per 100,000 in Asians, and 2.7 per 100,000 in Hispanics (E. M. Ward et al., 2015). Despite these age and race-related differences, the incidence of LCIS appears to be relatively stable over time (Eheman et al., 2009; E. M. Ward et al., 2015). Between 1999 and 2004, the annual percent change in the incidence of LCIS was 0.8, leading to only a slight increase in incidence (Eheman et al., 2009). When assessing LCIS incidence trends over a longer time period, 1992 – 2011, increases in incidence were reflected by annual percent changes that ranged from 1.2 to 4.4 based on age category (E. M. Ward et al., 2015). The greatest increase (annual percent change of 4.4) was demonstrated among women aged 50 – 69 years, and this included a significant increase in incidence until 2001, followed by a non-significant decline until 2004, and a non-significant increase until 2011 (E. M. Ward et al., 2015). The small increases in LCIS incidence were similar to those seen for ductal carcinoma in situ between 1999 and 2011, when annual percent changes ranged from 0.4 to 2.0 based on age category (E. M. Ward et al., 2015).

With the slight increase in LCIS incidence in recent years, it is important to be aware of the risk that LCIS poses to patients who are found to have this lesion in their breast. LCIS is thought to be a marker for an increased risk of breast cancer, rather than a true cancer (Chuba et al., 2005; Oppong & King, 2011; E. M. Ward et al., 2015). There are a few reasons for this. First, the invasive breast cancer that may subsequently develop following the diagnosis and treatment of LCIS is not limited to the same breast in which LCIS occurred, but may occur in either breast with approximately equal frequencies (Chuba et al., 2005; King et al., 2015; Wong, King, Boileau, Barry, & Golshan, 2017). Furthermore, the invasive breast cancer that may develop is not limited to lobular histology, but may also be of ductal histology (e.g. invasive ductal carcinoma instead of invasive lobular carcinoma) (Chuba et al., 2005; Wong et al., 2017). In fact, more than 40% of patients develop invasive ductal carcinoma, while only 20 – 23% develop invasive lobular carcinoma (Chuba et al., 2005; Wong et al., 2017). The overall risk of developing invasive breast cancer following a diagnosis of LCIS is 7 – 11% at 10 years and 13 – 20% at 20 years (Chuba et al., 2005; Wong et al., 2017). The risk of invasive cancer is greatest among patients aged 60 – 69 years compared to other age groups (Chuba et al., 2005). Furthermore, although the risk of developing invasive breast cancer in general is greatest among whites, there are no racial differences in the risk of developing invasive breast cancer following a diagnosis of LCIS (Chuba et al., 2005).

Because LCIS is not believed to be a true cancer, it is not treated like a typical breast cancer. In general, breast cancer is treated with surgery, followed by radiation, chemotherapy and/or hormone therapy. In contrast, LCIS may not require any treatment at all. There are several recommended options for the management of LCIS, including surveillance, chemoprevention, and prophylactic mastectomy (Oppong & King, 2011; E. M. Ward et al., 2015). Surveillance entails obtaining a mammogram annually as well as having a clinical breast exam every 6 – 12 months in an effort to detect any cancer that may develop as early as possible (Oppong & King, 2011). Chemoprevention involves taking an estrogen receptor modulator, such as tamoxifen or raloxifene, to decrease the risk of developing breast cancer (Oppong & King, 2011). Finally, prophylactic mastectomy involves removing the breasts in order to decrease the risk of breast cancer, and may be followed by breast reconstruction for cosmesis. The patient and their healthcare providers together decide which management option is best for the patient. Based on current recommendations, no single option is preferred to the others. However, a recent analysis of patients with LCIS treated at a single institution in New York demonstrated that surveillance alone is the option chosen most often (78%), followed by chemoprevention (17%) and then prophylactic mastectomy (5%) (King et al., 2015).

With multiple management options available, it is unclear how demographic factors such as age, race and insurance type are associated with the type of

management received; specifically, whether surgery was received and the type of surgery received. This is of interest because prior research has shown that demographic variables may have an impact on the treatment received for other types of breast lesions. For instance, race has been shown to play a role in the treatment of invasive breast cancer (Bradley, Given, & Roberts, 2002; Li, Malone, & Daling, 2003; Sail, Franzini, Lairson, & Du, 2012). Black patients less frequently received standard treatment (breast-conserving surgery plus radiation, or total mastectomy), and more frequently received inappropriate treatment compared to their white counterparts (Li et al., 2003). On the other hand, Asians were more likely to receive standard treatment than whites (Li et al., 2003). Blacks were also less likely to receive chemotherapy and radiotherapy for breast cancer treatment (Sail et al., 2012). Racial differences also exist in the management of ductal carcinoma in situ, for which non-whites were more likely to get unilateral mastectomy, while whites were more likely to get bilateral mastectomy (E. M. Ward et al., 2015). In addition, age also appears to impact the treatment of invasive breast cancer (Bradley et al., 2002; Markossian & Hines, 2012). With each year increase in age, patients have 5% increased odds of not receiving surgery at all (Bradley et al., 2002). Similarly, patients greater than 65 years of age were less likely to receive radiation or surgery compared to patients younger than 40 years of age (Markossian & Hines, 2012). Among patients with ductal carcinoma in situ, patients older than age 59 years were less likely to undergo bilateral mastectomy,

and were more likely to undergo breast-conserving surgery compared to those aged 50 – 59 years (E. M. Ward et al., 2015). Furthermore, insurance type is associated with how a patient's breast cancer is treated (Bradley et al., 2002; Freedman et al., 2011). Patients with Medicaid were less likely to receive radiation following breast-conserving surgery compared to patients who do not have Medicaid (Bradley et al., 2002). Patients without insurance were less likely to receive appropriate surgery, hormone therapy and chemotherapy compared to patients with private insurance (Freedman et al., 2011). Among patients with ductal carcinoma in situ, those with private insurance were more likely to undergo bilateral mastectomy compared to those with Medicaid, Medicare or no insurance (E. M. Ward et al., 2015).

Although demographic and socioeconomic factors have been shown to impact the management of invasive breast cancer, it remains unclear how such factors are associated with the management of LCIS. Therefore, the purpose of this study was to identify whether demographic disparities exist in the management of LCIS and to quantify the risk associated with such disparities. Our primary goal was to assess whether race-related differences exist in the management of LCIS. Of secondary interest was to assess whether age and insurance-related differences exist in the management of LCIS. The specific aims and hypotheses were as follows:

- Specific Aim 1: To identify racial differences in whether a patient received no surgery, partial mastectomy or complete mastectomy for LCIS.

  - Hypothesis 1: White patients were more likely to receive prophylactic mastectomy than Black and Hispanic patients.
- Specific Aim 2: To identify age-related differences in whether a patient received no surgery, partial mastectomy or complete mastectomy for LCIS.
  - Hypothesis 2: Younger patients were more likely to receive prophylactic mastectomy than older patients.
- Specific Aim 3: To identify insurance-related differences in whether a patient received no surgery, partial mastectomy or complete mastectomy for LCIS.
  - Hypothesis 3: Patients with insurance were more likely to receive prophylactic mastectomy than patients without insurance.

Knowledge gained from this study will provide more insight into the factors related to treatment choice. Because the management of LCIS includes both invasive and non-invasive options, this study will improve our understanding of how demographic and socioeconomic variables are associated with the treatment received when the treatment options are more variable. This will enable health care providers to have more informed discussions with their patients as they manage LCIS.

CHAPTER 2

METHODS

This retrospective study was performed using secondary data analysis. The Surveillance, Epidemiology and End Results (SEER) database was used to identify patients diagnosed with LCIS over a ten-year period, 2005 – 2014 (Surveillance, Epidemiology, and End Results program [SEER], 2016). SEER is a publically available, de-identified database maintained by the National Cancer Institute that contains demographic, tumor, and treatment-related information regarding approximately 28% of the United States population (SEER, 2016). Demographic, clinical and treatment information was obtained from the database. The study included women diagnosed with LCIS (i.e., incident cases) between 2005 and 2014. Patients younger than age 18 years were excluded because current treatment guidelines do not necessarily apply to children. Patients were also excluded if their treatment status (e.g., surgery, etc.) was unknown. Temple University's Institutional Review Board reviewed the protocol for this study to ensure protection of human subjects.

The main dependent variable was treatment type (i.e., no surgery, partial mastectomy, and complete mastectomy) where "complete mastectomy" included total mastectomy, modified radical mastectomy and radical mastectomy. The primary independent variable was race (non-Hispanic white, non-Hispanic Black,

Hispanic, Asian, and other/unknown). Both age at diagnosis (in years) and insurance type (uninsured/unknown, insured, Medicaid) were assessed as effect modifiers. Potential confounders and covariates included: year of diagnosis; United States (US) region of residence (i.e., Alaska, East, Northern Plains, Pacific Coast, Southwest); proportion of residents in county greater than age 65 years; proportion of residents in county with less than a high school education; proportion of residents in county with a Bachelor's degree; proportion of residents in county who were unemployed; and the median family income of residents in the county.

Patients were stratified by race (non-Hispanic white, non-Hispanic Black, Hispanic, Asian, and other/unknown), and racial differences in variables related to clinical features and treatment were assessed. Chi-square tests compared categorical variables and one-way ANOVA compared group means for continuous variables.

To assess whether age was an effect modifier of the association between race and type of treatment received, a multinomial logistic regression model was run including the interaction or product term of race*age. The interaction term was significant; thus, age was considered an effect modifier. Similarly, to assess whether insurance type was an effect modifier of the association between race and type of treatment received, a multinomial logistic regression model was run including the interaction of race*insurance type. However, the interaction term was not significant, thus; insurance type was not considered an effect modifier. Because

only the age variable was an effect modifier, multinomial logistic regression was performed with the study sample stratified by age category.

To assess whether a variable was a confounder of the association between race and treatment type, multinomial logistic regression with the study sample stratified by age was performed with each variable in question independently added as a covariate. The crude odds ratio was compared to the odds ratio adjusted for the variable in question. If the odds ratios differed by more than 10%, the variable in question was considered a confounder. Variables assessed for confounding included insurance type, year of diagnosis, US region, tumor size, proportion of residents in county greater than age 65 years, proportion of residents in county with less than a high school education, proportion of residents in county with a Bachelor's degree, proportion of residents in county who were unemployed, and median family income of residents in the county. No variable acted as a confounder.

In the final model, unadjusted multinomial logistic regression with stratification by age category was performed to assess the association between race and treatment type. Relative risk ratios (RRR) and respective 95% confidence intervals (CI) were calculated. Although insurance type did not appear to act as an effect modifier or confounder, another stratified multinomial logistic regression model was run that included insurance type as a covariate in order to assess whether insurance type had any impact at all on the association between race and treatment type.

Statistical analysis was performed using Stata version 12.1 (StataCorp LP, College Station, TX, USA). A p-value of < 0.05 was used to determine significance for all statistical tests.

CHAPTER 3

RESULTS

The study sample (N=16,646) was 75.6% non-Hispanic white, 8.0% non-Hispanic Black, 9.3% Hispanic, 5.1% non-Hispanic Asian, and 2.1% unknown/other race (Table 1). White patients were older (mean age 55.4 years versus 54.9 years for Blacks, 52.0 years for Hispanics, and 51.4 years for Asians; $p < 0.001$). More whites and Asians were insured than Blacks and Hispanics (73.9% for whites and 77.0% for Asians versus 66.5% for Blacks, and 66.0% for Hispanics; $p < 0.001$). Moreover, a higher proportion of Blacks and Hispanics had Medicaid than whites and Asians (10.2% for Blacks and 12.0% for Hispanics versus 3.2% for whites and 5.2% for Asians; $p < 0.001$). As for county-level variables, white and Asian patients resided in counties with a greater proportion of residents with a Bachelor's degree (34.5% for whites and 37.7% for Asians, versus 32.5% for Blacks and 33.3% for Hispanics; $p < 0.001$) and higher median family incomes ($79,000 for whites and $86,400 for Asians, versus $67,800 for Blacks and $74,800 for Hispanics; $p < 0.001$) (Table 1).

Table 1
Demographic and Clinical Characteristics of the Study Sample by Race (N = 16,646)

Characteristic	White, n (%)	Black, n (%)	Hispanic, n (%)	Asian, n (%)	Other or Unknown, n (%)	p-value
Year of Diagnosis						< 0.001*
2005	1,069 (8.5)	105 (7.9)	113 (7.3)	48 (5.7)	29 (8.2)	
2006	1,180 (9.4)	109 (8.2)	105 (6.8)	67 (8.0)	22 (6.3)	
2007	1,221 (9.7)	125 (9.4)	129 (8.4)	68 (8.1)	32 (9.1)	
2008	1,296 (10.3)	117 (8.8)	150 (9.7)	85 (10.1)	21 (6.0)	
2009	1,408 (11.2)	124 (9.3)	149 (9.7)	71 (8.5)	28 (8.0)	
2010	1,276 (10.1)	150 (11.3)	152 (9.9)	87 (10.4)	30 (8.5)	
2011	1,229 (9.8)	126 (9.5)	146 (9.5)	87 (10.4)	36 (10.3)	
2012	1,259 (10.0)	135 (10.2)	153 (9.9)	107 (12.7)	33 (9.4)	
2013	1,311 (10.4)	171 (12.9)	211 (13.7)	104 (12.4)	65 (18.5)	
2014	1,335 (10.6)	168 (12.6)	232 (15.1)	116 (13.8)	56 (15.9)	
Mean Age in Years (SE)	55.4 (0.09)	54.9 (0.30)	52.0 (0.25)	51.4 (0.34)	52.4 (0.53)	< 0.001*
Age Category in Years						< 0.001*
< 45	1,593 (12.7)	211 (15.9)	346 (22.5)	198 (23.6)	65 (18.5)	
45 – 54	5,425 (43.1)	496 (37.3)	716 (46.5)	397 (47.3)	179 (50.9	
55 – 64	3,007 (23.9)	381 (28.7)	281 (18.3)	144 (17.1)	64 (18.2)	
65 – 74	1,752 (13.9)	168 (12.6)	155 (10.1)	73 (8.7)	30 (8.5)	
≥ 75	807 (6.4)	74 (5.6)	42 (2.7)	28 (3.3)	14 (4.0)	
Age 65+ Years	13.9	12.9	13.1	13.4	13.7	< 0.001*
Insurance Type						< 0.001*
Uninsured/Unknown	2,888 (23.0)	310 (23.3)	339 (22.0)	149 (17.7)	171 (48.6)	
Medicaid	401 (3.2)	135 (10.2)	185 (12.0)	44 (5.2)	18 (5.1)	
Insured	9,295 (73.9)	885 (66.5)	1,016 (66.0)	647 (77.0)	163 (46.3)	

Table 1 (*continued*)

Characteristic	White, n (%)	Black, n (%)	Hispanic, n (%)	Asian, n (%)	Other or Unknown, n (%)	p-value
Region						< 0.001*
Alaska	0	0	0	0	13 (3.7)	
East	6,439 (51.2)	816 (61.4)	526 (34.2)	232 (27.6)	139 (39.5)	
Northern Plains	1,448 (11.5)	237 (17.8)	19 (1.2)	23 (2.7)	30 (8.5)	
Pacific Coast	4,303 (34.2)	275 (20.7)	885 (57.5)	580 (69.1)	162 (46.0)	
Southwest	394 (3.1)	2 (0.2)	110 (7.1)	5 (0.6)	8 (2.3)	
< High School Education	12.1	13.7	15.6	13.0	12.4	< 0.001*
Bachelor's Degree	34.5	32.5	33.3	37.7	33.8	< 0.001*
Unemployed	8.8	10.2	9.3	8.3	9.1	< 0.001*
Median Family Income in Dollars	79,000	67,800	74,800	86,400	80,700	< 0.001*
Mean Tumor Size in Centimeters (SE)	1.3 (0.50)	1.3 (0.69)	1.5 (2.12)	1.2 (0.70)	1.3 (1.65)	0.001*
Treatment Type						< 0.001*
No Surgery	1,110 (8.8)	156 (11.7)	127 (8.3)	67 (8.0)	110 (31.3)	
Partial Mastectomy	8,603 (68.4)	968 (72.8)	1,116 (72.5)	631 (75.1)	215 (61.1)	
Complete Mastectomy	2,871 (22.8)	206 (15.5)	297 (19.3)	142 (16.9)	27 (7.7)	

Notes: SE = standard error.
**p-value < 0.05.*

In addition, Hispanic patients had the largest mean tumor size (1.5 cm versus 1.3 cm for whites, 1.3 cm for Blacks, and 1.2 cm for Asians; $p = 0.001$). The predominant treatment was partial mastectomy for all races. However, a larger proportion of whites underwent complete mastectomy compared to other races (22.8% versus 15.5% for Blacks, 19.3% for Hispanics, and 16.9% for Asians; $p < 0.001$) (Table 1).

Stratified multinomial logistic regression models revealed that particular racial groups had significantly higher odds of receiving different treatment than whites (Table 2). Among patients 65 – 74 years, Blacks were less likely to undergo partial mastectomy than no surgery compared to whites (RRR = 0.61, 95% CI 0.40 – 0.95). Moreover, Blacks in all but the youngest age group were less likely to undergo complete mastectomy than no surgery compared to whites (age 45 – 54 years: RRR = 0.48, 95% CI 0.34 – 0.69; age 55 – 64 years: RRR = 0.46, 95% CI 0.30 – 0.70; age 65 – 74 years: RRR = 0.38, 95% CI 0.21 – 0.69; age ≥ 75: RRR = 0.35, 95% CI 0.13 – 0.95). There were no significant differences in treatment type among Hispanics. In all age groups, patients of other/unknown race were less likely to undergo partial (RRR range: 0.19 –0.28) or complete mastectomy (RRR range: 0.04 – 0.14) than no surgery compared to whites (Table 2). There were less consistent findings for other race and age strata.

Table 2
Multinomial Logistic Regression of Treatment Type on Race, Stratified by Age

Treatment Type	**Age Category (years)**				
	< 45, RRR (95% CI)	**45 – 54, RRR (95% CI)**	**55 – 64, RRR (95% CI)**	**65 – 74, RRR (95% CI)**	**≥ 75, RRR (95% CI)**
No Surgery	Reference	Reference	Reference	Reference	Reference
Partial Mastectomy					
White	Reference	Reference	Reference	Reference	Reference
Black	1.74 (0.92 – 3.29)	0.76 (0.57 – 1.02)	0.77 (0.55 – 1.09)	0.61 (0.40 – 0.95)*	0.62 (0.32 – 1.18)
Hispanic	1.42 (0.88 – 2.27)	1.06 (0.80 – 1.40)	1.11 (0.71 – 1.74)	1.01 (0.58 – 1.75)	0.76 (0.28 – 2.03)
Asian	1.15 (0.67 – 1.99)	1.57 (1.03 – 2.41)*	0.74 (0.44 – 1.26)	0.96 (0.45 – 2.06)	1.61 (0.37 – 6.96)
Other or Unknown	0.22 (0.12 – 0.38)*	0.28 (0.21 – 0.40)*	0.24 (0.14 – 0.42)*	0.19 (0.09 – 0.39)*	0.20 (0.07 – 0.58)*
Complete Mastectomy					
White	Reference	Reference	Reference	Reference	Reference
Black	1.19 (0.59 – 2.38)	0.48 (0.34 – 0.69)*	0.46 (0.30 – 0.70)*	0.38 (0.21 – 0.69)*	0.35 (0.13 – 0.95)*
Hispanic	0.94 (0.56 – 1.59)	0.82 (0.60 – 1.13)	0.75 (0.45 – 1.25)	1.05 (0.56 – 1.97)	1.65 (0.55 – 4.93)
Asian	0.58 (0.30 – 1.10)	1.07 (0.66 – 1.71)	0.48 (0.26 – 0.92)*	0.92 (0.38 – 2.24)	1.50 (0.27 – 8.40)
Other or Unknown	0.09 (0.04 – 0.23)*	0.08 (0.04 – 0.16)*	0.14 (0.06 – 0.33)*	0.04 (0.01 – 0.31)*	~

Notes. RRR = relative risk ratio. CI = confidence interval. ~ = Unable to calculate due to insufficient data.
**p-value < 0.05.*

In the additional stratified multinomial logistic regression model that included insurance type as a covariate, racial differences in treatment were also noted (Table 3). Results were similar to those reported above for the unadjusted model. Among patients 65 – 74 years, Blacks were less likely to undergo partial mastectomy than no surgery compared to whites (RRR = 0.62, 95% CI 0.40 – 0.96). Moreover, Blacks in all but the youngest age group were less likely to undergo complete mastectomy than no surgery compared to whites (RRR range: 0.33 – 0.51). There were no significant differences in the type of treatment received among Hispanics. In all age groups, patients of other/unknown race were significantly less likely to undergo partial (RRR range: 0.22 –0.32) or complete mastectomy (RRR range: 0.05 – 0.18) than no surgery compared to whites. There were less consistent findings for other race and age strata. Asians were less likely to undergo complete mastectomy than no surgery compared to whites if they were aged 55 – 64 years (RRR = 0.43, 95% CI 0.23 – 0.83) (Table 3).

Table 3
Multinomial Logistic Regression of Treatment Type on Race, Stratified by Age, Adjusted for Insurance Type

Treatment Type	Age Category (years) < 45, RRR (95% CI)	45 – 54, RRR (95% CI)	55 – 64, RRR (95% CI)	65 – 74, RRR (95% CI)	≥ 75, RRR (95% CI)
No Surgery	Reference	Reference	Reference	Reference	Reference
Partial Mastectomy					
White	Reference	Reference	Reference	Reference	Reference
Black	1.80 (0.95 – 3.41)	0.79 (0.59 – 1.06)	0.74 (0.52 – 1.05)	0.62 (0.40 – 0.96)*	0.60 (0.31 – 1.15)
Hispanic	1.38 (0.85 – 2.22)	1.11 (0.83 – 1.47)	1.14 (0.73 – 1.80)	1.00 (0.58 – 1.74)	0.76 (0.28 – 2.05)
Asian	1.12 (0.65 – 1.95)	1.53 (1.00 – 2.35)	0.69 (0.40 – 1.17)	0.93 (0.43 – 1.99)	1.58 (0.36 – 6.84)
Other or Unknown	0.25 (0.14 – 0.45)*	0.32 (0.22 – 0.45)*	0.27 (0.15 – 0.49)*	0.22 (0.10 – 0.47)*	0.22 (0.07 – 0.67)*
Complete Mastectomy					
White	Reference	Reference	Reference	Reference	Reference
Black	1.23 (0.61 – 2.48)	0.51 (0.36 – 0.73)*	0.43 (0.28 – 0.66)*	0.37 (0.21 – 0.68)*	0.33 (0.12 – 0.93)*
Hispanic	0.90 (0.53 – 1.52)	0.85 (0.62 – 1.18)	0.78 (0.46 – 1.31)	1.02 (0.55 – 1.92)	1.74 (0.57 – 5.26)
Asian	0.56 (0.29 – 1.07)	1.01 (0.63 – 1.63)	0.43 (0.23 – 0.83)*	0.85 (0.35 – 2.08)	1.49 (0.27 – 8.41)
Other or Unknown	0.11 (0.05 – 0.29)*	0.10 (0.05 – 0.19)*	0.18 (0.08 – 0.41)*	0.05 (0.01 – 0.41)*	~

Notes. RRR = relative risk ratio. CI = confidence interval. ~ = Unable to calculate due to insufficient data.
**p-value < 0.05.*

CHAPTER 4

DISCUSSION

In this analysis of a large cancer database, we found significant racial disparity in socioeconomic factors among women with LCIS when assessing descriptive statistics. Moreover, we noted significant race-related differences in the type of treatment received. The majority of women with LCIS underwent partial mastectomy. This is similar to prior studies in which the predominant treatment was breast-conserving surgery (E. M. Ward et al., 2015; Wong et al., 2017). However, the number and proportion of prophylactic mastectomies performed for both invasive and in situ breast cancers seems to be increasing (McLaughlin, Lillquist, & Edge, 2009; Portschy, Marmor, Nzara, Virnig, & Tuttle, 2013; Yao, Stewart, Winchester, & Winchester, 2010). The rate at which mastectomy was performed for LCIS increased by 50% between 2000 and 2009 (Portschy et al., 2013). The goal of this study was to determine if demographic differences existed in the type of mastectomy received, if the patient underwent surgery at all. Our first specific aim was to identify racial differences in whether a patient received no surgery, partial mastectomy or complete mastectomy for LCIS. We found that the proportion of women with LCIS who underwent complete mastectomy was greatest among whites compared to other races. Blacks within most age categories were significantly less likely to undergo complete mastectomy than whites. Because

research on race-related disparity in the management of LCIS is sparse, we used data regarding the treatment of invasive breast cancer to help formulate our aims and hypotheses. Similar to the findings of our study, prior research has shown that Blacks and other racial minorities were less likely to undergo prophylactic mastectomy or complete mastectomy for treatment of their breast cancer compared to their white counterparts (Brown, Shao, Jatoi, Shriver, & Zhu, 2016; Kim, McCarthy, Bristol, & Armstrong, 2017; McLaughlin et al., 2009; E. P. Ward, Unkart, Bryant, Murphy, & Blair, 2017; Xie et al., 2017; Yao et al., 2010). For example, Whites with invasive breast cancer were more likely to undergo contralateral prophylactic mastectomy than Blacks (Kim et al., 2017; E. P. Ward et al., 2017; Yao et al., 2010). Moreover, whites with early-stage breast cancer had 132% increased odds of undergoing contralateral prophylactic mastectomy compared to Blacks (OR 2.32; 95% CI 1.76 – 3.06) (Kim et al., 2017). The limited number of studies focusing on LCIS in particular reported similar findings (Portschy et al., 2013; Xie et al., 2017). For example, Blacks with LCIS underwent partial mastectomy more frequently, while whites underwent bilateral mastectomy more frequently (Xie et al., 2017). Thus, there is clearly a difference in the type of surgery a patient receives, and this difference is impacted by race. The second specific aim of the current study was to identify whether age was an effect modifier for the relationship between race and LCIS treatment. While age was an effect modifier; however, we identified no clear pattern regarding age and treatment type. Blacks and patients of

other/unknown race were less likely than whites to get complete mastectomy, and this finding was demonstrated among most age groups. This is in contrast to prior research that has demonstrated a significant association between age and the type of treatment received. Although no studies have demonstrated that age is an effect modifier of the association between race and LCIS treatment, prior research has shown that younger women with early-stage breast cancer more frequently undergo contralateral prophylactic mastectomy than older women (Kim et al., 2017; E. P. Ward et al., 2017; Yao et al., 2010). For example, women in age categories less than 60 years of age were more likely to undergo contralateral prophylactic mastectomy compared to older women (aged 60 years or more) (Kim et al., 2017). One study that focused on LCIS in particular found that factors such as younger age and white race were associated with an increased likelihood of undergoing mastectomy compared to older age and minority race (Portschy et al., 2013).

Finally, the third specific aim of the current study was to identify whether insurance type was an effect modifier for the relationship between race and whether patients received no surgery, partial mastectomy or complete mastectomy for LCIS. Prior research has suggested that the type of insurance that a patient has is associated with receipt of prophylactic mastectomy (McLaughlin et al., 2009; E. P. Ward et al., 2017; Yao et al., 2010). For instance, patients with invasive breast cancer who were uninsured or had Medicaid were less likely to undergo contralateral prophylactic mastectomy compared to patients with private insurance

(E. P. Ward et al., 2017). We found that insurance type was neither an effect modifier nor confounder of the association between race and treatment type. Even when insurance type was included as a covariate in the multinomial regression model, the relative risk ratios in the adjusted model were essentially unchanged from those in the unadjusted model. However, the insurance variable used in our analysis included a uninsured/unknown category that included 23.1% of our study sample. When separated into its components, only 1.3% of the patients in our sample were uninsured and 21.8% had an unknown type of insurance. Thus, although our study may have demonstrated that insurance plays little to no role in LCIS treatment choice, further research is warranted using a sample for which more detailed insurance information is available.

The information obtained from this has study has important implications for public health. A cancer diagnosis may induce great physical, emotional and financial burdens on those affected. As described before, patients with LCIS are at greater risk of subsequently developing breast cancer. The duration of time at risk is greater for younger women than it is for older women. Thus, although an older woman may not develop breast cancer during the fewer number of remaining years in her lifetime, a younger woman, with more years of life to live, might. Longer follow up is needed in younger women with LCIS to determine long-term breast cancer risk and whether that risk may have been decreased by undergoing a complete mastectomy rather than non-surgical management when initially

diagnosed with LCIS. Because we demonstrated that certain racial groups were less likely to get complete mastectomy, these groups may be disproportionately affected by breast cancer in the long term. Thus further research is warranted, as it may allow us to adjust our treatment practices and decrease the risk of cancer and the associated burden.

The current study was the first to use a large national database to access LCIS in particular, and the association between race and the management of LCIS. However, this study does have some limitations. We were unable to assess the use of chemoprevention as a management option because the SEER database does not contain a variable related to the use of tamoxifen or raloxifene. Knowledge of the number of patients who received chemoprevention would have been very valuable for data analysis and interpretation. The insurance variable used in this analysis was limited in that it contained a large proportion of unknown data and its coding did not include categories for private insurance or Medicare. SEER's insurance variable was recoded in 2007. Thus patients diagnosed before 2007 have an insurance type that is coded differently than those diagnosed after 2007. These factors may have affected the accuracy of our results regarding insurance type. Because of this, it may be worthwhile to perform an analysis that only includes data on patients diagnosed after 2007. Also, although large and considered to be the gold standard for national cancer incidence registry data, the database used for this analysis includes only about 28% of the US population. Thus, our results may not be

fully generalizable to the US population. In addition, results of this analysis were based on secondary data analysis using a database that may contain missing data or coding errors. This might have affected the accuracy of the results obtained in this study.

CHAPTER 5

CONCLUSION

While there were significant racial differences in socioeconomic variables in descriptive analyses, they did not confound the relationship between race and treatment of patients with LCIS. Disparities in treatment were most notable among Blacks and patients of other/unknown race. Knowledge gained from this study provides more insight into the factors related to treatment choice, and how demographic variables are associated with the treatment received when the treatment options are more variable than those for a typical breast cancer. Although further research into the factors affecting the decision to proceed with surveillance or surgery among women with LCIS is warranted, the results of this study will enable health care providers to have more informed discussions with their patients as they manage LCIS.

REFERENCES CITED

Bradley, C. J., Given, C. W., & Roberts, C. (2002). Race, socioeconomic status, and breast cancer treatment and survival. *Journal of the National Cancer Institute, 94*(7), 490-496.

Brown, D., Shao, S., Jatoi, I., Shriver, C. D., & Zhu, K. (2016). Trends in use of contralateral prophylactic mastectomy by racial/ethnic group and ER/PR status among patients with breast cancer: A SEER population-based study. *Cancer Epidemiology, 42*, 24-31. doi:10.1016/j.canep.2016.02.011 [doi]

Chuba, P. J., Hamre, M. R., Yap, J., Severson, R. K., Lucas, D., Shamsa, F., & Aref, A. (2005). Bilateral risk for subsequent breast cancer after lobular carcinoma-in-situ: Analysis of surveillance, epidemiology, and end results data. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 23*(24), 5534-5541. doi:23/24/5534 [pii]

Cutuli, B., De Lafontan, B., Kirova, Y., Auvray, H., Tallet, A., Avigdor, S., . . . Delva, C. (2015). Lobular carcinoma in situ (LCIS) of the breast: Is long-term outcome similar to ductal carcinoma in situ (DCIS)? analysis of 200 cases. *Radiation Oncology (London, England), 10*, 110-015-0379-7. doi:10.1186/s13014-015-0379-7 [doi]

Eheman, C. R., Shaw, K. M., Ryerson, A. B., Miller, J. W., Ajani, U. A., & White, M. C. (2009). The changing incidence of in situ and invasive ductal and lobular breast carcinomas: United States, 1999-2004. *Cancer Epidemiology, Biomarkers & Prevention : A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology, 18*(6), 1763-1769. doi:10.1158/1055-9965.EPI-08-1082 [doi]

Freedman, R. A., Virgo, K. S., He, Y., Pavluck, A. L., Winer, E. P., Ward, E. M., & Keating, N. L. (2011). The association of race/ethnicity, insurance status, and socioeconomic factors with breast cancer care. *Cancer, 117*(1), 180-189. doi:10.1002/cncr.25542 [doi]

Han, Y. Y., Talbott, E., & Donovan, M. (2011). Time trends and racial differences in female breast cancer incidence in Pennsylvania, 1985-2004. *Journal of Women's Health (2002),* doi:10.1089/jwh.2010.2082 [doi]

Kim, Y., McCarthy, A. M., Bristol, M., & Armstrong, K. (2017). Disparities in contralateral prophylactic mastectomy use among women with early-stage breast cancer. *NPJ Breast Cancer, 3*, 2-017-0004-z. eCollection 2017. doi:10.1038/s41523-017-0004-z [doi]

King, T. A., Pilewskie, M., Muhsen, S., Patil, S., Mautner, S. K., Park, A., . . . Morrow, M. (2015). Lobular carcinoma in situ: A 29-year longitudinal experience evaluating

clinicopathologic features and breast cancer risk. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 33*(33), 3945-3952. doi:10.1200/JCO.2015.61.4743 [doi]

Li, C. I., Malone, K. E., & Daling, J. R. (2003). Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Archives of Internal Medicine, 163*(1), 49-56. doi:ioi10945 [pii]

Markossian, T. W., & Hines, R. B. (2012). Disparities in late stage diagnosis, treatment, and breast cancer-related death by race, age, and rural residence among women in Georgia. *Women & Health, 52*(4), 317-335. doi:10.1080/03630242.2012.674091 [doi]

McLaughlin, C. C., Lillquist, P. P., & Edge, S. B. (2009). Surveillance of prophylactic mastectomy: Trends in use from 1995 through 2005. *Cancer, 115*(23), 5404-5412. doi:10.1002/cncr.24623 [doi]

Oppong, B. A., & King, T. A. (2011). Recommendations for women with lobular carcinoma in situ (LCIS). *Oncology (Williston Park, N.Y.), 25*(11), 1051-6, 1058. doi:167891 [pii]

Portschy, P. R., Marmor, S., Nzara, R., Virnig, B. A., & Tuttle, T. M. (2013). Trends in incidence and management of lobular carcinoma in situ: A population-based

analysis. *Annals of Surgical Oncology, 20*(10), 3240-3246. doi:10.1245/s10434-013-3121-4 [doi]

Sail, K., Franzini, L., Lairson, D., & Du, X. (2012). Differences in treatment and survival among African-American and Caucasian women with early stage operable breast cancer. *Ethnicity & Health, 17*(3), 309-323. doi:10.1080/13557858.2011.628011 [doi]

Surveillance, Epidemiology, and End Results (SEER) program (www.seer.cancer.gov) research data (1973-2014), National Cancer Institute, DCCPS, surveillance research program, released April 2017, based on the November 2016 submission

Ward, E. M., DeSantis, C. E., Lin, C. C., Kramer, J. L., Jemal, A., Kohler, B., . . . Gansler, T. (2015). Cancer statistics: Breast cancer in situ. *CA: A Cancer Journal for Clinicians, 65*(6), 481-495. doi:10.3322/caac.21321 [doi]

Ward, E. P., Unkart, J. T., Bryant, A., Murphy, J., & Blair, S. L. (2017). Influence of distance to hospital and insurance status on the rates of contralateral prophylactic mastectomy, a national cancer data base study. *Annals of Surgical Oncology, 24*(10), 3038-3047. doi:10.1245/s10434-017-5985-1 [doi]

Wong, S. M., King, T., Boileau, J. F., Barry, W. T., & Golshan, M. (2017). Population-based analysis of breast cancer incidence and survival outcomes in women diagnosed with lobular carcinoma in situ. *Annals of Surgical Oncology, 24*(9), 2509-2517. doi:10.1245/s10434-017-5867-6 [doi]

Xie, Z. M., Sun, J., Hu, Z. Y., Wu, Y. P., Liu, P., Tang, J., . . . Yang, M. T. (2017). Survival outcomes of patients with lobular carcinoma in situ who underwent bilateral mastectomy or partial mastectomy. *European Journal of Cancer (Oxford, England : 1990), 82*, 6-15. doi:S0959-8049(17)30994-2 [pii]

Yao, K., Stewart, A. K., Winchester, D. J., & Winchester, D. P. (2010). Trends in contralateral prophylactic mastectomy for unilateral cancer: A report from the national cancer data base, 1998-2007. *Annals of Surgical Oncology, 17*(10), 2554-2562. doi:10.1245/s10434-010-1091-3 [doi]