Published in final edited form as:

Ann Epidemiol. 2013 April ; 23(4): 227–232. doi:10.1016/j.annepidem.2012.12.013.

Differences between Hispanic and non-Hispanic White Women with Breast Cancer for Clinical Characteristics and their Correlates

Avonne E Connor, PhD¹, Richard N Baumgartner, PhD¹, Dongyan Yang, MD¹, Martha L Slattery, PhD², Anna R Giuliano, PhD³, Betsy C. Risendal, PhD⁴, Madiha M Abdel-Maksoud, MD, PhD⁴, and Kathy B Baumgartner, PhD¹

¹University of Louisville, School of Public Health & Information Sciences, Department of Epidemiology & Population Health, Louisville, KY

²University of Utah, Department of Internal Medicine, Salt Lake City, UT

³H.Lee Moffit Cancer Center & Research Institute, Tampa, FL

⁴University of Colorado, School of Medicine, Denver, CO

Abstract

PURPOSE—Body size and ethnicity may influence breast cancer tumor characteristics at diagnosis. We compared Hispanic and non-Hispanic white cases for stage of disease, estrogen receptor status, tumor size, and lymph node status, and the associations of these with body size in the 4-Corners Breast Cancer Study (4-CBCS).

METHODS—1,527 Non-Hispanic white and 798 Hispanic primary incident breast cancer cases diagnosed between October 1999 and May 2004 were included. Odds ratios (OR) and 95% Confidence Intervals (CI) were calculated by multiple logistic regression.

RESULTS—Hispanic women were more likely to have larger (>1cm), ER- tumors, and >4 positive lymph nodes ($p < 0.003$). Lymph node status was not associated with body size. However, among non-Hispanic white women, obesity (BMI >30) and increased waist circumference (> 38.5 inches) were significantly, positively associated with ER- tumor status; ORs = 1.87, 95% CI 1.24–2.81 and 2.59, 95% CI 1.58–4.22, respectively. In contrast, among Hispanic women, obesity and waist circumference had inverse associations with ER- status (OR = 0.49, 95% CI 0.29–0.84) and (0.56, 95% CI 0.30–1.05), respectively.

CONCLUSIONS—Hispanic ethnicity may modify the association of body size and composition with ER- breast cancer. This finding could have relevance to clinical treatment and prognosis.

Keywords

Breast Neoplasms; Hispanic Americans; Obesity

© 2013 Elsevier Inc. All rights reserved.

Corresponding Author: Avonne Connor, MPH, Ph.D., University of Louisville, School of Public Health and Information Sciences, Department of Epidemiology and Population Health, 485 E. Gray St. Louisville, KY 40202, aeconn02@louisville.edu, Telephone: 502.852.6441, Fax: 502.852.3294.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Breast cancer risk in women is associated with body size and composition, however, this finding is dependent upon menopausal status (1, 2). Breast cancer prognosis also may be associated with increased adiposity, which has been linked with poor survival and increased risk for breast cancer recurrence (3–8). Some studies report that obesity is strongly associated with breast cancer prognostic markers, including positive estrogen receptor status (9, 10), increased tumor size (11–13), advanced stage of disease (14, 15) and positive nodal status (12, 16). Furthermore, breast cancer treatment is based on the evaluation of these prognostic markers and some studies suggest that treatment is further associated with post-diagnostic changes in weight and body composition that impact survival, and that this association may depend upon pre-diagnosis body weight (17, 18). Thus, establishing the associations of body size with these markers at the time of diagnosis is important because it may illuminate the pathways by which obesity influences breast cancer prognosis.

We tested the hypothesis that the following body size measures, body mass index (BMI), waist circumference, and waist-hip-ratio (WHR) are associated with baseline prognostic markers using data for breast cancer cases from the 4-Corners Breast Cancer Study (4-CBCS). The purpose of the 4-CBCS was to evaluate the associations between various risk factors for breast cancer in Hispanic and non-Hispanic white (NHW) women residing in the Southwestern United States.

METHODS

Study Population

The study participants in the 4-CBCS were women between the ages of 25 and 79 living in Arizona, Colorado, New Mexico, and Utah. The methods for subject selection, participation rates, data collection, and quality control procedures, are described in previous publications (19–24). Cases were ascertained through the National Cancer Institute as Surveillance Epidemiology and End Results registries in New Mexico and Utah and through the Centers for Disease Control and Prevention National Program of Cancer Registries for Colorado or Arizona. All primary incident cases diagnosed with *in situ* or invasive breast cancer between October 1999 and May 2004 with histological confirmation were eligible. Registries provided information on estrogen and progesterone receptor tumor status for approximately 70% of cases (22). All study participants signed Informed Consent Documents prior to study enrollment. The study was approved by the Institutional Review Board for Human Subjects at each institution.

Data Description

In-person interviews were administered to participants by trained interviewers using a computerized questionnaire to collect data on demographic characteristics and breast cancer risk factors prior to the referent year (date of diagnosis). Ethnicity was based on self-report. Risk factors included reproductive history, medical and medication history, height, weight history, diet, physical activity, education, smoking history, and alcohol intake. All participants had a blood draw, and anthropometric measurements were obtained.

Body mass index for the referent year was based upon the self-reported weight and the measured height collected by the interviewer at time of interview, and expressed as weight (kg)/height (m²). Levels of body size were defined using international BMI cut-points of <25 as normal weight, 25–29.9 as overweight, and 30+ as obese. Self-reported BMI at age 15, age 30, and at age 50 were also considered in analyses. BMI levels at ages 15 and 30 were defined as the following quartiles: BMI at age 15, <17.9, 17.9–19.5, 19.5–21.2, and >21.2; BMI at age 30, <20.5, 20.5–22.1, 22.1–24.4, and >24.4. BMI at age 50 was analyzed

using the international cut-points. Changes in BMI between ages and the referent year were calculated and analyzed as continuous variables. Waist and hip circumferences were measured in duplicate at the time of interview and to the nearest 0.5 inches. For analyses, waist circumferences were categorized into quartiles, based upon the normal distribution of the sample as follows: <30.6 (referent), 30.6–34.1, 34.1–38.5, and >38.5 inches. Waist-hip ratios were calculated and were categorized as >0.8, 0.8–0.9, and >0.9.

An algorithm based upon age <57 years at referent date and responses to eight questions regarding menstrual status, hormone replacement use, and surgical or medical menopause was used to determine menopausal status, as previously described (22). Postmenopausal women were further stratified based on their recent exposure to hormones, which was defined as HRT use within the past 2 years or pre- or peri-menopausal status during the two years prior to the referent date (22). Women who were peri-menopausal at the time of interview were grouped with pre-menopausal women in analyses. Parity, or number of live births, was categorized as: nulliparous; 1–2 live births; 3–4 live births; and 5 or more live births. Family history of breast cancer was determined by report of first degree relatives. Education was categorized as: less than high school graduate; high school graduate or GED; some college; and bachelors or more. Cigarette smoking status was categorized as current, former, or never smoker. Recent hormone exposure was based on recent hormone exposure within 2 years of the referent year. Age at menarche was categorized as: < 12 years; 12 years; 13 years; and 14 years of age or more. Self-reported history of diabetes was based on the following responses: “yes”; “no”; or “borderline”. Self-reported history of mammography screening was recorded as “yes” or “no”.

The clinical and tumor characteristics, such as stage, lymph node status, tumor size, and estrogen- receptor status were obtained from the cancer registries (25). Cancer stage groupings were coded as in situ (stage 0) versus invasive disease. Estrogen receptor status and lymph node status were both coded as positive versus negative. Tumor size was coded as less than 1 cm or greater than or equal to 1 cm.

Data Analysis

A total of 2,325 breast cancer cases were included for analyses, 1,527 NHW and 798 Hispanic/AIAN. Descriptive statistics were calculated using chi-squared tests for categorical variables and t-tests for continuous variables. Multiple logistic regression models were used for this case-case comparison to calculate the association of body composition and obesity measures with the breast cancer prognostic markers. Covariates included in analysis were age, ethnicity, menopausal status, education, family history, age at menarche, parity, smoking status, time to interview, study center, recent hormone exposure, history of diabetes, and history of mammography screening. Models were then stratified by ethnicity to test for effect modification and divergent patterns within the data, and p-values for interaction tests were calculated by including multiplicative interaction terms in the multivariable logistic regression models if there was evidence of divergent patterns. The statistical significance of the interactions was evaluated using the difference in maximum likelihood estimates. All p-values are two-sided. SAS statistical software (version 9.2, SAS Institute, Cary, NC) was used to conduct all analyses.

RESULTS

The mean age of women in the present analyses was 54.2 (standard deviation (SD) = 11.2) years. Hispanic women were somewhat younger than NHW women, with a mean age of 52.2 (SD= 11.2) years for Hispanic women and 55.3 (SD= 11.1) years for NHW women. NHW women, in comparison to Hispanic women reported higher education levels, lower

parity, more family history of breast cancer, and more recent exposure to exogenous hormones (table 1).

Hispanic women had larger tumors ($p < 0.0001$), were more likely to have positive lymph node involvement ($p = 0.0034$), and estrogen-receptor-negative tumors ($p = 0.0020$) (table 2). Hispanic women had significantly higher means for all body composition measures than NHW women (table 3). The higher waist circumferences in Hispanic women suggest more centralized adiposity than NHW women (Hispanic mean=36.0, SD=5.5 vs. NHW mean=34.2, SD=5.7) (table 3). The ethnic groups were closely similar for BMI at age 15, with mean BMI = 19.8, (SD=3.2) for Hispanic women, vs. mean BMI=19.7, (SD=2.9) for NHW women (table 3).

Odds ratios for body composition measures and prognostic characteristics are shown in Table 4. All odds ratios are stratified by ethnicity and have been adjusted for age, menopausal status, education, center, and time to interview. There were divergent results between the ethnic groups for the association of current waist circumference with estrogen receptor negative (ER-) tumor status. Among NHW women, increased waist circumference (greater than 38.5 inches vs. less than 30.6 inches) was associated significantly with an increased risk for ER- tumor status, (odds ratio (OR) = 2.59, 95% Confidence Interval (CI) 1.58–4.22) (table 4). In contrast, there was an inverse association with increased centralized adiposity and ER- status, among Hispanic women; however, the point estimate was not statistically significant (OR = 0.56, 95% CI 0.30–1.05) (table 4). We also examined waist circumference using the cut-points for the clinical identification of metabolic syndrome among women (26) (0–35 versus > 35 inches) and found a significant positive association for ER- breast cancer among NHW women with a waist circumference greater than 35 inches (OR=1.74, 95% CI 1.25–2.42) and a non-significant association among Hispanic cases (OR=0.98, 95% CI 0.65–1.47). The corresponding interaction between ethnicity and waist circumference on ER status was highly significant ($p_{\text{interaction}} = 0.0001$). Waist circumference was also associated with increased tumor size among NHW women, however the largest effect found was among cases who had waist circumferences between 34.1–38.5 inches compared to less than 30.6 inches (OR=1.71, 95% CI 1.17–2.49) (table 4).

Increased body size, measured as BMI at referent year, was associated with ER- tumor status and with a divergent pattern between the ethnic groups. Among NHW women, there was a statistically significant, positive association for risk of ER- tumor status in obese compared to normal weight (BMI 30 vs. <25 kg/m²), (OR = 1.87, 95% CI 1.24–2.81); conversely, an inverse association was found for Hispanic women (OR = 0.49, 95% CI 0.29–0.84) (table 4). The formal test of interaction between ethnicity and BMI was statistically significant ($p_{\text{interaction}} = 0.0003$). Although, WHR had a statistically significant positive association with risk of ER-tumors in NHW women: (WHR 0.8–0.9; OR=1.99, 95% CI 1.40–2.82 and WHR >0.9; OR=2.09, 95% CI 1.20–3.66) there was no association in Hispanic women, so a similar, divergent pattern between the ethnic groups was not found (table 4). Changes in BMI between ages and referent year were also modeled. There was evidence for effect modification of the association between change in BMI between age 15 and the referent year (Hispanics OR=0.96, 95% CI 0.93–1.00, vs. NHW OR=1.04, 95% CI 1.01–1.07; $p_{\text{interaction}} = 0.001$) (table 4). These associations for ER- tumor status were similar when stratified by menopausal status (data not shown).

Table 4 also shows the associations between measures of body size and breast cancer stage by ethnicity. Multiple logistic regression models were constructed comparing *in-situ* versus invasive cancer. Invasive stage was significantly associated with the highest tertiles of BMI at referent year compared to normal BMI in NHW women (OR= 1.64, 95% CI 1.14–2.36); however there was no association in Hispanic women in the same risk category (OR=1.19,

95% CI 0.74–1.91) (table 4). Invasive stage was also positively associated with changes in BMI between ages 15 to 30 years, age 15 to referent year, and for increased waist circumference, and WHR (table 4). The addition of family history, age at menarche, parity, history of diabetes, history of mammography screening, and smoking status did not alter the divergent pattern or greatly change the effect estimates (data not shown).

DISCUSSION

In this population based case-case analysis, various markers for adiposity were hypothesized to be associated with clinical, breast cancer prognostic markers, including ER status, breast cancer stage, tumor size, and lymph node status. Our findings suggest that obesity, as measured by BMI, waist circumference, and WHR, is associated with invasive stage and ER- tumor status in NHW women with breast cancer. Moreover, the associations with ER-tumor status by BMI are modified by Hispanic ethnicity.

In a previous 4-CBCS publication, Slattery et al. (22) reported that the relationship between obesity and breast cancer risk differs between Hispanic and NHW women. Their case-control analysis evaluated the association between ER status with BMI at referent year and at age 15, height, weight gain between age 15 and referent year, and WHR. BMI at referent year was associated with a reduction in risk for ER- tumors among obese Hispanics (OR= 0.45 95% CI 0.26–0.76), while a non-significant positive association was observed among obese NHW women (OR= 1.40, 95% CI 0.95–2.07) (22). An increased risk for ER- breast cancer was also found among NHW women with WHR > 0.9 compared to <0.8 (OR= 2.04, 95% CI 1.20–3.50), while a non-significant inverse association was found among Hispanics (OR= 0.79, 95% CI 0.39–1.57) (22). A recent 4-CBCS report analyzed the relationships between behavioral risk factors and tumor characteristics (27), including the association between BMI and ER status. Among women less than 50 years, ethnicity modified the association between obesity and ER status; there was an inverse association among obese Hispanic cases for ER- tumors (OR= 0.29, 95% CI 0.13–0.66) but a significant positive association among NHW cases (OR= 2.47, 95% CI 1.08–5.67) (27). For this research, our analyses not only investigated the associations between BMI and ER status, but also examined the effects of waist circumference, BMI at ages 30 and 50, and changes in BMI between selected ages. We also evaluated the associations between these measures of adiposity and other clinical markers for breast cancer. Based on our findings, waist circumference is an important marker of central adiposity among NHW breast cancer cases that should be considered in the obesity and ER status relationship.

Although we found a significant association for high WHR and ER- breast cancer among NHW women, ethnic-specific results were more divergent for waist circumference. Waist circumference has been suggested to be a better predictor of central, abdominal or visceral obesity than WHR, BMI, or percent body fat (28). Increased waist circumference is positively correlated with circulating levels of inflammatory markers, Type 2 diabetes, and insulin resistance (29). In the general population, Hispanic women have a higher prevalence of obesity and Type 2 diabetes (30) and for our study, Hispanics had higher levels for all BMI and waist circumference at all ages when compared to NHW women. Nevertheless, the underlying mechanisms for these divergent associations are unknown.

The relationship between obesity and ER tumor status and the potential mechanisms contributing to these relationships and subsequent phenotypes have been explored in epidemiological literature. In a study of Hispanic and NHW breast cancer cases from New Mexico, none of the relevant adiposity measures (BMI, waist circumference, WHR) were found to be associated with risk of ER- tumors (12). Paradoxically, other studies have found that obesity, measured by BMI, is linked to postmenopausal ER+ breast cancer and not ER-

breast cancer (31–34). The relationship between obesity and ER+ breast cancer is thought to reflect increased estrogen synthesis in adipose stores and greater bioavailability (35). With the case of the association between obesity and ER- tumors, it has been speculated that insulin and the adipocytokine leptin may play a role in this relationship (36). Leptin, vascular endothelial growth factor, and heparin-binding epidermal growth factor-like growth factor may stimulate ER- tumors. Moreover, there is the assumption that the action of estrogen is not influenced by mechanisms related to hormonal, paracrine, and autocrine factors (37). It is plausible that leptin and insulin act synergistically in the development of this metastatic tumor phenotype (36), as plasma leptin and insulin levels have been reported to be positively correlated with ER- tumors (38). Clearly, more research is warranted to obtain a better understanding of the possible mechanisms behind the obesity and ER- breast cancer association.

There are possible limitations and strengths to the present study. Response rates were consistently lower among Hispanic cases for all study sites and it is possible that the non-respondents' characteristics could be different from those who participated in the study, which could create selection bias. Response rates were also fairly low among NHW cases. However, our study is one of few that included a substantial number of Hispanic cases from a multi-site population-based study, unlike previous studies with similar research aims. There is the possibility for recall bias in relation to self-reported body weight and height at the various time points selected; nonetheless, the accuracy of recalled body weight and height is good. In a previous report of the validity of self-reported past body weight in U.S. men and women, recalled past weight was strongly correlated with previously measured weight, with correlations reported as 0.74 for women, and 41% of women estimating their past weight within 5 pounds (39).

In spite of these limitations, our data suggest that obesity measured by BMI and waist circumference is significantly and positively associated with ER- breast cancer among NHW, but inversely associated in Hispanic women. Our results also suggest a possible association between BMI, waist circumference, WHR and invasive stage of disease. Our findings for ER- breast cancer build upon those previously reported by other researchers from the 4-CBCS (22, 27) as well as a previous report from the New Mexico site of the Health, Eating, Activity and Lifestyle study which suggests that Hispanic ethnicity may modify the hormone-mediated effects of obesity on breast cancer (12). It could be speculated that the effect modification presented in our results could be due to genetic differences between Hispanic and NHW women, and that certain genetic variants could alter obesity-related risk factors for ER- tumors. These hypotheses should be investigated further, and should be explored with other tumor phenotypes, including triple negative breast cancer. A previous 4-CBCS case-case analysis which included a subset of cases from Colorado, reported that Hispanics were almost three times more likely to have HER2+ breast tumors when compared to NHW cases; however, this study did not test the hypothesis that obesity markers are major contributing factors to the association between ethnicity and tumor phenotypes(40). In conclusion, our findings suggest that there is more to the estrogen, obesity and ER status relationship, as leptin and insulin might play significant roles in the obesity and ER-breast cancer association. Furthermore, these findings could have relevance to clinical treatment and prognosis.

Acknowledgments

This study was funded by grants: CA 078682, CA 078762, CA 078552, and CA 078802. This research also was supported by the Utah Cancer Registry, which is funded by Contract #N01-PC-67000 from the National Cancer Institute, with additional support from the State of Utah Department of Health, the New Mexico Tumor Registry, and the Arizona and Colorado cancer registries, funded by the Centers for Disease Control and Prevention National Program of Cancer Registries and additional state support. The contents of this manuscript are solely the

responsibility of the authors and do not necessarily represent the official view of the National Cancer Institute. We would also like to acknowledge the contributions of Tim Byers, Sandra Edwards, and Roger Edwards.

List of Abbreviations and Acronyms

4-CBCS	4-Corner's Breast Cancer Study
NHW	Non-Hispanic White
BMI	Body mass index
WHR	Waist-hip-ratio
ER	Estrogen receptor
SD	Standard deviation
OR	Odds Ratio
CI	Confidence Interval

References

1. Morimoto LM, White E, Chen Z, Chlebowski RT, Hays J, Kuller L, et al. Obesity, body size, and risk of postmenopausal breast cancer: the Women's Health Initiative (United States). *Cancer causes & control* : CCC. 2002; 13(8):741–51. Epub 2002/11/08.
2. Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter DJ, Manson JE, et al. Dual effects of weight and weight gain on breast cancer risk. *JAMA : the journal of the American Medical Association*. 1997; 278(17):1407–11. Epub 1997/11/14. [PubMed: 9355998]
3. Chen X, Lu W, Zheng W, Gu K, Chen Z, Zheng Y, et al. Obesity and weight change in relation to breast cancer survival. *Breast Cancer Res Treat*. 2010; 122(3):823–33. Epub 2010/01/09. [PubMed: 20058068]
4. Conroy SM, Maskarinec G, Wilkens LR, White KK, Henderson BE, Kolonel LN. Obesity and breast cancer survival in ethnically diverse postmenopausal women: the Multiethnic Cohort Study. *Breast Cancer Res Treat*. 2011; 129(2):565–74. Epub 2011/04/19. [PubMed: 21499688]
5. Carmichael AR. Obesity and prognosis of breast cancer. *Obes Rev*. 2006; 7(4):333–40. Epub 2006/10/14. [PubMed: 17038127]
6. Carmichael AR, Bendall S, Lockerbie L, Prescott RJ, Bates T. Does obesity compromise survival in women with breast cancer? *Breast*. 2004; 13(2):93–6. Epub 2004/03/17. [PubMed: 15019687]
7. Dal Maso L, Zucchetto A, Talamini R, Serraino D, Stocco CF, Vercelli M, et al. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. *Int J Cancer*. 2008; 123(9):2188–94. Epub 2008/08/20. [PubMed: 18711698]
8. Petrelli JM, Calle EE, Rodriguez C, Thun MJ. Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of US women. *Cancer Causes Control*. 2002; 13(4):325–32. Epub 2002/06/21. [PubMed: 12074502]
9. Maehle BO, Tretli S. Pre-morbid body-mass-index in breast cancer: reversed effect on survival in hormone receptor negative patients. *Breast Cancer Res Treat*. 1996; 41(2):123–30. Epub 1996/01/01. [PubMed: 8944330]
10. Canchola AJ, Anton-Culver H, Bernstein L, Clarke CA, Henderson K, Ma H, et al. Body size and the risk of postmenopausal breast cancer subtypes in the California Teachers Study cohort. *Cancer causes & control* : CCC. 2012 Epub 2012/01/31.
11. Maehle BO, Tretli S, Skjaerven R, Thorsen T. Premorbid body weight and its relations to primary tumour diameter in breast cancer patients; its dependence on estrogen and progesterone receptor status. *Breast Cancer Res Treat*. 2001; 68(2):159–69. Epub 2001/11/02. [PubMed: 11688519]
12. Baumgartner KB, Hunt WC, Baumgartner RN, Crumley DD, Gilliland FD, McTiernan A, et al. Association of body composition and weight history with breast cancer prognostic markers: divergent pattern for Hispanic and non-Hispanic White women. *Am J Epidemiol*. 2004; 160(11):1087–97. Epub 2004/11/25. [PubMed: 15561988]

13. Daling JR, Malone KE, Doody DR, Johnson LG, Gralow JR, Porter PL. Relation of body mass index to tumor markers and survival among young women with invasive ductal breast carcinoma. *Cancer*. 2001; 92(4):720–9. Epub 2001/09/11. [PubMed: 11550140]
14. Ewertz M, Jensen MB, Gunnarsdottir KA, Hojris I, Jakobsen EH, Nielsen D, et al. Effect of obesity on prognosis after early-stage breast cancer. *J Clin Oncol*. 2011; 29(1):25–31. Epub 2010/12/01. [PubMed: 21115856]
15. Cui Y, Whiteman MK, Flaws JA, Langenberg P, Tkaczuk KH, Bush TL. Body mass and stage of breast cancer at diagnosis. *Int J Cancer*. 2002; 98(2):279–83. Epub 2002/02/22. [PubMed: 11857420]
16. Daniell HW. Increased lymph node metastases at mastectomy for breast cancer associated with host obesity, cigarette smoking, age, and large tumor size. *Cancer*. 1988; 62(2):429–35. Epub 1988/07/15. [PubMed: 3383142]
17. Thivat E, Therondel S, Lapirot O, Abrial C, Gimbergues P, Gadea E, et al. Weight change during chemotherapy changes the prognosis in non metastatic breast cancer for the worse. *BMC Cancer*. 2010; 10:648. Epub 2010/11/27. [PubMed: 21108799]
18. Caan BJ, Kwan ML, Hartzell G, Castillo A, Slattery ML, Sternfeld B, et al. Pre-diagnosis body mass index, post-diagnosis weight change, and prognosis among women with early stage breast cancer. *Cancer Causes Control*. 2008; 19(10):1319–28. Epub 2008/08/30. [PubMed: 18752034]
19. Murtaugh MA, Herrick JS, Sweeney C, Baumgartner KB, Guiliano AR, Byers T, et al. Diet composition and risk of overweight and obesity in women living in the southwestern United States. *J Am Diet Assoc*. 2007; 107(8):1311–21. Epub 2007/07/31. [PubMed: 17659896]
20. Slattery ML, Baumgartner KB, Byers T, Guiliano A, Sweeney C, Herrick J, et al. Genetic, anthropometric, and lifestyle factors associated with IGF-1 and IGFBP-3 levels in Hispanic and non-Hispanic white women. *Cancer causes & control : CCC*. 2005; 16(10):1147–57. Epub 2005/10/11.
21. Slattery ML, Edwards S, Murtaugh MA, Sweeney C, Herrick J, Byers T, et al. Physical activity and breast cancer risk among women in the southwestern United States. *Ann Epidemiol*. 2007; 17(5):342–53. Epub 2007/04/28. [PubMed: 17462544]
22. Slattery ML, Sweeney C, Edwards S, Herrick J, Baumgartner K, Wolff R, et al. Body size, weight change, fat distribution and breast cancer risk in Hispanic and non-Hispanic white women. *Breast Cancer Res Treat*. 2007; 102(1):85–101. Epub 2006/11/03. [PubMed: 17080310]
23. Slattery ML, Sweeney C, Herrick J, Wolff R, Baumgartner K, Giuliano A, et al. ESR1, AR, body size, and breast cancer risk in Hispanic and non-Hispanic white women living in the Southwestern United States. *Breast Cancer Res Treat*. 2007; 105(3):327–35. Epub 2006/12/26. [PubMed: 17187234]
24. Sweeney C, Edwards SL, Baumgartner KB, Herrick JS, Palmer LE, Murtaugh MA, et al. Recruiting Hispanic women for a population-based study: validity of surname search and characteristics of nonparticipants. *Am J Epidemiol*. 2007; 166(10):1210–9. Epub 2007/09/11. [PubMed: 17827445]
25. Division of Cancer Control and Population Sciences. The SEER program code manual. 3. Bethesda, MD: National Cancer Institute, U.S. Department of Health and Human Services; 1998.
26. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA : the journal of the American Medical Association*. 2001; 285(19):2486–97. Epub 2001/05/23. [PubMed: 11368702]
27. Abdel-Maksoud MF, Risendal BC, Slattery ML, Giuliano AR, Baumgartner KB, Byers TE. Behavioral risk factors and their relationship to tumor characteristics in Hispanic and non-Hispanic white long-term breast cancer survivors. *Breast Cancer Res Treat*. 2011 Epub 2011/08/09.
28. Rankinen T, Kim SY, Perusse L, Despres JP, Bouchard C. The prediction of abdominal visceral fat level from body composition and anthropometry: ROC analysis. *Int J Obes Relat Metab Disord*. 1999; 23(8):801–9. Epub 1999/09/22. [PubMed: 10490780]
29. Ackermann D, Jones J, Barona J, Calle MC, Kim JE, LaPia B, et al. Waist circumference is positively correlated with markers of inflammation and negatively with adiponectin in women

- with metabolic syndrome. *Nutr Res.* 2011; 31(3):197–204. Epub 2011/04/13. [PubMed: 21481713]
30. Zhang Q, Wang Y, Huang ES. Changes in racial/ethnic disparities in the prevalence of Type 2 diabetes by obesity level among US adults. *Ethn Health.* 2009; 14(5):439–57. Epub 2009/04/11. [PubMed: 19360513]
 31. Vrieling A, Buck K, Kaaks R, Chang-Claude J. Adult weight gain in relation to breast cancer risk by estrogen and progesterone receptor status: a meta-analysis. *Breast Cancer Res Treat.* 2010; 123(3):641–9. Epub 2010/08/17. [PubMed: 20711809]
 32. Yang XR, Chang-Claude J, Goode EL, Couch FJ, Nevanlinna H, Milne RL, et al. Associations of breast cancer risk factors with tumor subtypes: a pooled analysis from the Breast Cancer Association Consortium studies. *J Natl Cancer Inst.* 2011; 103(3):250–63. Epub 2010/12/31. [PubMed: 21191117]
 33. Suzuki R, Orsini N, Saji S, Key TJ, Wolk A. Body weight and incidence of breast cancer defined by estrogen and progesterone receptor status--a meta-analysis. *Int J Cancer.* 2009; 124(3):698–712. Epub 2008/11/07. [PubMed: 18988226]
 34. Setiawan VW, Monroe KR, Wilkens LR, Kolonel LN, Pike MC, Henderson BE. Breast cancer risk factors defined by estrogen and progesterone receptor status: the multiethnic cohort study. *Am J Epidemiol.* 2009; 169(10):1251–9. Epub 2009/03/26. [PubMed: 19318616]
 35. Althuis MD, Fergenbaum JH, Garcia-Closas M, Brinton LA, Madigan MP, Sherman ME. Etiology of hormone receptor-defined breast cancer: a systematic review of the literature. *Cancer Epidemiol Biomarkers Prev.* 2004; 13(10):1558–68. Epub 2004/10/07. [PubMed: 15466970]
 36. Stephenson GD, Rose DP. Breast cancer and obesity: an update. *Nutr Cancer.* 2003; 45(1):1–16. Epub 2003/06/07. [PubMed: 12791499]
 37. Vona-Davis L, Rose DP. Adipokines as endocrine, paracrine, and autocrine factors in breast cancer risk and progression. *Endocr Relat Cancer.* 2007; 14(2):189–206. Epub 2007/07/20. [PubMed: 17639037]
 38. Goodwin PJ, Ennis M, Fantus IG, Pritchard KI, Trudeau ME, Koo J, et al. Is leptin a mediator of adverse prognostic effects of obesity in breast cancer? *J Clin Oncol.* 2005; 23(25):6037–42. Epub 2005/09/02. [PubMed: 16135472]
 39. Perry GS, Byers TE, Mokdad AH, Serdula MK, Williamson DF. The validity of self-reports of past body weights by U.S. adults. *Epidemiology.* 1995; 6(1):61–6. Epub 1995/01/01. [PubMed: 7888448]
 40. Hines LM, Risendal B, Byers T, Mengshol S, Lowery J, Singh M. Ethnic disparities in breast tumor phenotypic subtypes in Hispanic and non-Hispanic white women. *J Womens Health (Larchmt).* 2011; 20(10):1543–50. Epub 2011/07/05. [PubMed: 21721934]

TABLE 1

Baseline data on selected study population characteristics, 4-Corners Breast Cancer Study (1999–2004)

Characteristics	Hispanic (n=798)		Non-Hispanic White (n=1527)		$\chi^2 p$ value
	No.	%	No.	%	
Age at Diagnosis					
Under 29	8	1.00	9	0.59	
30–39 years	85	10.65	90	5.9	
40–49 years	266	33.34	433	28.36	
50–59 years	228	28.57	453	29.67	<0.0001
60–69 years	148	18.54	356	23.32	
70–79 years	63	7.89	186	12.18	
Education					
< High School	245	30.70	64	4.19	
High school	221	27.69	308	20.17	
Some college	218	27.32	562	36.80	<0.0001
Bachelors or more	114	14.29	593	38.83	
Age at Menarche					
Less than 12	181	22.68	314	20.56	
12	207	25.94	407	26.65	
13	178	22.31	431	28.23	0.0064
14 or more	232	29.07	375	24.56	
Menopause Status					
Pre/Peri-menopausal	333	41.73	538	35.23	0.0021
Postmenopausal	465	58.27	989	64.77	
Number of live births					
None	77	9.65	260	17.03	
1–2	327	40.98	696	45.58	
3–4	283	35.46	478	31.30	<0.0001
5 or more	111	13.91	93	6.09	
Family History					
Yes	127	15.91	345	22.59	0.0005

Characteristics	Hispanic (n=798)		Non-Hispanic White (n=1527)		χ^2 p value
	No.	%	No.	%	
No	654	81.95	1160	75.97	
Unknown	17	2.13	22	1.44	
Recent Hormone Exposure					
Yes	611	76.57	1244	81.47	0.0052
No	187	23.43	283	18.53	
History of Type 2 Diabetes					
Yes	121	15.2	109	7.1	
Borderline	16	2.0	25	1.6	<0.0001
No	661	82.8	1392	91.2	
Smoking Status					
Current	96	12.03	204	13.36	
Former	172	21.55	482	31.57	<0.0001
Never	530	66.42	842	55.08	
Time to interview (months)	21.54	11.25	18.17	9.32	<0.001

TABLE 2
Baseline data on prognostic factors, 4-Corners Breast Cancer Study (1999–2004)

Prognostic Factor	Hispanic (n=798)		Non-Hispanic White (n=1527)		χ^2 p value
	No.	%	No.	%	
Stage					
<i>In-situ</i>	129	17.4	259	16.4	0.0594
Localized	361	46.0	806	54.0	
Regional	264	33.6	371	24.9	
Distant	7	0.9	17	1.1	
Unstaged	24	3.1	40	2.7	
Tumor Size (cm)					
<1	117	14.66	325	21.28	<0.0001
1	548	68.67	934	61.17	
Unknown	133	16.67	268	17.55	
	Hispanic (n= 662)		Non-Hispanic White (n= 1246)		
	No.	%	No.	%	
Estrogen receptor status *					0.0020
Positive	449	67.82	915	73.43	
Negative	138	20.85	191	15.33	
Unknown	75	11.33	140	11.24	
Lymph node status *					
1–3 nodes positive	161	24.32	222	17.82	
4 nodes positive	74	11.18	95	7.62	0.0034
All nodes examined negative	342	51.67	760	61.0	
Not examined	42	6.34	83	6.66	
Unknown	43	6.50	86	6.90	

* Based on invasive breast cancer cases only.

TABLE 3

Body composition data for all breast cancer cases, 4-Corners Breast Cancer Study (1999–2004)

Body composition	Hispanic (n=798)	Non-Hispanic White (n=1527)	<i>t</i> -test <i>p</i> value
	Mean (SD)	Mean (SD)	
Body mass index (kg/m ²)			
Referent Yr.	28.1 (5.8)	26.8 (6.1)	<0.0001
At age 15	19.8 (3.2)	19.7 (2.9)	<0.0001
At age 30	23.8 (4.1)	22.5 (3.9)	<0.0001
At age 50	27.2 (5.1)	25.9 (5.6)	<0.0001
Mean changes in Body mass index (kg/m ²)			
15 to 30 years	4.1 (3.8)	3.0 (3.4)	<0.0001
15 to 50 years	7.2 (5.3)	6.1 (4.9)	0.002
15 to referent yr.	8.2 (5.7)	7.3 (5.7)	0.002
30 to 50 years	3.6 (4.1)	3.4 (4.1)	0.430
30 to referent yr.	4.3 (3.9)	4.4 (4.1)	0.652
50 to referent yr.	1.4 (3.9)	1.6 (3.5)	0.298
Waist circumference (in) *	36.0 (5.5)	34.2 (5.7)	<0.0001
Waist-Hip Ratio *	0.84 (0.07)	0.80 (0.07)	<0.0001

* Anthropometrics that were measured at time of interview.

(SD) standard deviation.

TABLE 4
Baseline data on association of body composition with prognostic markers, stratified by ethnicity, 4-Corners Breast Cancer Study

	Stage <i>In-situ</i> vs. Invasive		ER Status [*] ER+ vs. ER-		Lymph Node Status [*] Negative vs. Positive		Tumor Size <1.0 cm vs. 1.0 cm	
	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White
Body mass index, (kg/m ²) Referent								
<25.00	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25.00–30.00	1.08 (0.68–1.70)	1.33 (0.97–1.84)	1.18 (0.74–1.87)	1.86 (1.26–2.74)	0.84 (0.55–1.29)	1.11 (0.81–1.52)	1.07 (0.65–1.76)	1.25 (0.92–1.70)
30.00	1.19 (0.74–1.91)	1.64 (1.14–2.36)	0.49 (0.29–0.84)	1.87 (1.24–2.81)	1.02 (0.67–1.57)	1.06 (0.75–1.51)	1.08 (0.65–1.80)	1.09 (0.79–1.51)
p trend	0.33	0.002	0.01	0.002	0.93	0.99	0.82	0.24
No.	790	1507	585	1103	577	1077	662	1256
Body mass index, (kg/m ²) age 15								
<17.90	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
17.90–19.50	1.40 (0.80–2.44)	1.43 (0.98–2.08)	0.96 (0.54–1.69)	1.12 (0.72–1.75)	0.64 (0.38–1.08)	1.23 (0.84–1.79)	0.68 (0.38–1.22)	1.02 (0.70–1.47)
19.50–21.20	1.30 (0.76–2.21)	1.22 (0.85–1.76)	0.77 (0.44–1.36)	0.92 (0.58–1.46)	0.84 (0.51–1.40)	1.09 (0.74–1.60)	1.23 (0.66–2.31)	1.03 (0.71–1.49)
21.2	1.47 (0.85–2.51)	1.49 (1.01–2.19)	0.87 (0.50–1.52)	1.18 (0.75–1.85)	1.11 (0.67–1.83)	0.93 (0.65–1.43)	0.95 (0.53–1.71)	1.11 (0.76–1.60)
p trend	0.20	0.11	0.63	0.76	0.48	0.90	0.67	0.68
No.	754	1456	559	1060	552	1034	633	1211
Body mass index, (kg/m ²) age 30								
<20.49	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
20.49–22.09	1.94 (1.04–3.63)	1.27 (0.89–1.81)	1.60 (0.83–3.08)	0.99 (0.62–1.56)	1.07 (0.60–1.93)	1.21 (0.84–1.74)	1.75 (0.90–3.40)	1.08 (0.76–1.52)
22.09–24.40	1.55 (0.88–2.75)	1.15 (0.81–1.63)	1.17 (0.61–2.24)	1.20 (0.77–1.87)	1.27 (0.72–2.23)	1.14 (0.78–1.65)	1.48 (0.80–2.72)	1.42 (0.99–2.03)
>24.40	1.48 (0.88–2.52)	2.05 (1.33–3.14)	0.88 (0.47–1.67)	1.20 (0.76–1.91)	1.21 (0.70–2.07)	0.93 (0.62–1.38)	1.56 (0.87–2.78)	1.22 (0.85–1.77)
p trend	0.20	0.001	0.08	0.03	0.85	0.50	0.98	0.44
No.	758	1478	558	1077	554	1056	258	418
Body mass index (kg/m ²), age 50								
<25.00	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25.00–30.00	1.41 (0.78–2.56)	1.12 (0.75–1.68)	1.08 (0.50–2.34)	1.27 (0.74–2.16)	0.78 (0.42–1.45)	1.00 (0.67–1.51)	0.97 (0.51–1.82)	0.88 (0.61–1.28)
30.00	1.63 (0.79–3.34)	1.30 (0.78–2.17)	0.89 (0.36–2.19)	1.50 (0.82–2.75)	0.78 (0.39–1.59)	0.72 (0.43–1.21)	0.83 (0.40–1.72)	0.87 (0.56–1.35)

	Stage <i>In-situ</i> vs. Invasive		ER Status* ER+ vs. ER-		Lymph Node Status* Negative vs. Positive		Tumor Size <1.0 cm vs. 1.0 cm	
	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White
p trend	0.04	0.40	0.42	0.11	0.63	0.82	0.50	0.64
No.	383	900	269	651	273	656	324	764
Changes in body mass index (BMI) (kg/m ²) by age								
15 to 30 yrs.	1.01 (0.96–1.07)	1.06 (1.02–1.11)	0.96 (0.91–1.02)	1.05 (1.00–1.10)	0.99 (0.94–1.04)	0.98 (0.94–1.03)	0.99 (0.93–1.04)	1.04 (1.00–1.09)
P trend	0.61	0.001	0.17	0.04	0.60	0.46	0.60	0.06
No.	738	1431	544	1037	539	1015	618	1190
15 to 50 yrs.	1.02 (0.96–1.07)	1.01 (0.97–1.05)	0.95 (0.88–1.03)	1.03 (0.99–1.08)	0.97 (0.92–1.02)	1.00 (0.96–1.04)	1.03 (0.97–1.09)	1.00 (0.97–1.04)
P trend	0.58	0.70	0.22	0.14	0.20	0.86	0.35	0.97
No.	364	859	254	618	258	623	309	727
15 to referent yr.	1.00 (0.97–1.04)	1.04 (1.01–1.07)	0.96 (0.93–1.00)	1.04 (1.01–1.07)	1.00 (0.97–1.03)	1.00 (0.97–1.02)	0.99 (0.96–1.03)	1.02 (1.00–1.05)
P trend	0.81	0.01	0.05	0.004	0.81	0.81	0.66	0.09
No.	751	1453	556	1059	550	1032	631	1208
30 to 50 yrs.	1.03 (0.96–1.11)	0.98 (0.94–1.03)	1.03 (0.96–1.11)	1.03 (0.97–1.08)	0.95 (0.89–1.02)	1.03 (0.98–1.07)	1.00 (0.93–1.07)	0.99 (0.95–1.03)
P trend	0.42	0.40	0.43	0.36	0.18	0.22	0.95	0.49
No.	375	895	264	647	269	654	317	759
30 to referent yr.	1.00 (0.96–1.04)	1.02 (0.99–1.05)	0.96 (0.92–1.01)	1.04 (1.01–1.08)	0.99 (0.95–1.03)	1.01 (0.98–1.04)	0.99 (0.95–1.04)	1.01 (0.98–1.04)
P trend	0.97	0.19	0.11	0.02	0.70	0.63	0.75	0.43
No.	755	1475	555	1076	552	1054	631	1228
50 to referent yr.	0.96 (0.89–1.04)	1.04 (0.99–1.09)	0.96 (0.88–1.04)	1.06 (0.99–1.13)	1.05 (0.97–1.12)	1.00 (0.94–1.05)	0.97 (0.90–1.06)	1.02 (0.97–1.06)
P trend	0.31	0.17	0.30	0.09	0.22	0.87	0.52	0.49
No.	381	898	267	650	271	655	322	762
Waist circumference (in), interview								
<30.6	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
30.6–34.1	1.39 (0.78–2.47)	1.14 (0.81–1.62)	0.68 (0.37–1.25)	1.73 (1.05–2.88)	1.19 (0.67–2.13)	0.96 (0.66–1.40)	1.72 (0.91–3.24)	1.35 (0.95–1.92)
34.1–38.5	2.21 (1.18–4.14)	1.47 (1.00–2.17)	0.73 (0.40–1.34)	3.22 (1.98–5.23)	1.25 (0.70–2.24)	1.12 (0.76–1.66)	1.82 (0.96–3.45)	1.71 (1.17–2.49)
>38.5	1.24 (0.70–2.19)	1.79 (1.20–2.67)	0.56 (0.30–1.05)	2.59 (1.58–4.22)	0.99 (0.55–1.79)	0.98 (0.67–1.43)	1.33 (0.72–2.46)	1.46 (1.01–2.09)
p- trend	0.59	<0.001	0.09	<0.001	0.83	0.91	0.99	0.03

	Stage <i>In-situ</i> vs. <i>Invasive</i>		ER Status* ER+ vs. ER-		Lymph Node Status* Negative vs. Positive		Tumor Size <1.0 cm vs. 1.0 cm	
	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White	Hispanic	Non-Hispanic White
No.	774	1486	575	1085	567	1063	650	1238
Waist/hip Ratio, interview								
<0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
0.8-0.9	1.21 (0.78-1.89)	1.23 (0.92-1.64)	1.18 (0.67-1.66)	1.99 (1.40-2.82)	1.19 (0.79-1.80)	1.05 (0.79-1.41)	1.22 (0.77-1.94)	1.10 (0.83-1.44)
>0.9	0.87 (0.49-1.56)	1.64 (1.14-2.36)	1.05 (0.67-1.66)	2.09 (1.20-3.66)	0.85 (0.48-1.53)	1.09 (0.68-1.75)	1.37 (0.70-2.67)	1.40 (0.87-2.25)
p trend	0.82	0.04	0.35	<0.001	0.82	0.65	0.31	0.18
No.	793	1510	587	1106	579	1080	665	1259

All models adjusted for center, menopausal status, age, education, and time to interview.

* Estrogen receptor status and lymph node status in logistic regression analysis restricted to invasive cases.

Body mass index and waist-hip ratio are for referent year.

Odds Ratio (95% Confidence Interval); p-trend values by chi-square test for linear trend.