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:

_____ _____

Saurabh Subhash Chavan Date

RECEIPT OF SURGICAL TREATMENT IN WOMEN WITH EARLY STAGE BREAST CANCER: DOES PLACE OF BIRTH MATTER?

by

Saurabh Subhash Chavan

Master of Public Health

Epidemiology

_____

Michael Goodman MD, MPH

Committee Chair

Ahmedin Jemal DVM, PhD

Committee Member

RECEIPT OF SURGICAL TREATMENT IN WOMEN WITH EARLY STAGE BREAST CANCER: DOES PLACE OF BIRTH MATTER?

by

Saurabh Subhash Chavan

Medicinae Baccalaureus, Bachelor of Surgery

Maharashtra University of Health Sciences

2010

Thesis Committee Chair: Michael Goodman MD, MPH

Thesis Committee Member: Ahmedin Jemal DVM, PhD

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
2013

ABSTRACT

RECEIPT OF SURGICAL TREATMENT IN WOMEN

WITH EARLY STAGE BREAST CANCER:

DOES PLACE OF BIRTH MATTER?

by Saurabh Subhash Chavan

Background: While effects of age, race, place of residence, and marital status on treatment receipt among female breast cancer patients have been well documented, place of birth is a relatively less studied factor. The purpose of this study was to assess the association between birth place and type of surgery performed for early-stage breast cancer among women of different racial and ethnic backgrounds.

Methods: Eligible cases (n=119,560) were selected from the SEER registries for the period 2004-2009. US born and foreign born patients of different racial/ethnic groups were compared to US born non-Hispanic Whites (NHW) with respect to receipt of breast conserving surgery (BCS) or mastectomy. Results of multivariable logistic regression analyses were expressed as adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI).

Results: Relative to US NHW, BCS was more common in foreign born Whites (OR=1.21. 95% CI: 1.15-1.28) and foreign born Blacks (OR=1.21. 95% CI: 1.15-1.28) Foreign born Asians received less BCS compared to both US NHW (OR=0.76, 95% CI: 0.72-0.80) and US Asians (OR=0.74, 95% CI: 0.64-0.86).

Conclusions: The differences in receipt of BCS or mastectomy were generally small but noticeable, particularly for Asians. The underlying cultural or economic factors affecting breast cancer treatment selection or receipt in different population subgroups need further examination

RECEIPT OF SURGICAL TREATMENT IN WOMEN WITH EARLY STAGE BREAST CANCER: DOES PLACE OF BIRTH MATTER?

by

Saurabh Subhash Chavan

Medicinae Baccalaureus, Bachelor of Surgery

Maharashtra University of Health Sciences

2010

Thesis Committee Chair: Michael Goodman MD, MPH

Thesis Committee Member: Ahmedin Jemal DVM, PhD

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
2013

ACKNOWLEDGEMENTS

I take this opportunity to express my sincere gratitude towards Dr Michael Goodman. His continued guidance and patience was critical for this project. I wish to express my gratitude to Dr Ahmedin Jemal for his constant inputs and support without which this would not be possible.

To Jena Black, without whom, it is not unjustified to say, most students (in our department) would find it hard to navigate through while present at Rollins.
She is our North Star.

To my family, who have given everything to see me where I am today and my little niece Khushi whose fond memories brighten even the greyest day.

To my friends, Dattatraya Patil, Pratik Pimple, Kashika Sahay and Trishna Narula who are an unending source of criticism and encouragement. To Neeta aunty for being closest to what I had for a mother in Atlanta.

Most of all, to Hardik Kothare, for being constantly present by my side, in thought and spirit.

TABLE OF CONTENTS

Introduction……1

Methods……..4

Results……...7

Discussion……..9

References……12

Tables……...……19

Appendix

IRB Exemption Letter

INTRODUCTION

Breast cancer is the most commonly diagnosed non-cutaneous malignancy and the second leading cause of cancer mortality among women in the US, with an estimated 232,340 new cases and 39,620 deaths in 2013 (1). While in the West breast cancer incidence rates have been stable or slightly decreasing, they are rising in the developing world (2).

Survival following breast cancer diagnosis has been increasing in all regions of the world (3-7) because of increased awareness, early detection, and improved treatment. However, relative survival (defined as survival in cancer patients divided by that expected in the general population of the same age, sex and race) varies considerably among different countries (8).

There is also substantial variation in survival rates within each country according to region, socioeconomic status, country of origin, and race and ethnicity. For example, although in the US 5 year relative survival for breast cancer is one of the highest in the world, (8) important disparities exist by race. African American women have lower breast cancer incidence than non-Hispanic Whites, but suffer from higher mortality, (1, 9) a discrepancy attributable to disparity in survival (3). This observed inequality in breast cancer survival can be due to differences in disease severity or less timely diagnosis; (10) however, it is important to point out that the disparity persists within each stage, (3) which may serve as an indication of important differences in treatment receipt.

Clinical factors that are considered when selecting treatment for breast cancer are tumour stage and grade, hormone receptor status, patient's age, general health and preferences, menopausal status, and presence of known mutations in such as BRCA1 or BRCA2 (11). Currently, early or local stages (stages I, II and IIIA) are treated with primary surgery with or without radiation, and with or without adjuvant hormonal therapy depending on the estrogen or

progesterone receptor (ER/PR) status (12). Surgery may involve local excision of different types (e.g. lumpectomy, segmental breast removal, quadrantectomy) or modified radical mastectomy (11). Radiation is considered post-surgery for larger tumours to prevent local spread and recurrence (12). Fixed Tamoxifen (anti-estrogen) dose for 5 years has been the standard therapy for ER positive tumours and is known to reduce recurrence rates (13). Tamoxifen is recommended in both pre and post-menopausal women, however in the latter group, it may be substituted by an aromatase inhibitor to complete the 5 year treatment duration (14). Aromatase Inhibitors are known to prolong disease free survival and time to recurrence in comparison with Tamoxifen (15, 16). Trastuzumab is a monoclonal antibody drug given to HER2-positive patients with metastatic cancer in addition to chemotherapy and it is known to improve survival and quality of life in these patients (17). Chemotherapy is used for early stage and stage IIIC operable breast cancer as poly-therapy in various combinations with younger women (<50 years of age) experiencing more improvement in annual risk of disease relapse and death by breast cancer than older women (18).

Previous studies noted that treatment receipt is not equally distributed across population groups (19, 20). For example, treatment delay has been shown to be affected by both socio-demographic (21, 22) and racial disparities (23-26). It has been reported that African American women are less likely to receive adjuvant therapy for breast cancer compared to their white counterparts (27). African American women are also at higher risk for not initiating radiation therapy after breast conserving therapy (28-30). Hispanic women are less likely to receive breast conserving therapy compared to white non-Hispanic women (31).

An important socio-demographic factor that received relatively little attention is place of birth. Several international studies have compared cancer risk and prognosis in native born patients to those of immigrants (32-35). In the United States, one recent study found that West Africa- and Jamaica-born black women had lower prevalence of ER negative tumours compared

to those born in East Africa, whose prevalence estimates were comparable to those of US born white women (36).

To our knowledge, treatment receipt among US and foreign born breast cancer patients has not been examined. In particular little is known about effect of birthplace on the decision to undergo a particular type of surgery among women with early stage disease. To address this issue, the current study will assess the association between country of birth and receipt of breast conserving surgery among female breast cancer cases reported to the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program.

METHODS

The SEER program maintains a cancer database that represents 28% of the US population (37). Data are routinely collected on demographics, tumour characteristics, treatment and vital status on cancer cases reported to the 18 SEER registries. We selected data from 2004 to 2009 from all SEER registries, restricting on female cases and thus identified 332,232 of women newly diagnosed as having breast cancer during those years. Since surgical treatment status was the primary outcome of interest, those women with unknown surgical treatment status were excluded (n=2,533; 0.76%) as were those who received no surgery (26,006; 7.83%), local tumour destruction (n=18; 0.01%), surgery not otherwise specified (n=460; 0.14%) and those with mastectomy not otherwise specified (n=859; 0.26%). Those with unknown place of birth (n= 180,662; 54.38%) were excluded as this was the independent variable of primary interest. Only patients with early stage breast cancer (I, IIA, IIB, IIIA) *except* stage 0 (n=600; 0.18%) were included. Only racial/ethnic groups with sufficient proportions of foreign born persons were kept in the final dataset and for this reason American Indians /Alaska Natives (n=1,573; 0.47%) were excluded.

Primary outcome of interest was receipt of surgical treatment comparing any breast conserving surgery (BCS) with any mastectomy. Patients treated with lumpectomy, segmental mastectomy or any other tissue sparing surgery, were included in the BCS group, and those with simple, radical or extended radical mastectomy were included in the mastectomy group. The main predictor variable was place of birth, and all participants were categorized as US born or foreign born. People born in the overseas US territories such as Puerto Rico or American Samoa were not considered in the US born group since the ethno-cultural context was more relevant for this study than the geo-political context. We further grouped foreign born patients according to the major geographical regions of the world (38). Place of birth, as recorded by SEER, was studied previously and it was found that completeness of the birthplace information is a more serious

limitation than accuracy of the recorded data (39). The countries of birth were grouped into the following regions: 1) The United States considered separately; 2) entire Latin America (Central and South America); 3) the Caribbean, 4) East Africa; 5) West Africa; 6) Europe, the Middle East and North Africa combined as one region and 7) East Asia, Oceania, South East Asia and Indochina also combined into a single category. We excluded South Asia since the ethnicity of US born individuals of Indian/Pakistani origin is not represented well in our data. Hybrid variables of race and place of origin (US or foreign and region wise) was also included in the analysis.

Age at diagnosis was dichotomized as less than 50 or at least 50 years and included as a covariate. Marital status at diagnosis was classified as single (never married), married, or divorced/separated/widowed. Tumour size (<2 cm vs. ≥2 cm) and grade were also included as covariates. Tumours recorded to be greater than 60 cm were excluded as unrealistic using mean tumour size plus two standard deviations as the cut-off point. Stage was categorized as I, IIA, IIB or IIIA. Area of residence at diagnosis was accounted for by categorizing it as metro, urban and rural. Counties in metro areas with populations fewer than 250,000 were considered as metro, non-metro counties with more than 20,000 population whether or not adjacent to a metro area were considered urban and non-metro counties with less than 20,000 population whether or not adjacent to a metro area were considered rural, thus coding the original nine divisions (40) into three groups.

We performed multivariable logistic regression analyses assessing the relation of place of birth and race to selection of surgery type while adjusting for covariates. The outcome of interest in all analyses was BCS (vs. mastectomy). To take into consideration known differences in receipt of treatment by race (19) we compared different racial-ethnic / place of birth categories (e.g. US born Asians or foreign born Blacks) to US born Non-Hispanic Whites (NHW) who were used as the reference category. In addition, we conducted within race / ethnicity analyses by

comparing foreign born to US born cases. The results of multivariable analyses were expressed as adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI). A two sided alpha error of <0.05 was used as the cut-off point to determine statistical significance. Statistical analyses were performed using SAS v9.3; Statistical Institute, Cary, NC, USA.

RESULTS

Among all study participants 57.5 % underwent BCS and the remaining 42.5% had mastectomy. Mean age at diagnosis among patients receiving any mastectomy (60.4 years) was slightly lower than that for the BCS group (61.9 years). As shown in Table 1, BCS was slightly more common among white women (58.4%), than among blacks (55.2%) and Asians (52.7%), but similar among those born in the US (57.9%) and abroad (56.2%). The proportion of women treated with BCS decreased with increasing disease stage, tumour size and grade (Table 1). The difference in frequency of BCS was particularly evident when comparing residents of metropolitan areas (58.2%) to those residing in small towns (52.6%) or rural areas (47.8%). The distributions of BCS and mastectomy were similar across marital status categories.

Multivariable analysis included 5,226 European Whites, 79 West African Blacks, 90 East African Blacks, 383 Caribbean Blacks, 8,478 Asia born Asians and 6,888 Hispanics born in Latin America. Among the US born participants 73,634 were NHW, 11,605 Blacks, 3,020 Asians and 5,455 Hispanics. Using US born NHW as reference, foreign born Whites and Blacks were about 20% more likely to undergo BCS (Table 3). The differences between US born NHW and US born Blacks, Asians or Hispanics were small (OR range 1.05-1.06) and in most analyses not statistically significant. As shown in Table 3, the only group that was significantly less likely to receive BCS compared to US born NHW were foreign born Asians/Pacific Islanders (OR=0.76; 95% CI: 0.72-0.80).

Table 4 presents the results of analyses comparing US born and foreign born breast cancer patients within each racial/ethnic group. Among Whites, foreign born women were more likely to undergo BCS than their US born counterparts (OR=1.21; 95% CI: 1.15-1.28); and among Asians the association was in the opposite direction (OR=0.74; 95% CI: 0.64-0.86). By contrast, no statistically significant place of birth related differences were observed among Blacks and Hispanics (Table 4).

Table 5 extends the above analyses by evaluating specific region of birth as the independent variable of interest. European Whites were more likely to receive BCS than US NHW (OR=1.30; 95% CI: 1.22-1.39). Neither West African nor East African Blacks were significantly different from US Whites in receipt of surgical treatment; however the corresponding association was statistically significant (OR=1.31; 95% CI: 1.04-1.66) for Caribbean born Blacks (Table 5). When the analyses by region of birth were repeated within each race / ethnicity category, only among Asians the result remained statistically significant with an OR of 0.72 and a 95% CI from 0.65 to 0.79.

DISCUSSION

Overall the likelihood of receiving either BCS or mastectomy in this study did not differ widely by place of birth. The only exceptions were the consistently lower frequency of BCS among foreign born Asians (regardless of the comparison group) and the apparently higher likelihood of BCS in foreign born Whites and Black relative to US born NHW.

Choice of type of surgery in early stage breast cancer has been linked to several factors including age, socioeconomic status, geographic area in which the patient lives, proximity to a radiation therapy center, presence of BRCA mutations, breast imaging results, availability of decision aids, tumour size, and surgeon's work load (41, 42). It also depends on multi-centricity of the tumours, whether or not the cancer is of the inflammatory type, whether there are diffuse malignant appearing calcifications present and prior radiation or ineligibility to receive radiation (43). Clinical trials indicate that post-diagnosis survival of early breast cancer patients is about the same regardless of the type of surgery (44-51). Studies comparing the psychosocial consequences of BCS and mastectomy demonstrated that BCS better serves to protect women's self-image (52) but requires additional adjustment related to radiation therapy (53). Factors affecting breast cancer recurrence after BCS or mastectomy are mostly surgery-specific although hormone receptor status appears to be a predictor of prognosis regardless of treatment type (54, 55). Recurrence after BCS was of particular concern in the earlier era, but modern series have shown similar rates of post-surgical recurrence (2% - 5%) given the effective use of systemic therapy (56).

Relatively little research is available on various aspects of cancer characteristics and prognosis by place of birth. One recent study found that tumour subtypes may differ by place of birth suggesting that similar histologic features of breast cancer in women born in the same geographic area may reflect common environmental exposures in early life (57). Another recent study found differences in breast cancer survival among Hispanic women of different ethnicities

and place of birth. Compared to US NHW, breast cancer mortality was higher by 6% in Cubans, 11% in Puerto Ricans, and 13% and 24%, respectively in US born and foreign born Mexican women (58).

An international study comparing data from several European countries and the US found no significant differences in breast cancer survival in women older than 65 years of age despite major differences in the type of surgery received (59). Our results showing differences in receipt of BCS between Asian women and other ethnic groups are supported by previous research. A population-based study by Prehn et al found that Asian / Pacific Islander women were more likely to receive mastectomies than US White women (58% vs. 42%) (60). Goel et al considered the effect of being US born vs being foreign born and found that foreign born Asian / Pacific Islander women were significantly less likely to receive BCS than US NHW and these differences persisted over time between 1992-2000 (61). A recent qualitative study observed that Chinese immigrant women may be less prone to share information about their cancer diagnosis with others, and may have different attitudes towards screening and treatment due to their beliefs regarding efficacy of Traditional Eastern and Western medicine (62). Although to our knowledge this is the first study that explores the effect of place of birth on receipt of surgery, it has several important limitations. Nearly 54% of the data were excluded due to missing place of birth. However, we found that the proportions of partial surgery and mastectomy were similar between those with known (58.83%) and unknown place of birth (57.52%). Kim et al examined patterns for missing data in SEER database and found that there were no such discernible patterns of association between probability of having missing data and patient's age, race, sex or registry (63) and this relates to lessened chances of bias due to missing data in our study. For many comparisons, our analyses were based on small numbers (e.g. there were only 79 West Africans). Nevertheless, the variability of estimates was consistently low with relatively precise 95%

confidence intervals. In addition, no information was available on years spent in the US and thus the effect of acculturation could not be studied in the current analysis.

In summary, we found only a few associations between receipt of surgical treatment and place of birth among early stage breast cancer patients. Nevertheless some observations are noteworthy. Foreign born Asian breast cancer patients appear to be less likely to receive breast conserving surgery (BCS) compared to US born whites or Asian-Americans. By contrast, non-Hispanic White and Black immigrants appear to be more likely to receive BCS compared to US whites. Further studies are needed to understand the cultural factors that may explain these observations.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA: a cancer journal for clinicians* 2013;63(1):11-30.

2. Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet* 2011;378(9801):1461-84.

3. Siegel R, DeSantis C, Virgo K, et al. Cancer treatment and survivorship statistics, 2012. *CA: a cancer journal for clinicians* 2012;62(4):220-41.

4. Van Ewijk RJ, Schwentner L, Wockel A, et al. Trends in patient characteristics, treatment and survival in breast cancer in a non-selected retrospective clinical cohort study of 2,600 patients. *Archives of gynecology and obstetrics* 2013;287(1):103-10.

5. Keinan-Boker L, Baron-Epel O, Fishler Y, et al. Breast cancer trends in Israeli Jewish and Arab Women, 1996-2007. *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)* 2013;22(2):112-20.

6. Jung KW, Park S, Kong HJ, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2009. *Cancer research and treatment : official journal of Korean Cancer Association* 2012;44(1):11-24.

7. Hanagiri T, Nagata Y, Monji S, et al. Temporal trends in the surgical outcomes of patients with breast cancer. *World journal of surgical oncology* 2012;10:108.

8. Coleman MP, Quaresma M, Berrino F, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *The lancet oncology* 2008;9(8):730-56.

9. Vital signs: racial disparities in breast cancer severity--United States, 2005-2009. *MMWR Morbidity and mortality weekly report* 2012;61(45):922-6.

10. Richards MA, Westcombe AM, Love SB, et al. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999;353(9159):1119-26.

11. Breast Cancer: Treatment. American Society of Clinical Oncologists; 2013. (http://www.cancer.net/cancer-types/breast-cancer/treatment). (Accessed February 25 2013).

12. Carlson RW. NCCN Guidelines for Patients. National Comprehensive Cancer Network, 2011:58-95.

13. Davies C, Godwin J, Gray R, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet* 2011;378(9793):771-84.

14. Martinez Guisado A, Sanchez Munoz A, de la Cabeza Lomas Garrido M, et al. Initialization of adjuvant hormonal treatment for breast cancer. *Advances in therapy* 2011;28 Suppl 6:66-84.

15. Howell A, Cuzick J, Baum M, et al. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. *Lancet* 2005;365(9453):60-2.

16. Forbes JF, Cuzick J, Buzdar A, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. *The lancet oncology* 2008;9(1):45-53.

17. Baselga J, Perez EA, Pienkowski T, et al. Adjuvant trastuzumab: a milestone in the treatment of HER-2-positive early breast cancer. *The oncologist* 2006;11 Suppl 1:4-12.

18. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;365(9472):1687-717.

19. Showalter SL, Grover S, Sharma S, et al. Factors Influencing Surgical and Adjuvant Therapy in Stage I Breast Cancer: A SEER 18 Database Analysis. *Annals of surgical oncology* 2012.

20. Markossian TW, Hines RB. Disparities in late stage diagnosis, treatment, and breast cancer-related death by race, age, and rural residence among women in Georgia. *Women & health* 2012;52(4):317-35.

21. Iskandarsyah A, Klerk CD, Suardi DR, et al. Psychosocial and Cultural Reasons for Delay in Seeking Help and Nonadherence to Treatment in Indonesian Women With Breast

Cancer: A Qualitative Study. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association* 2013.

22. Balasubramanian BA, Demissie K, Crabtree BF, et al. Black Medicaid beneficiaries experience breast cancer treatment delays more frequently than whites. *Ethnicity & disease* 2012;22(3):288-94.

23. Stuver SO, Zhu J, Simchowitz B, et al. Identifying women at risk of delayed breast cancer diagnosis. *Joint Commission journal on quality and patient safety / Joint Commission Resources* 2011;37(12):568-75.

24. Hedeen AN, White E. Breast cancer size and stage in Hispanic American women, by birthplace: 1992-1995. *American journal of public health* 2001;91(1):122-5.

25. Maly RC, Leake B, Mojica CM, et al. What Influences Diagnostic Delay in Low-Income Women with Breast Cancer? *Journal of Women's Health (15409996)* 2011;20(7):1017-23.

26. Rauscher GH, Ferrans CE, Kaiser K, et al. Misconceptions about breast lumps and delayed medical presentation in urban breast cancer patients. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2010;19(3):640-7.

27. Shelton RC, Hillyer GC, Hershman DL, et al. Interpersonal influences and attitudes about adjuvant therapy treatment decisions among non-metastatic breast cancer patients: an examination of differences by age and race/ethnicity in the BQUAL study. *Breast cancer research and treatment* 2013;137(3):817-28.

28. Royak-Schaler R, Pelser C, Langenberg P, et al. Characteristics associated with the initiation of radiation therapy after breast-conserving surgery among African American and white women diagnosed with early-stage breast cancer in Maryland, 2000-2006. *Annals of epidemiology* 2012;22(1):28-36.

29. Parise CA, Bauer KR, Caggiano V. Disparities in receipt of adjuvant radiation therapy after breast-conserving surgery among the cancer-reporting regions of California. *Cancer* 2012;118(9):2516-24.

30. Dragun AE, Huang B, Tucker TC, et al. Disparities in the application of adjuvant radiotherapy after breast-conserving surgery for early stage breast cancer: impact on overall survival. *Cancer* 2011;117(12):2590-8.

31. Bride MB, Neal L, Dilaveri CA, et al. Factors Associated With Surgical Decision Making in Women With Early-Stage Breast Cancer: A Literature Review. *Journal of women's health (2002)* 2013.

32. Pons-Vigues M, Puigpinos-Riera R, Rodriguez-Sanz M, et al. Preventive control of breast and cervical cancer in immigrant and native women in Spain: the role of country of origin and social class. *International journal of health services : planning, administration, evaluation* 2011;41(3):483-99.

33. Levine H, Afek A, Shamiss A, et al. Country of origin, age at migration and risk of cutaneous melanoma: A migrant cohort study of 1,100,000 Israeli men. *International journal of cancer Journal international du cancer* 2013.

34. Hemminki K, Ankerst DP, Sundquist J, et al. Prostate cancer incidence and survival in immigrants to Sweden. *World journal of urology* 2013.

35. Leiba A, Kark JD, Afek A, et al. Adolescent obesity and paternal country of origin predict renal cell carcinoma: a cohort study of 1.1 million 16 to 19-year-old males. *The Journal of urology* 2013;189(1):25-9.

36. Jemal A, Fedewa SA. Is the prevalence of ER-negative breast cancer in the US higher among Africa-born than US-born black women? *Breast cancer research and treatment* 2012;135(3):867-73.

37. National Cancer Institute. About the SEER Program. (http://www.seer.cancer.gov/about/). (Accessed March 23 2013).

38. National Cancer Institute. APPENDIX B SEER Place of Birth/Death Geocodes.; 2011. (http://seer.cancer.gov/manuals/2011/SPCSM_2011_AppendixB.pdf). (Accessed April 8 2013).

39. Gomez SL, Glaser SL, Kelsey JL, et al. Bias in completeness of birthplace data for Asian groups in a population-based cancer registry (United States). *Cancer causes & control : CCC* 2004;15(3):243-53.

40. United States Department of Agriculture. Rural-Urban Continuum Codes. 2012. (http://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx#.UVeJz1fPjmw). (Accessed March 3 2013).

41. Roder D, Zorbas H, Kollias J, et al. Factors Predictive of Treatment by Australian Breast Surgeons of Invasive Female Breast Cancer by Mastectomy rather than Breast Conserving Surgery. *Asian Pacific journal of cancer prevention : APJCP* 2013;14(1):539-45.

42. Bride MB, Neal L, Dilaveri CA, et al. Factors associated with surgical decision making in women with early-stage breast cancer: a literature review. *Journal of women's health (2002)* 2013;22(3):236-42.

43. McLaughlin SA. Surgical management of the breast: breast conservation therapy and mastectomy. *The Surgical clinics of North America* 2013;93(2):411-28.

44. Straus K, Lichter A, Lippman M, et al. Results of the National Cancer Institute early breast cancer trial. *Journal of the National Cancer Institute Monographs* 1992(11):27-32.

45. Sauer R, Schauer A, Rauschecker HF, et al. Therapy of small breast cancer: a prospective study on 1036 patients with special emphasis on prognostic factors. *International journal of radiation oncology, biology, physics* 1992;23(5):907-14.

46. Arriagada R, Le MG, Rochard F, et al. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1996;14(5):1558-64.

47. Lichter AS, Lippman ME, Danforth DN, Jr., et al. Mastectomy versus breast-conserving therapy in the treatment of stage I and II carcinoma of the breast: a randomized trial at the National Cancer Institute. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1992;10(6):976-83.

48. Fisher B, Anderson S, Redmond CK, et al. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. *The New England journal of medicine* 1995;333(22):1456-61.

49. [A randomized study of tumor resection versus mastectomy in breast cancer. 2. 6-year results of the DBCG-82TM (Danish Breast Cancer Cooperative Group) protocol]. *Ugeskrift for laeger* 1991;153(33):2272-6.

50. Noguchi M, Yagasaki R, Kawahara F, et al. Breast conserving treatment versus modified radical mastectomy in Japanese patients with operable breast cancer. *International surgery* 1997;82(3):289-94.

51. Effects of radiotherapy and surgery in early breast cancer. An overview of the randomized trials. Early Breast Cancer Trialists' Collaborative Group. *The New England journal of medicine* 1995;333(22):1444-55.

52. Schain WS, d'Angelo TM, Dunn ME, et al. Mastectomy versus conservative surgery and radiation therapy. Psychosocial consequences. *Cancer* 1994;73(4):1221-8.

53. Ganz PA, Schag AC, Lee JJ, et al. Breast conservation versus mastectomy. Is there a difference in psychological adjustment or quality of life in the year after surgery? *Cancer* 1992;69(7):1729-38.

54. Morris CR, Cohen R, Schlag R, et al. Increasing trends in the use of breast-conserving surgery in California. *American journal of public health* 2000;90(2):281-4.

55. Ballard-Barbash R, Potosky AL, Harlan LC, et al. Factors associated with surgical and radiation therapy for early stage breast cancer in older women. *Journal of the National Cancer Institute* 1996;88(11):716-26.

56. Edge SB. Advances in breast surgery, 2002-2012. *Journal of the National Comprehensive Cancer Network : JNCCN* 2013;11(1):53-9.

57. Han D, Nie J, Bonner MR, et al. Clustering of place of birth for women with breast cancer: differences by tumor characteristics. *Cancer causes & control : CCC* 2012.

58. Pinheiro PS, Williams M, Miller EA, et al. Cancer survival among Latinos and the Hispanic Paradox. *Cancer causes & control : CCC* 2011;22(4):553-61.

59. Kiderlen M, Bastiaannet E, Walsh PM, et al. Surgical treatment of early stage breast cancer in elderly: an international comparison. *Breast cancer research and treatment* 2012;132(2):675-82.

60. Prehn AW, Topol B, Stewart S, et al. Differences in treatment patterns for localized breast carcinoma among Asian/Pacific islander women. *Cancer* 2002;95(11):2268-75.

61. Goel MS, Burns RB, Phillips RS, et al. Trends in breast conserving surgery among Asian Americans and Pacific Islanders, 1992-2000. *Journal of general internal medicine* 2005;20(7):604-11.

62. Lee-Lin F, Menon U, Nail L, et al. Findings from Focus Groups Indicating what Chinese American Immigrant Women Think about Breast Cancer and Breast Cancer Screening. *Journal of obstetric, gynecologic, and neonatal nursing : JOGNN / NAACOG* 2012.

63. Kim HM, Goodman M, Kim BI, et al. Frequency and determinants of missing data in clinical and prognostic variables recently added to SEER. *Journal of registry management* 2011;38(3):120-31.

TABLES

Table 1. Demographic and cancer characteristics of female breast cancer patients from 2004-2009 in SEER Registry N (%)

Patient / Tumour Characteristics	BCS (n=68,798)	Mastectomy (n=50,792)	Total(n=119,560)
Age at diagnosis (years)			
<50	14,007 (51.3)	13,302 (48.7)	27,309
50+	54,761 (59.4)	37,490 (40.6)	92,251
Race			
White	55,620 (58.4)	39,606 (41.6)	95,226
Black	6,828 (55.2)	5,553 (44.8)	12,381
Asian or Pacific Islander	6,170 (52.7)	5,548 (47.3)	11,718
Unknown/Other	150 (63.8)	85 (36.2)	235
Born in the US			
Yes	54,327 (57.9)	39,553 (42.1)	93,880
No	14,441 (56.2)	11,239 (43.8)	25,680
Stage			
I	41,621 (68.6)	19,032 (31.4)	60,653
IIA	16,935 (54.6)	14,104 (45.4)	31,039
IIB	5,295 (38.5)	8,461 (61.5)	13,756
IIIA	2,672 (27.2)	7,149 (72.8)	9,821
Unknown	2,245 (52.3)	2,046 (47.7)	4,291
Tumour size			
< 2cm	47,573 (66.2)	24,340 (33.8)	71,913
2cm or more	20,622 (46.5)	23,740 (53.5)	44,362
Unknown	573 (17.4)	2,712 (82.6)	3,285
Grade			
Well differentiated/ I	16,716 (66.9)	8,281 (33.1)	24,995
Moderately differentiated/II	27,662 (58.2)	19,910 (41.8)	47,572
Poorly differentiated/ III	20,329 (52.1)	18,673 (47.9)	39,002
Undifferentiated/ IV	699 (48.9)	730 (51.1)	1,429
Unknown	3,364 (51.3)	3,198 (48.7)	6,562
Residence			
Metro	62,903 (58.2)	45,238 (41.8)	108,141
Urban	4,432 (52.6)	3,994 (47.4)	8,426
Rural	1,430 (47.8)	1,559 (52.2)	2,989
Unknown	3 (75.0)	1 (25.0)	4
Marital status at diagnosis			
Single (never married)	8,748 (56.1)	6,845 (43.9)	15,593
Married	38,012 (57.8)	27,727 (42.2)	65,739
Separated/Divorced/Widowed	20,375 (57.8)	14,881 (42.2)	35,256
Unknown	1,633 (54.9)	1,339 (45.1)	2,972

BCS – Breast conserving surgery

Table 2. Distribution of treatment received by combined measure of place of birth and race in female breast cancer patients from 2004-2009 in SEER Registry N (%)

	BCS (n=68,798)	Mastectomy (n=50,792)	Total (n=119,560)
Place of birth and Race			
US Whites [a]	42,957 (58.3)	30,677 (41.7)	73,634
Foreign born Whites [a]	5,042 (62.5)	3,029 (37.5)	8,071
US Blacks	6,384 (55.1)	5,221 (44.9)	11,605
Foreign born Blacks	444 (57.2)	332 (42.8)	776
US Asians/Pacific Islanders	1,791 (59.3)	1,229 (40.7)	3,020
Foreign born Asians/Pacific Islanders	4,379 (50.3)	4,319 (49.7)	8,698
Unknown Race	150 (63.8)	85 (36.2)	235
			119,560
US Hispanics [b]	3,089 (56.6)	2,366 (43.4)	5,455
Foreign born Hispanics [b]	4,532 (56.2)	3,534 (43.8)	8,066
			13,521

BCS – Breast conserving surgery
a – non-Hispanic
b – Whites only

Table 3. Adjusted odds ratios for partial surgery (BCS) received by combined measure of place of birth and race in female breast cancer patients from 2004-2009 in SEER Registry with US Whites as reference N (%)

	n	Adjusted OR	95% CI	p value
Place of birth and Race				
US Whites [a]	73,634	1.00	Referent	
Foreign born Whites [a]	8,071	1.21	(1.15, 1.28)	<0.0001
US Blacks	11,605	1.06	(1.02, 1.11)	0.0090
Foreign born Blacks	776	1.21	(1.15, 1.28)	<0.0001
US Asians/Pacific Islanders	3,020	1.05	(0.97, 1.14)	0.2046
Foreign born Asians/Pacific Islanders	8,698	0.76	(0.72, 0.80)	<0.0001
US Hispanics [b]	5,455	1.05	(0.99, 1.11)	0.1322
Foreign born Hispanics [b]	8,066	1.11	(1.05, 1.17)	<0.0001

a – non-Hispanic
b – Whites only

Table 4. Adjusted odds ratios for partial surgery (BCS) received by combined measure of place of birth and race in female breast cancer patients from 2004-2009 in SEER Registry with corresponding US races/ethnicity groups as reference N (%)

	n	Adjusted OR	95% CI	p value
Place or birth and Race				
US Whites [a]	73,634	1.00	Referent	
Foreign born Whites [a]	8,071	1.21	(1.15, 1.28)	<0.0001
US Blacks	11,605	1.00	Referent	
Foreign born Blacks	776	1.10	(0.93, 1.30)	0.2873
US Asians/Pacific Islanders	3,020	1.00	Referent	
Foreign born Asians/Pacific Islanders	8,698	0.74	(0.64, 0.86)	<0.0001
US Hispanics [b]	5,455	1.00	Referent	
Foreign born Hispanics [b]	8,066	1.06	(0.98, 1.15)	0.1330

a – non-Hispanic
b – Whites only

Table 5. Adjusted odds ratios for covariates of interest comparing receipt of partial breast surgery (BCS) place of birth and race in early stage female breast cancer patients from the SEER Registry from 2004-2009

	n	Adjusted OR	95% CI	p value
Place of birth and Race				
US Whites [a]	73,634	1.00	Referent	
European Whites [a,b]	5,226	1.31	(1.23, 1.40)	<0.0001
US Blacks	11,605	1.06	(1.02, 1.11)	0.0090
West African Blacks	79	0.85	(0.52, 1.41)	0.5284
East African Blacks	90	1.39	(0.85, 2.30)	0.1925
Caribbean Blacks	383	1.31	(1.04, 1.66)	0.0225
US Asians/Pacific Islanders	3,020	1.05	(0.97, 1.14)	0.2046
Asia born Asians/Pacific Islanders [c]	8,478	0.76	(0.72, 0.80)	<0.0001
US Hispanics [d]	5,455	1.05	(0.99, 1.11)	0.1322
Latin American Hispanics [d]	6,888	1.09	(1.03, 1.15)	0.0038
US Blacks	11,605	1.00	Referent	
West African Blacks	79	0.73	(0.44, 1.20)	0.2093
East African Blacks	90	1.25	(0.76, 2.04)	0.3886
Caribbean Blacks	383	1.20	(0.95, 1.52)	0.1307
US Asians/Pacific Islanders	3,020	1.00	Referent	
Asia born Asians/Pacific Islanders [c]	8,478	0.72	(0.65, 0.79)	<0.0001
US Hispanics [d]	5,455	1.00	Referent	
Latin American Hispanics [d]	6,888	1.04	(0.96, 1.13)	0.3811

a – non-Hispanic only
b – Includes Middle Eastern and North African peoples
c – all of Asia except the Middle East, South Asia combined with Oceania
d – White Hispanics only

EMORY UNIVERSITY
Institutional Review Board

April 3, 2013

RE: Determination: No IRB Review Required
Title: *Receipt of surgical treatment in early breast cancer: Does Place of Birth matter?*

PI: Saurabh Chavan

Dear Saurabh Chavan:

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the materials you provided, we have determined that it does not require IRB review because it does not meet the definition(s) of "research" involving "human subjects" or the definition of "clinical investigation" as set forth in Emory policies and procedures and federal rules, if applicable. Specifically, in this project, you will access publically available data through the Surveillance Epidemiology and End Results (SEER) database. You will use this publically available data to asses the effect of birth locale upon surgical treatment for breast cancer. No PHI or identifiers will be collected during this process and, as such, the project does not constitute human subjects research.

This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Thank you for consulting the IRB.

Sincerely,

Aric Edwards, BA
Research Protocol Analyst
This letter has been digitally signed