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Overall and abdominal adiposity and premenopausal breast cancer risk among Hispanic women: The Breast Cancer Health Disparities Study

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Abstract

Background—Few studies in Hispanic women have examined the relation between adult body size and risk of premenopausal breast cancer defined by hormone receptor status.

Methods—The Breast Cancer Health Disparities Study pooled interview and anthropometric data from two large U.S. population-based case-control studies. We examined associations of overall and abdominal adiposity with risk of estrogen receptor and progesterone receptor positive (ER+PR+) and negative (ER–PR–) breast cancer in Hispanic and non-Hispanic White (NHW) women, calculating odds ratios (OR) and 95% confidence intervals (CI).

Results—Among Hispanics, young-adult and current body mass index (BMI) were inversely associated with both ER+PR+ and ER-PR- breast cancer. For ER+PR+ disease, risk was substantially reduced among those with elevated BMI throughout adulthood (OR=0.35, 95% CI=0.19-0.62). Height and height-to-waist ratio were positively associated with ER-PR- breast cancer. After adjustment for current BMI, two-fold increased risks were seen for large waist and hip circumferences, regardless of tumor receptor status. Genetic ancestry appeared to modify some of the associations with overall and abdominal adiposity. Among NHWs, findings for overall

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Conflict of interest

None of the authors have any conflict of interest to report. Dr. Giuliano serves as a consultant and as a member of advisory boards at Merck & Co., Inc.

adiposity were similar to those for Hispanics, but there was no evidence of associations with abdominal adiposity.

Conclusions—Our findings for Hispanic women were generally similar to those reported for NHW women in other studies, with inverse associations for overall adiposity and positive associations for abdominal adiposity.

Impact—Abdominal obesity in young adulthood is an important risk factor for premenopausal breast cancer among Hispanic women.

Keywords

Breast cancer; BMI; body size; estrogen receptor status; genetic ancestry; Hispanics; Latinas; premenopausal; progesterone receptor status; weight gain

Introduction

Body mass index (BMI), a measure of overall adiposity, has been associated with decreased risk of premenopausal breast cancer (BC) (1-3), whereas waist circumference and waist-tohip ratio (WHR), two commonly used measures of abdominal or central adiposity, have been associated with increased risk (3-5). These findings are based on studies conducted in primarily non-Hispanic white (NHW) women. Only a few studies have reported on body size associations in premenopausal U.S. Hispanic women (6-10), and the findings are not consistent. Therefore, it is unclear whether the effects of overall and abdominal obesity on premenopausal BC risk in Hispanics are different from those in NHWs (11). Given the higher prevalence of overweight and obesity in Hispanics than NHWs (12), further investigation of the relation between body size and breast cancer risk in Hispanics is warranted.

In this report, we analyzed data for Hispanic and NHW women from two large populationbased case-control studies that were harmonized and pooled for the Breast Cancer Health Disparities Study (13). We assessed associations of overall and abdominal adiposity with risk of premenopausal BC defined by estrogen receptor (ER) and progesterone receptor (PR) status, which are important in characterizing risk profiles for hormone-related exposures such as body size (14). We also examined whether genetic ancestry among Hispanic women modified the body size associations, given our previous finding that overall and abdominal obesity are more common in Hispanic women with higher Indigenous American (IA) ancestry (15).

Materials and Methods

The Breast Cancer Health Disparities Study was approved by the institutional review board at each institution. Written informed consent was provided by all study participants.

San Francisco Bay Area Breast Cancer Study (SFBCS)

The SFBCS was conducted in Hispanic, African American and NHW women from the San Francisco Bay Area (16, 17). The Greater Bay Area Cancer Registry identified 17,537 cases aged 35-79 years with a first primary invasive BC diagnosed between April 1995 and April

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2002. Controls were identified through random-digit dialing and were frequency matched to cases on race/ethnicity and the expected 5-year age distribution of cases. Self-reported race/ ethnicity and eligibility for several studies were assessed by a telephone screening interview, with participation rates of 89% among 15,573 cases contacted (alive, valid address, no physician refusal) and 92% among 3,547 controls contacted. For the SFBCS, women eligible for an in-person interview included all Hispanic cases diagnosed from 1995-2002, all African American cases diagnosed from 1995-1999, and a sample of NHW cases diagnosed from 1995-1999. Given the large number of diagnoses in NHW women, they were randomly sampled at 10%. Interview data were obtained for 1,715 cases, including 1,119 (89%) Hispanics and 596 (86%) NHWs, and 2,108 controls, including 1,462 (88%) Hispanics and 646 (83%) NHWs. Median time between diagnosis and interview was 15.4 months. The pooled analysis included Hispanics and NHWs only; body size associations for African Americans were reported elsewhere (9).

4-Corners Breast Cancer Study (4-CBCS)

The 4-CBCS included NHW, Hispanic, and Native American (NA) women from nonreservation areas in Arizona, Colorado, New Mexico, and Utah (8). The state-wide cancer registries identified 5,256 cases aged 25-79 years with *in situ* or invasive BC diagnosed between October 1999 and May 2004; controls were selected from the populations living in the four states and were frequency matched to cases on race/ethnicity and expected 5-year age distribution. A total of 3,761 cases were contacted and 2,556 completed the in-person interview, including 873 Hispanics/NAs (63%) and 1,683 NHWs (71%). Of 6,152 controls contacted, 2,605 completed the interview, including 936 (36%) Hispanics/NAs and 1,669 (47%) NHWs. The number of NAs (55 cases, 73 controls) was too small for separate analysis and they were combined with Hispanics. Cases were restricted to those with a first primary invasive breast cancer (662 Hispanics/NAs, 1,246 NHWs). Median time between diagnosis and interview was 17.8 months.

Data Collection

The two studies used similar structured questionnaires in English or Spanish to collect information on body size and other BC risk factors up to the reference year (defined as the calendar year prior to diagnosis for cases or selection into the study for controls). Trained professional bilingual interviewers administered the questionnaires in English or Spanish and also measured standing height (with shoes removed) and weight (with light clothing) at the time of interview, using a portable stadiometer and scale, respectively. Waist and hip circumferences were measured using a linen tape (in SFBCS) or a flexible tape (in 4-CBCS). In SFBCS, height was measured to the nearest millimeter, weight to the nearest 0.20 kilogram, and waist and hip circumferences to the nearest millimeter. For each, three measurements were taken (except for two measurements of weight) and averaged (9). In 4-CBCS, height was measured to the nearest 0.25 inch (in), weight to the nearest 0.50 pound (lb), and waist and hip circumferences to the nearest 0.50 in. For each, two measurements were taken (if they differed by >0.5 in for height, >1.0 in for waist or hip circumferences, or >1.0 lb for weight, a third measurement was taken) and averaged (8). Information on estrogen receptor (ER) and progesterone receptor (PR) status was obtained from the

respective cancer registries and was available for most premenopausal cases (84% in SFBCS, 79% in 4-CBCS).

Study Variables

Data from the two studies were harmonized according to common definitions (13). Women were classified as premenopausal if they reported having menstrual periods during the reference year. Based on current language usage, a three-level acculturation index was created for Hispanics (low: Spanish speaking only; moderate: speaking more Spanish than English or Spanish and English equally; high: speaking more English than Spanish or English only). Current BMI was calculated as weight (in kg) divided by height (in meter) squared, based on measured height at interview and self-reported weight in the reference year. Self-reported weight before diagnosis was used since weight measured at interview may have been affected by disease- or treatment-related weight gain or loss. For study participants who declined the height measurement, self-reported height was used (3% of cases, 2% of controls); for individuals without self-reported weight, measured weight was used (1% of cases, 2% of controls). The two studies used slightly different approaches to assess young-adult weight. In SFBCS, young-adult BMI was based on self-reported weight at age 25-30 years for cases diagnosed from 1995-1998 and their matched controls, or on self-reported weight at age 20-29 years for cases diagnosed from 1998-2002 and their matched controls. In 4-CBCS, young-adult BMI was based on the average of weights reported at ages 15 years and 30 years. Weight gain was calculated as the difference between self-reported young-adult weight and self-reported weight in the reference year (or measured weight at interview if self-reported weight was not available). We calculated WHR as a measure of body fat distribution that reflects both adipose tissue (waist circumference) and muscle mass (hip circumference), and waist-to-height ratio (WHtR) as a measure of visceral adiposity independent of height (18). Current BMI was classified as underweight to normal weight (<25.0 kg/m²), overweight (25.0-29.9 kg/m²), or obese (30.0 kg/m^2) . All other body size variables were categorized according to the tertile or quartile distribution among premenopausal controls. We used the same cut-points for the two ethnic groups in order to facilitate the comparison of results. Additionally, we performed comparative analyses using ethnic-specific quantiles.

For a subset of study participants with stored DNA (in SFBCS, biospecimen collection began with cases diagnosed in April 1997 or later and their matched controls), we estimated genetic ancestry using 104 ancestry informative markers (AIMs) (13). Hispanic women were classified according to being above or below the median (46%) of Indigenous American (IA) ancestry among premenopausal controls.

Statistical Analyses

Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the associations with body size variables. Polytomous logistic regression was used to compare ER+PR+ and ER-PR- case groups to a common control group. Other case groups in premenopausal women (97 ER+PR-, 41 ER-PR+) were too small for separate analyses. We also stratified the analyses by study (SFBCS, 4-CBCS) to evaluate consistency of results.

Multivariate analyses were adjusted for age (continuous) and study, and additionally, for factors significantly associated with risk of ER+PR+ or ER-PR- BC in our dataset. For ER +PR+ BC, analyses were adjusted for education, BC family history, age at menarche, number of full-term pregnancies, age at first full-term pregnancy, lifetime duration of breast-feeding, oral contraceptive use, and alcohol consumption; for ER-PR- BC, analyses were adjusted for alcohol consumption. Analyses in Hispanics additionally adjusted for language acculturation. Analyses of overall adiposity measures (current BMI, young-adult BMI, and weight gain) were adjusted for waist circumference (adjustment for WHtR produced the same results, data not shown), and analyses of abdominal adiposity were adjusted for current BMI. Additional adjustment for genetic ancestry did not alter the results (data not shown). Variables were categorized as noted in the footnotes of the tables. Linear trends were assessed across ordinal values of categorical variables. Significant differences in ORs between case groups were tested using the Wald statistic *P*-value, calculated from the polytomous regression model. Two-sided *P*-values are reported for tests of trend and tests of heterogeneity, with *P*-values <0.05 considered statistically significant.

Analyses in premenopausal women included 1,262 Hispanics (497 cases, 765 controls) and 1,101 NHWs (448 cases, 653 controls), after excluding individuals with missing data on covariates (89 cases, 92 controls) or ER/PR status (241 cases). The analyses by genetic ancestry were based on 861 Hispanics (327 cases, 534 controls). Statistical analyses used SAS version 9.3 software (SAS Institute, Inc., Cary, NC).

Results

Compared to controls, cases had higher education, younger age at menarche, fewer full-term pregnancies, later age at first full-term pregnancy, shorter duration of breast-feeding, and were more likely to have a first-degree family history of breast cancer (Table 1). Among Hispanics, cases had higher English language acculturation than controls. Compared to NHW controls, higher proportions of Hispanic controls were overweight or obese (72% vs. 45%), had a waist size above the median of 87 cm (59% vs. 38%), and a young-adult BMI above the median of 21.7 kg/m² (63% vs. 35%) (Table 2). Furthermore, Hispanics with higher IA ancestry (above the median of 46%) had higher body size measures than those with lower IA ancestry.

Body size and ER+PR+ breast cancer

For ER+PR+ BC (Table 3), a suggestive positive trend with height was seen among Hispanics overall (P_{trend} =0.05), with a stronger association among SFBCS Hispanics (high vs. low quartile: OR=1.85, 95% CI=0.94-3.61, P_{trend} =0.02; data not shown). Higher youngadult and current BMI were associated with reduced risk, and adjustment for waist circumference strengthened the inverse associations. ORs for high (high vs. low quartile) young-adult BMI were similar for Hispanics (OR=0.41, $P_{trend} < 0.01$) and NHWs (OR=0.53, $P_{trend}=0.01$), and findings were similar in SFBCS and 4-CBCS (data not shown). For current obesity (30 vs. <25 kg/m²), inverse associations were statistically significant for Hispanics (OR=0.48, $P_{trend} < 0.01$) and NHWs in SFBCS (data not shown). For weight gain there was a suggestive inverse association among Hispanics, but the reduction in risk was statistically

Analyses of long-term elevated BMI showed that compared to women with both a lower young-adult BMI ($<21.8 \text{ kg/m}^2$) and current normal-weight BMI ($<25 \text{ kg/m}^2$), the greatest risk reductions of ER+PR+ BC were seen in Hispanics with higher young-adult BMI (21.8 kg/m^2) and current overweight (OR=0.39, 95% CI=0.24-0.63) or obesity (OR=0.35, 95% CI=0.19-0.62). Similarly, among NHWs, risk was significantly reduced among those with a higher young-adult BMI (21.8 kg/m^2) and current overweight (OR=0.49, 95% CI=0.26-0.91).

Among Hispanics, two-fold increased risk of ER+PR+ BC were associated with large waist and hip circumferences, and adjustment for current BMI strengthened the associations. For WHtR, the trend was of borderline significance (P_{trend} =0.06). There were no significant associations with WHR. Among NHWs, abdominal obesity was not associated with ER+PR + BC, neither overall (Table 3) nor in either study (data not shown);

Body size and ER-PR- breast cancer

For ER–PR– BC (Table 4), significant associations with body size were limited to Hispanic women. Height was associated with a two-fold increased risk, whereas young-adult BMI was associated with reduced risk, with a stronger inverse association after adjustment for abdominal obesity ($30 \text{ vs.} < 25 \text{ kg/m}^2$: OR=0.36, $P_{\text{trend}} < 0.01$). A significant inverse association also was seen for current BMI, when adjusted for abdominal obesity, although no significant association remained after additional adjustment for young-adult BMI.

Large waist and hip circumferences and high WHtR were associated with two-fold increased risks of ER–PR– BC in Hispanics, with stronger associations after adjustment for current BMI. Among NHWs, borderline trends were seen for WHtR ($P_{\text{trend}}=0.07$) and WHR ($P_{\text{trend}}=0.09$).

Joint associations of abdominal and overall obesity with breast cancer risk among Hispanics

Since the association with abdominal obesity among Hispanics did not differ significantly by ER/PR status, we examined the joint role of overall and abdominal obesity for all BCs combined (Table 5). Among overweight Hispanics (BMI 25.0-29.9 kg/m²), BC risk was significantly reduced among those with small waist (88 cm) or hip (106.3 cm) circumference or low WHR (0.85) or WHtR (0.56), but not among those with large waist or hip circumference or those with high WHR or WHtR. In contrast, among obese Hispanics (BMI 30 kg/m²), risk reductions were of similar magnitude, regardless of abdominal obesity.

Genetic ancestry, body size and breast cancer risk among Hispanics

In the subset of premenopausal Hispanics with available DNA, there was some variation in body size associations by genetic ancestry (Table 6). For ER+PR+ BC, there was a pattern of inverse associations with current BMI (P_{trend} =0.06 after adjustment for young-adult BMI)

For the analyses of abdominal obesity by genetic ancestry, all BCs were combined (Table 6). Associations of waist circumference ($P_{\text{trend}}=0.01$) and WHtR ($P_{\text{trend}}=0.07$) were somewhat stronger among Hispanics with higher (>46%) IA ancestry.

Discussion

This pooled case-control analysis of over 1,200 premenopausal Hispanic women is the largest study to date to evaluate associations between body size and BC risk in U.S. Hispanics. Regardless of tumor hormone receptor status, young-adult BMI was inversely associated with breast cancer risk, whereas height and waist and hip circumferences were associated with increased risk. Current BMI was associated with reduced risk of ER+PR+ BC, with the largest reductions in risk found in Hispanics who had an elevated BMI as young adults and currently were overweight or obese. Genetic ancestry of Hispanic women appeared to modify some of the body size associations. These findings provide evidence that overall and abdominal obesity play an important role in BC etiology among premenopausal Hispanic women, as has been reported for NHWs, and contribute to the sparse and inconsistent epidemiologic data on body size and premenopausal BC risk in Hispanics (6-9).

Adult obesity has been associated with reduced risk of premenopausal BC risk in metaanalyses of primarily NHW women (3, 19, 20). Similarly in Hispanic women, we found an inverse association with current obesity that was independent of young-adult BMI and abdominal obesity, although the association was limited to ER+PR+ BC. Furthermore, the reductions in risk were highest for women with higher adiposity throughout adulthood, thus emphasizing the importance of considering young-adult BMI when examining associations with current BMI and weight gain, especially in populations, such as Hispanics, who have a higher prevalence of overweight and obesity, even at young ages (12). In our pooled dataset, 36% of premenopausal Hispanic controls had a young-adult BMI in the highest quartile (>24.1 kg/m²) compared to 15% among NHWs. In contrast, for ER-PR- BC, no significant inverse associations remained for current BMI after adjustment for young-adult BMI and abdominal obesity, suggesting that current obesity may be an important protective factor for hormone responsive tumors only. The lower BC risk among obese women has been attributed to more frequent anovulatory menstrual cycles and lower estrogen concentrations (21), although there is evidence that menstrual cycle characteristics, self-reported infertility, and polycystic ovary syndrome do not explain the inverse associations with obesity (22, 23), suggesting the importance of other mechanisms yet to be identified.

Consistent with studies in NHW women (24-27), we found strong inverse associations with young-adult BMI in Hispanic women, both for ER+PR+ and ER-PR- BC. We previously reported inverse associations with adolescent obesity in Hispanics (8, 10) and NHWs (8), particularly in premenopausal women with lifelong obesity (10). Inverse associations with

childhood or adolescent obesity have also been reported for NHW women (22, 28-31). Although the underlying mechanisms remain unclear, these findings suggest that early-life adiposity exerts a long-lasting influence on premenopausal BC risk.

In Hispanics, waist and hip circumference and WHtR were strongly associated with increased risk of both ER+PR+ and ER-PR- BC. For ER+PR+ BC, however, associations emerged only after adjustment for current BMI, whereas for ER-PR- BC, adjustment for BMI strengthened the positive associations. Some studies in NHWs have also shown that adjustment for BMI strengthened the associations with waist (32, 33), hip (33), or WHR (32, 34). We found no association with WHR in Hispanics, but a strong association with WHtR, an abdominal obesity measure that has previously not been examined in Hispanic women. Positive associations with WHR have been reported for NHWs (35, 36), with associations limited to ER+PR+(37) or ER-(38) disease in some studies. In contrast to Hispanics, we found no evidence of association with abdominal obesity in NHWs, in agreement with other studies (9, 39-42), but unlike a recent meta-analysis that reported a positive association with WHR in NHW women (3). The reasons for the differences in abdominal obesity associations between Hispanics and NHWs in our pooled analysis are not obvious. Abdominal obesity may affect premenopausal BC risk through hormonal, metabolic and inflammatory mechanisms (2, 43), and it has been suggested that abdominal adipose tissue may be metabolically more active than peripheral adipose tissue (44).

The 4-CBCS, to our knowledge, is the only study that examined possible variations in body size associations among Hispanics by genetic ancestry (8). Using a different set of AIMs in a population with a more limited range of genetic admixture than the SFBCS, associations with BMI and WHR did not differ by genetic ancestry. In contrast, we found that associations with adiposity measures were different for Hispanics, depending on the degree of genetic admixture: inverse associations of ER+PR+ BC with BMI and weight gain were limited to Hispanics with lower IA ancestry, whereas for abdominal obesity, associations with BC risk overall were limited to those with higher IA ancestry. These results highlight the importance of genetic factors and call for further evaluation.

Our analysis has several strengths, including the population-based design, the large sample size, measurements of body size, comprehensive assessment of other BC risk factors by inperson interview, and availability of information on tumor ER and PR status for most cases. The use of measured height for BMI calculation was particularly important, since in the SFBCS, 22% of Hispanics did not know their height. Although we measured weight at interview, we used self-reported weight during the reference year to calculate BMI because of concern about disease- and treatment-related weight gain or loss. In a sensitivity analysis limited to women with both measured and self-reported weight and height, we found similar associations with BMI based on self-reported or measured height and weight (data not shown). Furthermore, the correlation between self-reported and measured weight was high both in premenopausal cases (r=0.88) and controls (r=0.91). Some limitations also need to be considered. Participation rates differed between the two studies, but the results for Hispanic women were generally consistent across the two studies. Although the pooled analysis included a large sample of premenopausal Hispanic women and was hypothesis driven, the sample size was limited for certain subgroup analyses that considered multiple

factors jointly and for analyses of ER–PR– disease. Furthermore, the investigation of modifying factors resulted in many comparisons, possibly leading to false-positive results. We relied on self-reported young-adult weight and the two studies assessed weight at different ages. Data harmonization to estimate average weight in a woman's twenties may not have been optimal and introduced non-differential misclassification, possibly causing the associations with weight gain to be attenuated. BMI, a widely used measure of body fat, does not distinguish between lean and fat mass (45), or account for differences in body fat between individuals with the same BMI or across different racial/ethnic groups (46-48). The analyses of abdominal obesity were based on measurements taken after diagnosis which may have introduced some misclassification. For example, within 12 months of treatment chemotherapy and endocrine therapy have been linked to increases in central fat, regardless of changes in body weight (49). Finally, our analyses by genetic ancestry were limited by the range of admixture, as only U.S. Hispanics were included.

In conclusion, our findings highlight that body size throughout the premenopausal years has a major influence on BC risk and suggest that, in Hispanics, associations with overall and abdominal obesity are similar to those previously reported for NHW women, especially when considering tumor hormone receptor status. The association between abdominal obesity and ER–PR– BC is particularly important since few risk factors have been identified for this tumor subtype (50-52), which is more common among Hispanics than NHWs (53). Given that obesity and weight gain are associated with increased BC risk after menopause, when BC is diagnosed more frequently than at younger ages, avoiding weight gain and maintaining a healthy weight are important in both Hispanic and non-Hispanic populations, even at a young age, because of the long-term adverse effects of obesity on cancer and other chronic disease risk later in life.

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References

- 1. World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity, and Prevention of Cancer: A Global Perspective. AICR; Washington, D.C.: 2007.
- Amadou A, Hainaut P, Romieu I. Role of obesity in the risk of breast cancer: lessons from anthropometry. J Oncol. 2013; 2013:906495. [PubMed: 23431300]
- 3. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, et al. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013
- Connolly BS, Barnett C, Vogt KN, Li T, Stone J, Boyd NF. A meta-analysis of published literature on waist-to-hip ratio and risk of breast cancer. Nutr Cancer. 2002; 44:127–38. [PubMed: 12734058]
- Harvie M, Hooper L, Howell AH. Central obesity and breast cancer risk: a systematic review. Obes Rev. 2003; 4:157–73. [PubMed: 12916817]
- Mayberry RM, Branch PT. Breast cancer risk factors among Hispanic women. Ethn Dis. 1994; 4:41–6. [PubMed: 7742731]
- Wenten M, Gilliland FD, Baumgartner K, Samet JM. Associations of weight, weight change, and body mass with breast cancer risk in Hispanic and non-Hispanic white women. Ann Epidemiol. 2002; 12:435–4. [PubMed: 12160603]
- 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; 102:85–101. [PubMed: 17080310]
- John EM, Sangaramoorthy M, Phipps AI, Koo J, Horn-Ross PL. Adult body size, hormone receptor status, and premenopausal breast cancer risk in a multiethnic population: the San Francisco Bay Area breast cancer study. Am J Epidemiol. 2011; 173:201–16. [PubMed: 21084558]
- Sangaramoorthy M, Phipps AI, Horn-Ross PL, Koo J, John EM. Early-life factors and breast cancer risk in Hispanic women: the role of adolescent body size. Cancer Epidemiol Biomarkers Prev. 2011; 20:2572–82. [PubMed: 22056503]
- Sexton KR, Franzini L, Day RS, Brewster A, Vernon SW, Bondy ML. A review of body size and breast cancer risk in Hispanic and African American women. Cancer. 2011; 117:5271–81. [PubMed: 21598244]
- Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014; 311:806–14. [PubMed: 24570244]
- Slattery ML, John EM, Torres-Mejia G, Lundgreen A, Herrick JS, Baumgartner KB, et al. Genetic variation in genes involved in hormones, inflammation and energetic factors and breast cancer risk in an admixed population. Carcinogenesis. 2012; 33:1512–21. [PubMed: 22562547]
- 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; 124:698–712. [PubMed: 18988226]
- 15. Ziv E, John EM, Choudhry S, Kho J, Lorizio W, Perez-Stable EJ, et al. Genetic ancestry and risk factors for breast cancer among Latinas in the San Francisco Bay Area. Cancer Epidemiol Biomarkers Prev. 2006; 15:1878–85. [PubMed: 17035394]
- John EM, Horn-Ross PL, Koo J. Lifetime physical activity and breast cancer risk in a multiethnic population: the San Francisco Bay area breast cancer study. Cancer Epidemiol Biomarkers Prev. 2003; 12:1143–52. [PubMed: 14652273]
- John EM, Phipps AI, Davis A, Koo J. Migration history, acculturation, and breast cancer risk in Hispanic women. Cancer Epidemiol Biomarkers Prev. 2005; 14:2905–13. [PubMed: 16365008]
- Molarius A, Seidell JC. Selection of anthropometric indicators for classification of abdominal fatness--a critical review. Int J Obes Relat Metab Disord. 1998; 22:719–27. [PubMed: 9725630]
- van den Brandt PA, Spiegelman D, Yaun SS, Adami HO, Beeson L, Folsom AR, et al. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. Am J Epidemiol. 2000; 152:514–27. [PubMed: 10997541]
- Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008; 371:569–78. [PubMed: 18280327]

- Potischman N, Swanson CA, Siiteri P, Hoover RN. Reversal of relation between body mass and endogenous estrogen concentrations with menopausal status. J Natl Cancer Inst. 1996; 88:756–8. [PubMed: 8637031]
- 22. Michels KB, Terry KL, Willett WC. Longitudinal study on the role of body size in premenopausal breast cancer. Arch Intern Med. 2006; 166:2395–402. [PubMed: 17130395]
- Palmer JR, Adams-Campbell LL, Boggs DA, Wise LA, Rosenberg L. A prospective study of body size and breast cancer in black women. Cancer Epidemiol Biomarkers Prev. 2007; 16:1795–802. [PubMed: 17855697]
- 24. 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. 1997; 278:1407–11. [PubMed: 9355998]
- 25. Chu SY, Lee NC, Wingo PA, Senie RT, Greenberg RS, Peterson HB. The relationship between body mass and breast cancer among women enrolled in the Cancer and Steroid Hormone Study. J Clin Epidemiol. 1991; 44:1197–206. [PubMed: 1941014]
- 26. Brinton LA, Swanson CA. Height and weight at various ages and risk of breast cancer. Ann Epidemiol. 1992; 2:597–609. [PubMed: 1342311]
- Berstad P, Coates RJ, Bernstein L, Folger SG, Malone KE, Marchbanks PA, et al. A case-control study of body mass index and breast cancer risk in white and African-American women. Cancer Epidemiol Biomarkers Prev. 2010; 19:1532–44. [PubMed: 20501755]
- Coates RJ, Uhler RJ, Hall HI, Potischman N, Brinton LA, Ballard-Barbash R, et al. Risk of breast cancer in young women in relation to body size and weight gain in adolescence and early adulthood. Br J Cancer. 1999; 81:167–74. [PubMed: 10487629]
- Weiderpass E, Braaten T, Magnusson C, Kumle M, Vainio H, Lund E, et al. A prospective study of body size in different periods of life and risk of premenopausal breast cancer. Cancer Epidemiol Biomarkers Prev. 2004; 13:1121–7. [PubMed: 15247122]
- 30. Baer HJ, Colditz GA, Rosner B, Michels KB, Rich-Edwards JW, Hunter DJ, et al. Body fatness during childhood and adolescence and incidence of breast cancer in premenopausal women: a prospective study. Breast Cancer Research. 2005; 7:R314–R25. [PubMed: 15987426]
- 31. Baer HJ, Tworoger SS, Hankinson SE, Willett WC. Body fatness at young ages and risk of breast cancer throughout life. Am J Epidemiol. 2010; 171:1183–94. [PubMed: 20460303]
- Huang Z, Willett WC, Colditz GA, Hunter DJ, Manson JE, Rosner B, et al. Waist circumference, waist:hip ratio, and risk of breast cancer in the Nurses' Health Study. Am J Epidemiol. 1999; 150:1316–24. [PubMed: 10604774]
- Lahmann PH, Hoffmann K, Allen N, van Gils CH, Khaw KT, Tehard B, et al. Body size and breast cancer risk: findings from the European Prospective Investigation into Cancer And Nutrition (EPIC). Int J Cancer. 2004; 111:762–71. [PubMed: 15252848]
- 34. Sonnenschein E, Toniolo P, Terry MB, Bruning PF, Kato I, Koenig KL, et al. Body fat distribution and obesity in pre- and postmenopausal breast cancer. Int J Epidemiol. 1999; 28:1026–31. [PubMed: 10661643]
- Mannisto S, Pietinen P, Pyy M, Palmgren J, Eskelinen M, Uusitupa M. -size indicators and risk of breast cancer according to menopause and estrogen-receptor status. Int J Cancer. 1996; 68:8–13. [PubMed: 8895532]
- 36. Hall IJ, Newman B, Millikan RC, Moorman PG. Body size and breast cancer risk in black women and white women: the Carolina Breast Cancer Study. Am J Epidemiol. 2000; 151:754–64. [PubMed: 10965972]
- Huang WY, Newman B, Millikan RC, Schell MJ, Hulka BS, Moorman PG. Hormone-related factors and risk of breast cancer in relation to estrogen receptor and progesterone receptor status. Am J Epidemiol. 2000; 151:703–14. [PubMed: 10752798]
- Harris HR, Willett WC, Terry KL, Michels KB. Body fat distribution and risk of premenopausal breast cancer in the Nurses' Health Study II. J Natl Cancer Inst. 2011; 103:273–8. [PubMed: 21163903]
- Swanson CA, Coates RJ, Schoenberg JB, Malone KE, Gammon MD, Stanford JL, et al. Body size and breast cancer risk among women under age 45 years. Am J Epidemiol. 1996; 143:698–706. [PubMed: 8651232]

- 40. Kaaks R, Van Noord PA, Den Tonkelaar I, Peeters PH, Riboli E, Grobbee DE. Breast-cancer incidence in relation to height, weight and body-fat distribution in the Dutch "DOM" cohort. Int J Cancer. 1998; 76:647–51. [PubMed: 9610720]
- 41. Tehard B, Clavel-Chapelon F. Several anthropometric measurements and breast cancer risk: results of the E3N cohort study. Int J Obes (Lond). 2006; 30:156–63. [PubMed: 16231021]
- 42. Friedenreich CM, Courneya KS, Bryant HE. Case-control study of anthropometric measures and breast cancer risk. Int J Cancer. 2002; 99:445–52. [PubMed: 11992416]
- 43. Kaaks R. Nutrition, hormones, and breast cancer: is insulin the missing link? Cancer Causes Control. 1996; 7:605–25. [PubMed: 8932921]
- 44. Ballard-Barbash R. Anthropometry and breast cancer. Body size--a moving target. Cancer. 1994; 74:1090–100. [PubMed: 8039144]
- 45. Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK, Erwin PJ, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obes (Lond). 2010; 34:791–9. [PubMed: 20125098]
- Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? Am J Epidemiol. 1996; 143:228–39. [PubMed: 8561156]
- 47. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obes Rev. 2002; 3:141–6. [PubMed: 12164465]
- Flegal KM, Shepherd JA, Looker AC, Graubard BI, Borrud LG, Ogden CL, et al. Comparisons of percentage body fat, body mass index, waist circumference, and waist-stature ratio in adults. Am J Clin Nutr. 2009; 89:500–8. [PubMed: 19116329]
- Cheney CL, Mahloch J, Freeny P. Computerized tomography assessment of women with weight changes associated with adjuvant treatment for breast cancer. Am J Clin Nutr. 1997; 66:141–6. [PubMed: 9209182]
- 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; 13:1558–68. [PubMed: 15466970]
- Ma H, Bernstein L, Pike MC, Ursin G. Reproductive factors and breast cancer risk according to joint estrogen and progesterone receptor status: a meta-analysis of epidemiological studies. Breast Cancer Res. 2006; 8:R43. [PubMed: 16859501]
- 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; 103:250–63. [PubMed: 21191117]
- Banegas MP, Li CI. Breast cancer characteristics and outcomes among Hispanic Black and Hispanic White women. Breast Cancer Res Treat. 2012; 134:1297–304. [PubMed: 22772379]

Table 1

Characteristics of Study Population

		Preme	nopausa	al wome	en
		ises 945)		trols ,418)	
	n	_% 1	n	% ¹	P^2
Study				-	
San Francisco Bay Area Breast Cancer Study	430	46	666	47	
4-Corners Breast Cancer Study	515	54	752	53	
Estrogen receptor (ER) and progesterone receptor (PR) status					
ER+PR+	575	61			
ER+PR-	86	9			
ER-PR+	37	4			
ER-PR-	247	26			
Age 3 (years)					
<40	212	22	342	24	
40-49	564	60	837	59	
50-59	169	18	239	17	
Ethnicity/English language acculturation					
Hispanic - low acculturation	54	6	157	11	< 0.0
Hispanic - moderate acculturation	196	21	339	24	
Hispanic - high acculturation	247	26	269	19	
Non-Hispanic White	448	47	653	46	
Percent Indigenous American admixture ⁴					
46	187	57	267	50	0.07
>46	140	43	267	50	
Education					
Some high school or less	148	16	313	22	< 0.0
High school graduate	192	20	250	18	
Some college or higher	605	64	855	60	
Family history of breast cancer in first-degree relatives					
No	795	84	1278	90	< 0.01
Yes	150	16	140	10	
Age at menarche (years)					
<12	222	24	280	20	< 0.0
12-13	497	53	713	50	
14	226	24	425	30	
Full-term pregnancies					
Nulliparous	195	21	211	15	< 0.0
1-2	474	50	619	44	
3-4	227	24	469	33	

		Preme	nopaus	al wome	en
		nses 945)		trols ,418)	
	n	_% 1	n	_% 1	P ²
5	49	5	119	8	
Age at first full-term pregnancy (years)					
Nulliparous	195	21	211	15	
<25	376	40	669	47	< 0.01
25-29	207	22	321	23	
30	167	18	217	15	
Lifetime breastfeeding (months)					
Nulliparous	195	21	211	15	< 0.01
0	198	21	238	17	
1-12	294	31	463	33	
13-24	119	13	250	18	
25	139	15	256	18	
Oral contraceptive use					
Current	110	12	175	12	0.06
Former	648	69	886	62	
Never	187	20	357	25	
Alcohol consumption (g/day) ⁵					
0	473	50	783	55	0.09
0.1-9.9	314	33	435	31	
10.0-19.9	94	10	121	9	
20.0	64	7	79	6	

¹Percentages may not add up to 100% due to rounding.

 $^2 \mathrm{Mantel}\text{-}\mathrm{Haenszel}$ Chi-square test for difference between cases and controls.

 $^3\mathrm{Age}$ at diagnosis (cases) or selection into the study (controls).

 $^4\mathrm{Among}$ Hispanics only; based on the median in premenopausal controls.

⁵ In the reference year.

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Table 2

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Body Size Characteristics among Premenopausal Controls, by Ethnicity and Genetic Admixture among Hispanics

	Non-Hispanic Whites (n=653)	ispanic ites (53)		Hisp (n=	Hispanics (n=765)		Hispanics	anics		
						Indigenou American Admixture 46% (n=267)	Indigenous American dmixture 1.2 46% (n=267)	Indigenous American Admixture >46% (n=267)	enous rican ure 1,2 %67)	
	u	% ³	u	% 3	P^4	u	°%	u	% ³	P^{5}
Current height (m) 6.7										
Q1: <1.54	45	٢	309	41	<0.01	LL	29	129	48	<0.01
Q2: 1.54-1.59	128	20	229	30		85	32	78	29	
Q3: 1.60-1.64	190	29	161	21		69	26	51	19	
Q4: >1.64	290	44	64	8		36	13	6	4	
Young-adult BMI (kg/m ²) 6,8										
Q1: <20.1	220	35	117	16	<0.01	43	17	38	15	0.02
Q2: 20.1-21.7	189	30	149	21		63	25	47	19	
Q3: 21.8-24.1	128	21	210	29		76	30	63	25	
Q4: >24.1	88	14	250	34		73	28	104	41	
Current BMI (kg/m ²) 9										
<25.0	364	56	212	28	<0.01	83	31	60	23	<0.01
25.0-29.9	160	25	286	37		113	42	94	35	
30.0	129	20	265	35		71	27	113	42	
Weight gain (kg) ^{6,10}										
Q1: <7.5	195	35	154	23	<0.01	57	25	47	20	0.11
Q2: 7.5-13.6	98	17	124	19		45	19	40	17	
Q3: 13.7-22.7	144	25	206	31		74	32	76	33	
Q4: >22.7	129	23	178	27		57	25	70	30	
Waist (cm) δ										
Q1: <78.7	245	39	106	14	<0.01	45	17	21	8	<0.01

	H-noN IW n=	Non-Hispanic Whites (n=653)		Hisp (n=	Hispanics (n=765)		Hispanics	anics		
						Indigenou Americar Admixture 46% (n=267)	Indigenous American dmixture 1,2 46% (n=267)	Indigenous American Admixture >46% (n=267)	digenous merican nixture 1,2 >46% n=267)	
	u	% 3	u	% 3	P^4	u	°% ³	u	% ³	P^{5}
Q2: 78.8-87.0	145	23	196	26		78	29	73	28	
Q3: 87.1-97.7	116	18	227	30		73	28	85	32	
Q4: >97.7	126	20	219	29		68	26	84	32	
Hip (cm) δ										
Q1: <99.1	179	28	166	22	<0.01	60	23	56	21	0.65
Q2: 99.2-106.1	161	26	184	25		99	25	67	25	
Q3: 106.2-115.2	149	24	197	26		73	28	70	27	
Q4: >115.2	143	23	202	27		65	25	70	27	
Waist-to-hip ratio 6										
Q1: <0.77	258	41	87	12	<0.01	38	14	15	9	$<\!0.01$
Q2: 0.78-0.82	177	28	168	23		99	25	51	19	
Q3: 0.83-0.86	109	17	236	32		91	35	85	32	
Q4: >0.86	88	14	257	34		69	26	112	43	
Waist-to-height ratio 6										
Q1: <0.49	274	43	71	10	<0.01	36	14	11	4	<0.01
Q2: 0.50-0.55	154	24	191	26		75	28	61	23	
Q3: 0.56-0.62	102	16	242	32		81	31	91	35	
Q4: >0.62	102	16	244	33		72	27	100	38	
$^{\prime}$ Based on the median among Hispanic premenopausal controls.	Hispanic pr	emenopa	usal con	ttrols.						
² Information on genetic admixture was available for	ture was av	ailable fu	or a subs	set of 8 [,]	41 Hispan	ic preme	a subset of 841 Hispanic premenopausal cases and 1,080 Hispanic premenopausal controls for whom a blood or mouthwash sample was collected.	cases and	1 1,080 H	ispanic pı
3 Percentages may not add up to 100% due to rounding.	o 100% du	to round	ling.							

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⁴ Mantel-Haenszel Chi-square test for difference between premenopausal Hispanic controls and premenopausal NHW controls. ⁵ Mantel-Haenszel Chi-square test for difference between genetic ancestry groups among premenopausal Hispanic controls.

 δ Based on quartiles among all premenopausal controls.

7 Based on measured height at interview (for SFBCS participants, self-reported adult height was used when measured height was not available).

April 1995 to April 1998 and matched controls and between ages 20-29 for cases diagnosed from May 1998 to April 2002 and matched controls), and measured height at interview (for SFBCS participants, 8 Based on self-reported averaged weight at age 15 and age 30 for 4-CBCS cases and controls, self-reported weight in the 20's for SFBCS cases and controls (between ages 25-30 for cases diagnosed from self-reported adult height was used when measured height was not available).

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9 Based on self-reported weight in reference year (or measured weight at interview if self-reported weight in reference year was not available) and measured height at interview (or self-reported adult height for SFBCS participants for whom measured height was not available). 10 Based on self-reported weight in reference year (or measured weight at interview when self-reported weight was not available) minus self-reported young-adult weight; excludes 92 premenopausal cases and 125 premenopausal controls who lost weight. **NIH-PA** Author Manuscript

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Overall and Abdominal Adiposity Associations with ER+PR+ Breast Cancer in Premenopausal Women, by Ethnicity

			V	All		H	Hispanics		Non-Hispanic Whites	c Whites
	ER+PR+ cases (n=575)	Controls (n=1,418)			ER+PR+ cases (n=285)	Controls (n=765)		ER+PR+ cases (n=290)	Controls (n=653)	
	u	п	OR ¹ (95%CI)	OR ² (95%CI)	u	u	OR ² (95%CI)	u	u	OR ³ (95%CI)
Current height (m) ^{4,5}										
Q1: <1.54	110	354	1.0	1.0	93	309	1.0	17	45	1.0
Q2: 1.54-1.59	139	357	1.12 0.82-1.52	1.12 0.82-1.53	80	229	1.08 0.75-1.56	59	128	1.13 0.58-2.20
Q3: 1.60-1.64	171	351	1.39 1.02-1.89	1.41 1.03-1.93	81	161	1.47 1.00-2.16	90	190	1.21 0.64-2.31
Q4: >1.64	155	354	$1.26\ 0.90-1.77$	1.34 0.95-1.88	31	64	1.40 0.83-2.36	124	290	1.24 0.66-2.34
			$P_{\rm trend} = 0.09$	$P_{\mathrm{trend}}=0.04$			$P_{ m trend}=0.05$			$P_{\rm trend} = 0.47$
Young-adult BMI (kg/m ²) 4,6	n ²) 4.6									
Q1: <20.1	190	337	1.0	1.0	59	117	1.0	131	220	1.0
Q2: 20.1-21.7	163	338	$0.84\ 0.64-1.10$	0.81 0.61-1.07	83	149	0.99 0.63-1.55	80	189	0.70 0.49-1.01
Q3: 21.8-24.1	120	338	0.66 0.49-0.88	0.63 0.46-0.85	78	210	0.72 0.46-1.14	42	128	0.55 0.35-0.87
Q4: >24.1	91	338	0.51 0.37-0.70	0.44 0.30-0.63	60	250	0.41 0.24-0.69	31	88	0.53 0.30-0.95
			$P_{\rm trend} <\! 0.01$	$P_{\rm trend} <\! 0.01$			$P_{\rm trend} <\! 0.01$			$P_{\mathrm{trend}} = 0.01$
Current BMI (kg/m ²) 7										
<25.0	294	576	1.0	1.0	119	212	1.0	178	364	1.0
25.0-29.9	148	446	0.69 0.53-0.88	$0.64 \ 0.48-0.84$	84	286	0.53 0.36-0.79	64	160	0.76 0.51-1.13
30.0	133	394	0.67 0.51-0.87	$0.58\ 0.40-0.84$	82	265	0.48 0.29-0.81	51	129	0.73 0.42-1.29
			$P_{\rm trend} <\! 0.01$	$P_{\rm trend} <\! 0.01$			$P_{\rm trend} <\! 0.01$			$P_{\mathrm{trend}} = 0.20$
Current BMI (kg/m ²) 7,8 , adjusted	. ⁸ , adjusted for	for young-adult BMI	BMI							
<25.0			1.0	1.0			1.0			1.0
25.0-29.9			0.75 0.58-0.96	0.67 0.50-0.88			0.53 0.36-0.80			0.82 0.55-1.24
30.0			0.85 0.62-1.17	0.69 0.46-1.03			0.54 0.31-0.95			0.93 0.50-1.70
			$P_{\mathrm{trend}}=0.17$	$P_{\mathrm{trend}}=0.03$			$P_{ m trend}=0.02$			$P_{\mathrm{trend}} = 0.62$
Weight gain (kg) ^{4,9}										

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			V	All		H	Hispanics	Z	Non-Hispanic Whites	c Whites
	ER+PR+ cases (n=575)	Controls (n=1,418)			ER+PR+ cases (n=285)	Controls (n=765)		ER+PR+ cases (n=290)	Controls (n=653)	
	u	u	OR ¹ (95%CI)	OR ² (95%CI)	u	u	OR ² (95%CI)	п	n	OR ³ (95%CI)
Q1: <7.5	170	349	1.0	1.0	75	154	1.0	95	195	1.0
Q2: 7.5-13.6	69	222	0.66 0.47-0.92	0.67 0.47-0.94	36	124	0.59 0.36-0.97	33	98	0.70 0.43-1.15
Q3: 13.7-22.7	139	350	0.83 0.63-1.10	0.83 0.61-1.13	67	206	0.67 0.43-1.04	72	144	1.05 0.68-1.63
Q4: >22.7	124	307	0.80 0.59-1.07	0.83 0.57-1.21	64	178	0.70 0.42-1.17	60	129	1.02 0.58-1.79
			$P_{\rm trend} = 0.21$	$P_{\rm trend} = 0.34$			$P_{\rm trend} = 0.16$			$P_{\mathrm{trend}}=0.83$
Young-adult BMI (kg/m ²⁾ $^{6.10}$ and current BMI (kg/m ²) 7	m^2) 6,10 and c	urrent BMI (k	$g/m^2)^7$							
<21.8/<25	242	436	1.0	1.0	89	136	1.0	153	300	1.0
<21.8/25-25.9	83	185	0.82 0.60-1.13	0.74 0.52-1.04	38	98	0.55 0.33-0.93	45	85	0.93 0.58-1.48
<21.8/ 30	28	56	0.89 0.54-1.47	0.74 0.42-1.30	15	32	0.60 0.27-1.33	13	24	0.94 0.42-2.13
21.8/<25	48	113	0.82 0.56-1.22	0.77 0.52-1.15	29	64	0.70 0.40-1.21	19	49	$0.82 \ 0.45 - 1.49$
21.8 / 25-25.9	63	245	0.52 0.37-0.73	0.46 0.32-0.67	45	177	0.39 0.24-0.63	18	68	0.49 0.26-0.91
21.8 / 30	100	318	0.58 0.43-0.79	0.46 0.30-0.70	64	219	0.35 0.19-0.62	36	66	0.63 0.33-1.19
			$P_{\rm interaction} = 0.64$	$P_{\rm interaction} = 0.74$			$P_{ m interaction} = 0.94$			$P_{ m interaction} = 0.63$
Waist (cm) ⁴										
Q1: <78.7	171	351	1.0	1.0	56	106	1.0	115	245	1.0
Q2: 78.8-87.0	129	341	0.83 0.63-1.11	0.94 0.70-1.26	67	196	0.87 0.54-1.38	62	145	$0.94\ 0.63-1.40$
Q3: 87.1-97.7	130	343	0.89 0.66-1.19	1.14 0.82-1.58	73	227	$1.19\ 0.73 - 1.96$	57	116	1.04 0.66-1.63
Q4: >97.7	131	345	0.82 0.61-1.10	1.39 0.92-2.10	81	219	2.11 1.15-3.88	50	126	0.81 0.44-1.47
			$P_{\rm trend} = 0.25$	$P_{\mathrm{trend}}=0.11$			$P_{\mathrm{trend}} = 0.01$			$P_{\mathrm{trend}} = 0.76$
$\operatorname{Hip}\left(\operatorname{cm}\right)^{4}$										
Q1: <99.1	146	345	1.0	1.0	65	166	1.0	81	179	1.0
Q2: 99.2-106.1	139	345	0.98 0.74-1.31	$1.10\ 0.82-1.47$	69	184	1.19 0.78-1.83	70	161	1.01 0.67-1.52
Q3: 106.2-115.2	140	346	0.97 0.73-1.29	1.26 0.92-1.72	71	197	1.42 0.90-2.24	69	149	1.06 0.68-1.66
Q4: >115.2	136	345	0.92 0.69-1.24	1.64 1.09-2.44	72	202	2.18 1.25-3.80	64	143	1.18 0.64-2.15
			$P_{\rm trend} = 0.59$	$P_{\rm trend} = 0.02$			$P_{\rm trend} = 0.01$			$P_{\rm trend} = 0.63$

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Waist-to-hip ratio⁴

			V	IIV			Hispanics	Z	Non-Hispanic Whites	: Whites
	ER+PR+ cases (n=575)	Controls (n=1,418)			ER+PR+ cases (n=285)	Controls (n=765)		ER+PR+ cases (n=290)	Controls (n=653)	
	ц	п	OR ¹ (95%CI)	OR ² (95%CI)	a	п	OR ² (95%CI)	u	п	OR ³ (95%CI)
Q1: <0.77	161	345	1.0	1.0	45	87	1.0	116	258	1.0
Q2: 0.78-0.82	151	345	0.99 0.75-1.30	1.05 0.79-1.40	60	168	0.82 0.50-1.34	91	177	1.16 0.82-1.65
Q3: 0.83-0.86	127	345	0.87 0.65-1.18	0.97 0.71-1.32	84	236	0.97 0.60-1.56	43	109	0.87 0.56-1.36
Q4: >0.86	122	345	0.85 0.62-1.16	1.02 0.73-1.42	88	257	1.13 0.69-1.85	34	88	0.78 0.47-1.29
			$P_{\rm trend} = 0.23$	$P_{\rm trend} = 0.97$			$P_{\rm trend} = 0.32$			$P_{\rm trend} = 0.32$
Waist-to-height ratio	4									
Q1: <0.49	172	345	1.0	1.0	49	71	1.0	123	274	1.0
Q2: 0.50-0.55	140	345	$0.84\ 0.63-1.11$	0.94 0.70-1.26	65	191	$0.66\ 0.40-1.09$	75	154	1.04 0.72-1.52
Q3: 0.56-0.62	122	344	0.81 0.60-1.11	1.07 0.75-1.51	79	242	0.98 0.57-1.68	43	102	0.92 0.56-1.53
Q4: >0.62	127	346	0.78 0.57-1.06	1.30 0.84-2.01	84	244	1.50 0.80-2.84	43	102	0.87 0.45-1.67
			$P_{\mathrm{trend}} = 0.12$	$P_{\mathrm{trend}} = 0.26$			$P_{ m trend}=0.06$			$P_{\rm trend} = 0.70$
lOdds ratios and 95% confidence intervals, adjusted for age (years, cc school, high school graduate, post high school education), family histt birth (<20, 20-24, 25-29, 30, nulliparous), lifetime number of monthiconsumption in reference year (g/day; 0, 0, 1-4, 9, 5-9, 9, 10-19.9, 20).	confidence inter duate, post high 9, 30, nulliparc ce year (g/day; (vals, adjustec school educ: ous), lifetime), 0.1-4.9, 5-5	I for age (years, cont ation), family history number of months o 9.9, 10-19.9, 20).	inuous), study (SFB ' of breast cancer in - f breastfeeding (null	CS, 4-CBCS first degree r liparous, 0, 1-	(), ethnicity/ elatives (no -6, 7-12, 13	acculturation (low, r , yes), age at menarc -24, >24), hormonal	noderate, hig the (<12, 12, 12, contraception	h, non-Hispa 13, 14), par 1 use (never,	¹ Odds ratios and 95% confidence intervals, adjusted for age (years, continuous), study (SFBCS, 4-CBCS), ethnicity/acculturation (low, moderate, high, non-Hispanic white), education (less than high school high school graduate, post high school education), family history of breast cancer in first degree relatives (no, yes), age at menarche (<12, 12, 13, 14), parity (nulliparous, 1-2, 3-4, 5), age at first birth (<20, 20-24, 25-29, 30, nulliparous), lifetime number of months of breastfeeding (nulliparous, 0, 1-6, 7-12, 13-24, >24), hormonal contraception use (never, former, current), and average alcohol consumption in reference year (g/day; 0, 0.1-4.9, 5-9.9, 10-19.9, 20).
² Overall obesity measures additionally adjusted for waist circumference (continuous) and abdominal obesity measures additionally adjusted for current BMI (continuous).	tres additionally	adjusted for	waist circumference	(continuous) and ab	dominal obe	sity measur	es additionally adjus	ted for curren	ıt BMI (conti	inuous).
3 Adjusted for all variables above except acculturation.	bles above excep	ot acculturation	on.							
⁴ Based on quartiles among all premenopausal controls.	ong all premenc	ppausal contr	ols.							
5 Based on measured height at interview (for SFBCS participants, self-reported adult height was used when measured height was not available).	sight at interviev	v (for SFBCS	5 participants, self-re-	ported adult height v	vas used whe	en measured	l height was not avai	llable).		
⁶ Based on self-reported averaged weight at age 15 and age April 1995 to April 1998 and matched controls and betwee self-reported adult height was used when measured height	d averaged weig 38 and matched ht was used whe	ht at age 15 a controls and en measured	and age 30 for 4-CBCS ca between ages 20-29 for cc height was not available).	CS cases and control for cases diagnosed able).	s, self-report from May 19	ed weight ii 998 to April	a the 20's for SFBC ⁶ 2002 and matched c	S cases and cc controls), and	ontrols (betw measured he	6 seed on self-reported averaged weight at age 15 and age 30 for 4-CBCS cases and controls, self-reported weight in the 20's for SFBCS cases and controls (between ages 25-30 for cases diagnosed from April 1995 to April 1995 to April 1998 and matched controls), and measured height at interview (for SFBCS participants, self-reported adult height was used when measured height was not available).
7 Based on self-reported weight in reference year (or measured weight for SFBCS participants for whom measured height was not available).	d weight in refer for whom meas	ence year (or sured height v	r measured weight at was not available).	interview if self-rep	oorted weight	t in referenc	e year was not avail:	able) and mea	isured height	7 Based on self-reported weight in reference year (or measured weight at interview if self-reported weight in reference year was not available) and measured height at interview (or self-reported adult height for SFBCS participants for whom measured height was not available).
8 Adjusted additionally for young-adult BMI (continuous).	for young-adult	BMI (contin	uous).							

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 9 Based on self-reported weight in reference year (or measured weight at interview when self-reported weight was not available) minus self-reported young-adult weight; excludes 62 premenopausal ER+PR + cases and 125 premenopausal controls who lost weight.

 $^{IO}\mathrm{Based}$ on the median among all premenopausal controls.

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Overall and Abdominal Body Size Associations with ER-PR- Breast Cancer in Premenopausal Women, by Ethnicity

FP.P. (0:231) (0:1413) <th <="" colspa="2" t<="" th=""><th></th><th></th><th></th><th>V</th><th>All</th><th></th><th></th><th>Hispanics</th><th>Ż</th><th>Non-Hispanic Whites</th><th>c Whites</th></th>	<th></th> <th></th> <th></th> <th>V</th> <th>All</th> <th></th> <th></th> <th>Hispanics</th> <th>Ż</th> <th>Non-Hispanic Whites</th> <th>c Whites</th>				V	All			Hispanics	Ż	Non-Hispanic Whites	c Whites
n n $0R^4$ (95%C) $0R^2$ (95%C) n n $0R^2$ (95%C) 70 468 10 10 394 10 75 466 107075-1.55 110076-1.60 59 394 10 75 466 107075-1.55 1.0076-1.60 59 394 10 75 466 107075-1.55 1.0076-1.60 45 222 1.13073-1.75 75 466 100 76 47 38 117 201124325 84 446 100 10 46 157 10 84 446 10 10 46 157 10 84 446 090641-126 082058-1.17 51 230 056020663 95 459 063043093 044028-069 38 339 056020663 106 57 10 230 05602066 56 049025606 65 394 080057-140 0590355099		ER-PR- cases (n=247)	Controls (n=1,418)			ER-PR- cases (n=142)	Controls (n=765)		ER-PR- cases (n=105)	Controls (n=653)		
70 468 1.0 1.0 5.9 3.4 1.0 75 466 1.070751.55 1.10076-1.60 45 2.22 113073-1.75 102 482 1.50103-2.19 1.52103-2.24 38 117 2.01124-3.25 $P_{read} = 0.03$ 88 446 1.0 1.0 46 1.57 1.0 84 446 0.90.064-1.26 0.82.058-1.17 51 2.30 0.77.048-1.24 84 446 0.90.064-1.26 0.82.058-1.17 51 2.30 0.77.048-1.24 99 456 0.80.054-1.26 0.82.058-1.17 51 2.30 0.77.048-1.24 91 7 7 1.0 7 1.0 7 1.0 7 446 0.90.064-1.26 0.82.058-1.17 51 2.30 0.77.048-1.24 8 410 0.01 1.0 7 2.22 1.0 1.0 <		u	u	OR ^I (95%CI)	OR ² (95%CI)	u	u	OR ² (95%CI)	u	u	OR ³ (95%CI)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Current height (m) ^{4,5}											
75 466 107 0.75-1.55 1.10 0.76-1.60 45 222 1.13 0.73-1.75 102 482 1.50 1.03.2.19 1.52 1.03.2.24 38 1.17 2.01 1.34.325 $p_{read} = 0.03$ $p_{read} = 0.03$ $p_{read} = 0.03$ $p_{read} = 0.03$ $p_{read} < 0.01$ 88 446 1.0 1.0 46 1.7 $p_{read} < 0.01$ 84 446 0.90 0.64+1.26 0.82 0.58+1.17 51 2.00 0.77 0.48+1.24 84 446 0.90 0.64+1.26 0.82 0.58+1.17 51 2.00 0.77 0.48+1.24 84 446 0.90 0.64+1.26 0.82 0.58+1.17 51 2.00 0.77 0.48+1.24 90 0.410 2.80.69 38 0.36 0.20 0.63 38 0.36 0.20 0.63 106 576 1.0 0.40 0.28 0.69 38 399 0.36 0.20 0.63 106 576 1.0 1.0 1.0 1.0 1.0 1.0 106 57 1.0 2.6 0.90 0.53 0.5	T1:<1.56	70	468	1.0	1.0	59	394	1.0	11	74	1.0	
	T2: 1.56-1.63	75	466	1.07 0.75-1.55	1.10 0.76-1.60	45	252	1.13 0.73-1.75	30	214	0.89 0.42-1.88	
$T_{pend} = 0.03$ $P_{mend} = 0.03$ $P_{mend} = 0.03$ T_{p} 446 1.0 1.0 46 1.0 84 446 0.90.064-1.26 0.82.058-1.17 51 230 0.70.048-1.24 84 446 0.90.064-1.26 0.82.058-1.17 51 230 0.70.048-1.24 84 446 0.90.064-1.26 0.82.0589 38 339 0.36.020-0.63 75 446 0.90.071-1.38 0.44.028.069 38 339 0.36.020-0.63 106 576 1.0 1.0 1.0 $P_{mend} = 0.02$ $P_{mend} = 0.02$ $P_{mend} = 0.04$ 76 446 0.99.071-1.38 0.80.055-1.15 48 286 0.68.042-1.10 75 446 0.90.071-1.38 0.80.055-1.15 48 286 0.49.025-0.96 76 446 0.90.069-1.40 0.59.055-0.16 $P_{mend} = 0.05 P_{mend} = 0.04 P_{mend} = 0.04 8.adjusted for young-adult BMI P_{mend} = 0.93 P_{mend} = 0.05 $	T3: >1.63	102	482	1.50 1.03-2.19	1.52 1.03-2.24	38	117	2.01 1.24-3.25	64	365	1.01 0.50-2.03	
$ \begin{array}{llllllllllllllllllllllllllllllllllll$				$P_{\rm trend} = 0.03$	$P_{\rm trend} = 0.03$			$P_{\rm trend} < 0.01$			$P_{\mathrm{trend}}=0.80$	
88 446 10 10 46 10 10 46 10 10 84 446 090.0441.26 082.058-1.17 51 230 0.77.048-1.24 59 459 0.63.043-0.93 0.44.0.28-0.69 38 339 0.36.0.20-0.63 76 446 0.90.071-1.38 0.44.0.28-0.90 41 20 $p_{rend} < 0.01$ 76 446 0.99.0.71-1.38 0.80.0.55-1.15 48 286 0.68.042-1.10 76 446 0.99.0.71-1.38 0.80.0.55-1.15 48 286 0.49.0.25-0.96 65 394 0.99.0.51-1.40 0.59.0.35-0.99 41 265 0.49.0.25-0.96 65 394 0.98.0.69-1.40 0.50.0.35-0.15 48 286 0.68.042-1.10 8 adjusted for young-adult BMI $P_{rend} = 0.05$ $P_{rend} = 0.05$ $P_{rend} = 0.04$ $P_{rend} = 0.04$ 8 adjusted for young-adult BMI 1.0 1.0 1.0 $P_{rend} = 0.44$ $P_{rend} = 0.44$ 8 adjuste	Young-adult BMI (kg/m ²) ^{4,6}											
84 446 0.90 0.64+1.26 0.82 0.58+1.17 51 230 0.77 0.48-1.24 59 459 0.63 0.43-0.93 0.44 0.28-0.69 38 339 0.36 0.20-0.63 7 $P_{wend} = 0.02$ $P_{wend} = 0.02$ $P_{wend} < 0.01$ $P_{wend} < 0.01$ $P_{wend} < 0.01$ 106 576 1.0 1.0 53 212 1.0 76 446 0.90 0.71-1.38 0.80 0.55-1.15 48 286 0.68 0.42-1.10 65 394 0.99 0.71-1.38 0.80 0.55-1.15 48 286 0.69 0.42-1.10 65 394 0.99 0.71-1.38 0.80 0.55-1.15 48 286 0.69 0.42-1.10 65 394 0.98 0.69-1.31 P_wend = 0.05 41 265 0.49 0.25-0.96 $R_{uend} = 0.93 P_{wend} = 0.05 P_{wend} = 0.05 P_{wend} = 0.04 P_{wend} = 0.04 R_{uend} = 0.93 P_{wend} = 0.05 P_{wend} = 0.05 P_{wend} = 0.41 P_{wend} = 0.41 R_{uend} = 0.26 P_{wend} = 0.26 P_{wen$	T1: <20.6		446	1.0	1.0	46	157	1.0	42	289	1.0	
59 459 0.63 0.43 0.03 0.44 0.28 0.69 38 339 0.36 0.20 0.63 $P_{tend} = 0.02$ $P_{tend} < 0.01$ $P_{tend} < 0.01$ $P_{tend} < 0.01$ $P_{tend} < 0.01$ 106 576 1.0 1.0 53 212 1.0 76 446 0.99 0.71-1.38 0.80 0.55-1.15 48 286 0.43 0.1.10 65 394 0.98 0.69-1.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 65 394 0.98 0.69-1.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 65 394 0.98 0.60-1.31 P_{tend} = 0.05 41 265 0.49 0.25-0.96 8 P_{tend} = 0.93 P_{tend} = 0.05 41 266 0.49 0.25-0.96 8 265 0.49 0.25-0.96 0.49 0.25-0.96 8 P_{tend} = 0.93 P_{tend} = 0.05 1.0 0.30 0.30 0.30 1.0 8	T2: 20.6-23.1	84	446	0.90 0.64-1.26	0.82 0.58-1.17	51	230	0.77 0.48-1.24	33	216	0.87 0.51-1.47	
$P_{\text{tend}} = 0.02$ $P_{\text{tend}} < 0.01$ $P_{\text{tend}} < 0.01$ 106 576 1.0 5.3 212 1.0 76 446 0.99 0.71-1.38 0.80 0.55-1.15 48 286 0.68 0.42-1.10 65 394 0.98 0.691.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 65 394 0.98 0.691.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 65 394 0.98 0.691.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 65 394 0.98 0.60-1.31 $P_{\text{tend}} = 0.05$ $P_{\text{tend}} = 0.04$ $P_{\text{tend}} = 0.04$ 6 1.0 1.0 1.0 1.0 $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.41$ 7 411 $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.41$ $P_{\text{tend}} = 0.41$ 7 414 $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.41$ 7 414 $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.34$ $P_{\text{tend}} = 0.41$ <	T3: >23.1	59	459	0.63 0.43-0.93	$0.44\ 0.28-0.69$	38	339	0.36 0.20-0.63	21	120	0.67 0.32-1.37	
				$P_{\rm trend} = 0.02$	$P_{\rm trend} < 0.01$			$P_{\rm trend} <\!\! 0.01$			$P_{\mathrm{trend}}=0.27$	
	Current BMI $(kg/m^2)^7$											
76 446 0.99 0.71-1.38 0.80 0.55-1.15 48 286 0.68 0.42-1.10 65 394 0.98 0.69-1.40 0.59 0.35-0.99 41 265 0.49 0.25-0.96 $P_{\rm rend} = 0.93$ $P_{\rm rend} = 0.05$ $P_{\rm rend} = 0.05$ $P_{\rm rend} = 0.04$ 7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 1.0 2.78 , adjusted for young-adult BMI 1.0 1.0 1.0 7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 $1.3080-1.61$ 0.89 0.60-1.31 0.82 0.49-1.37 0.82 0.49-1.37 $1.20808-1.99$ 0.76 0.43-1.33 0.73 0.33-1.55 0.73 0.33-1.55 $P_{\rm rend} = 0.26$ $P_{\rm rend} = 0.34$ $P_{\rm rend} = 0.41$ $P_{\rm rend} = 0.41$ 75 414 1.0 1.0 0.73 0.52-1.10 0.53 0.52-1.53 75 414 1.0 1.0 1.0	<25.0	106	576	1.0	1.0	53	212	1.0	53	364	1.0	
65 394 0.98 0.69-1.40 0.59 0.35 0.39 41 265 0.49 0.25 0.96 $P_{\rm tend} = 0.93$ $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.04$ 7.8 $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.04$ 7.8 $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.05$ 1.0 1.0 1.0 1.0 1.0 $1.13 0.80 - 1.61$ $0.89 0.60 - 1.31$ $0.73 0.32 - 1.37$ $1.13 0.80 - 1.61$ $0.89 0.60 - 1.31$ $0.73 0.33 - 1.55$ $1.28 0.83 - 1.99$ $0.76 0.43 - 1.33$ $0.73 0.33 - 1.55$ $P_{\rm tend} = 0.26$ $P_{\rm tend} = 0.34$ $P_{\rm tend} = 0.41$ 75 414 1.0 1.0 1.0 75 414 1.0 $0.90 0.63 - 1.30$ $0.79 0.54 - 1.16$ 36 $0.29 0.37 - 1.03$	25.0-29.9	76	446	0.99 0.71-1.38	0.80 0.55-1.15	48	286	$0.68\ 0.42-1.10$	28	160	1.01 0.57-1.78	
7.8 , adjusted for young-adult BMI $P_{\rm tend} = 0.05$ $P_{\rm tend} = 0.04$ 7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 1.0 1.0 1.13 0.890.60-1.31 0.820.49-1.37 1.2 0.820.43-1.33 0.730.35-1.55 1.2 0.83-1.99 0.760.43-1.33 0.730.35-1.55 $P_{\rm tend} = 0.26$ $P_{\rm tend} = 0.34$ $P_{\rm tend} = 0.41$ 75 414 1.0 1.0 75 337 0.900.65-1.30 0.790.54-1.16 63 337 0.900.65-1.30 36	30.0	65	394	0.98 0.69-1.40	0.59 0.35-0.99	41	265	0.49 0.25-0.96	24	129	0.85 0.38-1.87	
7.8 , adjusted for young-adult BMI 1.0 1.0 1.0 1.0 1.0 1.0 1.0 $1.13 0.80-1.61$ $0.89 0.60-1.31$ $0.82 0.49-1.37$ $1.28 0.83-1.99$ $0.76 0.43-1.33$ $0.73 0.35-1.55$ $P_{tend} = 0.26$ $P_{tend} = 0.34$ $P_{tend} = 0.41$ 75 414 1.0 1.0 63 37 $0.90 0.63-1.30$ $0.79 0.54-1.16$ 36 0.229 $0.62 0.37-1.03$				$P_{\rm trend} = 0.93$	$P_{\mathrm{trend}}=0.05$			$P_{\mathrm{trend}}=0.04$			$P_{\mathrm{trend}}=0.72$	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Current BMI (kg/m ²) $7,8$, adju	usted for young	g-adult BMI									
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	<25.0			1.0	1.0			1.0			1.0	
1.28 0.83-1.99 0.76 0.43-1.33 0.73 0.35-1.55 $P_{\text{tend}} = 0.26$ $P_{\text{tend}} = 0.34$ 0.73 0.35-1.55 75 414 1.0 1.0 46 183 1.0 63 397 0.90 0.63-1.30 0.79 0.54-1.16 36 229 0.62 0.37-1.03	25.0-29.9			1.13 0.80-1.61	0.89 0.60-1.31			$0.82 \ 0.49 - 1.37$			1.01 0.56-1.82	
$P_{\text{trend}} = 0.26$ $P_{\text{trend}} = 0.34$ $P_{\text{trend}} = 0.41$ 75 414 1.0 1.0 46 183 1.0 63 377 0.90 0.63-1.30 0.79 0.54-1.16 36 229 0.62 0.37-1.03	30.0			1.28 0.83-1.99	$0.76\ 0.43-1.33$			0.73 0.35-1.55			0.86 0.36-2.04	
75 414 1.0 1.0 46 183 1.0 63 397 0.90 0.63-1.30 0.79 0.54-1.16 36 229 0.62 0.37-1.03				$P_{\rm trend} = 0.26$	$P_{\rm trend} = 0.34$			$P_{\rm trend} = 0.41$			$P_{\mathrm{trend}}=0.77$	
75 414 1.0 1.0 1.0 46 183 1.0 63 397 0.90 0.63-1.30 0.79 0.54-1.16 36 229 0.62 0.37-1.03	Weight gain (kg) ^{4,9}											
63 397 0.90 0.63-1.30 0.79 0.54-1.16 36 229 0.62 0.37-1.03	T1: <9.1	75	414	1.0	1.0	46	183	1.0	29	231	1.0	
	T2: 9.1-18.1	63	397	0.90 0.63-1.30	0.79 0.54-1.16	36	229	0.62 0.37-1.03	27	168	$1.06\ 0.58-1.94$	

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	ER-PR- cases (n=247)	Controls (n=1,418)			ER-PR- cases (n=142)	Controls (n=765)		ER-PR- cases (n=105)	Controls (n=653)	
	u	u	OR ¹ (95%CI)	OR ² (95%CI)	u	п	OR ² (95%CI)	u	п	OR ³ (95%CI)
T3: >18.1	76	417	1.05 0.74-1.50	0.75 0.47-1.18	44	250	0.65 0.36-1.16	32	167	0.91 0.43-1.93
			$P_{\rm trend} = 0.79$	$P_{\rm trend} = 0.20$			$P_{\rm trend} = 0.14$			$P_{\rm trend} = 0.83$
Waist (cm) ⁴										
T1: <81.3	72	463	1.0	1.0	31	158	1.0	41	305	1.0
T2: 81.4-93.6	79	458	1.16 0.81-1.66	1.33 0.91-1.93	52	289	1.36 0.81-2.29	27	169	1.17 0.67-2.03
T3: >93.6	86	459	1.29 0.91-1.84	1.86 1.16-3.01	54	301	2.17 1.13-4.17	32	158	1.45 0.70-2.98
			$P_{\rm trend} = 0.16$	$P_{\rm trend} = 0.01$			$P_{\rm trend} = 0.02$			$P_{\rm trend} = 0.32$
Hip (cm) ⁴										
T1:<101.6	72	455	1.0	1.0	39	216	1.0	33	239	1.0
T2: 101.7-111.7	74	457	1.06 0.74-1.50	1.18 0.82-1.70	45	261	1.33 0.82-2.19	29	196	1.05 0.60-1.82
T3: >111.7	91	469	1.27 0.91-1.79	1.77 1.13-2.77	53	272	2.39 1.31-4.35	38	197	1.17 0.58-2.33
			$P_{\rm trend} = 0.16$	$P_{\rm trend} = 0.02$			$P_{\rm trend} = 0.01$			$P_{\rm trend} = 0.68$
Waist-to-hip ratio ⁴										
T1: <0.79	67	455	1.0	1.0	28	135	1.0	39	320	1.0
T2: 0.79-0.85	87	455	1.35 0.95-1.93	1.41 0.98-2.02	49	271	$1.09\ 0.64-1.84$	38	184	1.68 1.02-2.77
T3: >0.85	83	470	1.34 0.92-1.95	1.46 0.98-2.19	60	342	1.26 0.73-2.17	23	128	1.57 0.85-2.89
			$P_{\rm trend} = 0.14$	$P_{\rm trend} = 0.07$			$P_{\rm trend} = 0.36$			$P_{\rm trend} = 0.09$
Waist-to-height ratio ⁴										
T1: <0.51	69	455	1.0	1.0	27	123	1.0	42	332	1.0
T2: 0.52-0.59	79	455	1.22 0.85-1.75	1.43 0.98-2.11	50	291	1.17 0.68-2.03	29	164	1.43 0.82-2.48
T3: >0.59	89	470	1.40 0.97-2.03	2.19 1.33-3.60	60	334	2.11 1.07-4.15	29	136	1.99 0.94-4.23
			$P_{\rm trend} = 0.07$	$P_{\rm trend} < 0.01$			$P_{\mathrm{trend}}=0.02$			$P_{\rm trend} = 0.07$

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² Overall obesity measures additionally adjusted for waist circumference (continuous) and abdominal obesity measures additionally adjusted for current BMI (continuous).

 3 Adjusted for all variables above except acculturation.

 4 Based on tertiles among all premenopausal controls.

5 Based on measured height at interview (for SFBCS participants, self-reported adult height was used when measured height was not available).

April 1995 to April 1998 and matched controls and between ages 20-29 for cases diagnosed from May 1998 to April 2002 and matched controls), and measured height at interview (for SFBCS participants, 6° Based on self-reported averaged weight at age 15 and age 30 for 4-CBCS cases and controls, self-reported weight in the 20's for SFBCS cases and controls (between ages 25-30 for cases diagnosed from self-reported adult height was used when measured height was not available).

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7 Based on self-reported weight in reference year (or measured weight at interview if self-reported weight in reference year was not available) and measured height at interview (or self-reported adult height for SFBCS participants for whom measured height was not available).

 $^{8}_{
m Adjusted}$ additionally for young-adult BMI (continuous).

9 Based on self-reported weight in reference year (or measured weight at interview when self-reported weight was not available) minus self-reported young-adult weight; excludes 17 premenopausal ER–PR - cases and 125 premenopausal controls who lost weight.

Table 5

Abdominal Adiposity Associations with Premenopausal Breast Cancer in Hispanic Women, by Current BMI

		Н	lispanics
	Cases (n=497)	Controls (n=765)	
	n	n	OR ¹ (95%CI)
Current BMI ² (kg/m ²) and waist	circumference (cm) ³		
<25.0/ 88.0	167	185	1.0
<25.0/>88.0	21	20	1.25 0.64-2.45
25.0-29.9 / 88.0	62	159	0.49 0.33-0.71
25.0-29.9 / >88.0	93	120	0.99 0.68-1.43
30.0 / 88.0	16	29	0.65 0.33-1.28
30.0 / >88.0	122	235	0.63 0.45-0.88
			$P_{\text{interaction}} = 0.15$
Current BMI ² (kg/m ²) and hip c	ircumference (cm) ⁴		
<25.0/ 106.3	158	185	1.0
<25.0/>106.3	30	21	1.51 0.81-2.81
25.0-29.9 / 106.3	72	159	0.62 0.43-0.90
25.0-29.9 / >106.3	83	120	0.84 0.58-1.22
30.0 / 106.3	17	29	0.76 0.39-1.49
30.0 / >106.3	121	235	0.64 0.45-0.89
			$P_{\text{interaction}} = 0.38$
Current BMI ² (kg/m ²) and waist	-to-hip ratio ³		
<25.0/ 0.85	162	181	1.0
<25.0/>0.85	26	24	1.39 0.75-2.59
25.0-29.9 / 0.85	96	195	0.61 0.43-0.86
25.0-29.9 / >0.85	59	84	0.98 0.64-1.50
30.0 / 0.85	68	131	0.62 0.42-0.92
30.0 / >0.85	70	133	0.67 0.45-0.99
			$P_{\text{interaction}} = 0.44$
Current BMI ² (kg/m ²) and waist	-to-height ratio 4		
<25.0/ 0.56	176	187	1.0
<25.0/>0.56	12	18	0.67 0.31-1.49
25.0-29.9 / 0.56	66	160	0.47 0.32-0.68
25.0-29.9 / >0.56	89	119	0.95 0.66-1.38
30.0 / 0.56	12	27	0.49 0.23-1.02
30.0 / >0.56	126	237	0.62 0.44-0.86
			$P_{\text{interaction}} = 0.05$

¹Odds ratios and 95% confidence intervals, adjusted for age (years, continuous), study (SFBCS, 4-CBCS), ethnicity/acculturation (low, moderate, high, non-Hispanic white), education (less than high school, high school graduate, post high school education), family history of breast cancer in first degree relatives (no, yes), age at menarche (<12, 12, 13, 14), parity (nulliparous, 1-2, 3-4, 5), age at first birth (<20, 20-24, 25-29, 30, nulliparous), lifetime number of months of breastfeeding (nulliparous, 0, 1-6, 7-12, 13-24, >24), hormonal contraception use (never, former, current), average alcohol consumption in reference year (g/day; 0, 0.1-4.9, 5-9.9, 10-19.9, 20).

²Based on self-reported weight in reference year (or measured weight at interview if self-reported weight in reference year was not available) and measured height at interview (or self-reported adult height for SFBCS participants for whom measured height was not available).

 ${}^{\mathcal{S}}\textsc{Based}$ on median among all Hispanic premenopausal controls.

⁴Based on WHO categories.

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Body Size Associations in Premenopausal Hispanic Women, by Genetic Ancestry and ER/PR Status

Table 6

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			Indigenous American Ancestry 12 46%	ıs stry 12				Indigenous American Ancestry >46%	stry 1,2	
	Controls (n=267)	ER+PR+ cases (n=102)		ER-PR- cases (n=55)		Controls (n=267)	ER+PR+ cases (n=85)		ER-PR- cases (n=38)	
	u	u	OR ³ (95%CI)	u	OR ⁴ (95%CI)	u	u	OR ³ (95%CI)	u	OR ⁴ (95%CI)
Current height (m) 5.6										
T1: <1.53	64	16	1.0	14	1.0	107	26	1.0	12	1.0
T2: 1.53-1.58	87	34	1.38 0.67-2.85	16	0.86 0.38-1.96	88	31	0.97 0.48-1.97	11	0.97 0.39-2.41
T3: >1.58	116	52	1.61 0.81-3.19	25	0.98 0.46-2.11	72	28	1.20 0.57-2.52	15	1.50 0.61-3.64
			$P_{\mathrm{trend}} = 0.18$		$P_{\rm trend} = 0.97$			$P_{\mathrm{trend}} = 0.63$		$P_{\rm trend} = 0.37$
Young-adult BMI (kg/m ²) 5,7	2									
T1: <21.3	83	50	1.0	25	1.0	60	24	1.0	8	1.0
T2: 21.3-24.0	113	29	0.43 0.23-0.81	15	0.86 0.39-1.88	94	31	1.31 0.64-2.66	14	0.91 0.39-2.13
T3: >24.0	71	23	0.39 0.18-0.86	15	1.37 0.56-3.35	113	30	0.38 0.16-0.93	16	0.24 0.08-0.78
			$P_{\rm trend} < 0.01$		$P_{\rm trend} = 0.54$			$P_{ m trend}=0.05$		$P_{\mathrm{trend}} = 0.02$
Current BMI (kg/m ²) 8										
<25.0	95	54	1.0	24	1.0	77	33	1.0	14	1.0
25.0-29.9	87	26	0.37 0.19-0.71	14	0.52 0.24-1.15	73	34	1.16 0.51-2.60	16	1.13 0.41-3.15
30.0	73	21	0.39 0.15-1.00	16	0.68 0.23-2.03	102	16	0.84 0.30-2.37	9	1.07 0.32-3.65
			$P_{ m trend}=0.02$		$P_{\rm trend} = 0.36$			$P_{\mathrm{trend}} = 0.68$		$P_{\rm trend} = 0.93$
Current BMI (kg/m ²) 8,9 adjusted for young-adult BMI	isted for young	-adult BMI								
<25.0			1.0		1.0			1.0		1.0
25.0-29.9			0.39 0.20-0.77		$0.54\ 0.24$ -1.20			1.15 0.50-2.63		1.34 0.45-3.97
30.0			0.49 0.17-1.39		0.64 0.19-2.19			$1.06\ 0.35-3.14$		1.67 0.43-6.56
			$P_{\mathrm{trend}}=0.06$		$P_{\rm trend} = 0.32$			$P_{\mathrm{trend}} = 0.94$		$P_{\mathrm{trend}} = 0.46$
Weight gain (kg) 5,10										
T1: <10.0	85	46	1.00	26	1.00	71	26	1.00	12	1.00

				Indigenous	us 12					Indigenous	IS 1,2	
				American Ancestry 46%	estry					American Ancestry > 46%	sury	
	Con (n≡)	Controls (n=267)	ER+PR+ cases (n=102)		ER-PR- cases (n=55)			Controls (n=267)	ER+PR+ cases (n=85)		ER-PR- cases (n=38)	
	u	e	u	OR ³ (95%CI)	u	OR ⁴ (95%CI)	5%CI)	u	u	OR ³ (95%CI)	u	OR ⁴ (95%CI)
T2: 10.0-19.3	2	75	24	0.61 0.32-1.15	6	0.37 0.16-0.87	6-0.87	76	16	0.64 0.28-1.46	9	0.45 0.15-1.34
T3:>19.3	7	73	20	$P_{ m trend} = 0.045$	13	$0.41 \ 0.15-1.09$ $P_{\rm trend} = 0.04$	5-1.09 0.04	86	32	$1.25\ 0.54-2.88$ $P_{\rm trend} = 0.55$	17	$P_{\rm trend} = 0.66$
	Controls (n=267)	All cases (n=187)			Controls (n=267)	All cases (n=140)						
	ц	u	OR ³	OR ³ (95%CI)	п	n	OR ³ (95%CI)	%CI)				
Waist (cm) ⁵									I			
T1: <84.5	68	98	1.0		35	75	1.0					
T2: 84.6-95.3	62	85	1.290	1.29 0.77-2.18	47	89	2.01 1.05-3.85	-3.85				
T3: >95.3	53	81	$P_{ m trend}^{1.65}$ 0	$1.65\ 0.84-3.26$ $P_{\rm trend}=0.14$	57	66	$2.96\ 1.36-6.41$ $P_{\rm trend} = 0.01$	-6.41 .01				
Hip (cm) ⁵												
T1: <102.0	70	06	1.0		51	91	1.0					
T2: 102.1-112.0	53	88	0.820	$0.82\ 0.48-1.40$	39	80	1.19 0.64-2.22	-2.22				
T3: >112.0	60	86	1.45~0 $P_{ m trend^{-1}}$	$1.45 \ 0.77$ -2.74 $P_{\rm trend} = 0.32$	49	92	$\frac{1.62\ 0.78-3.37}{P_{\rm trend}=0.20}$	-3.37 .20				
Waist-to-hip ratio 5												
T1: <0.81	75	103	1.0		35	62	1.0					
T2: 0.81-0.86	57	93	$0.93\ 0$	0.93 0.57-1.53	43	90	1.12 0.60-2.09	-2.09				
T3: >0.86	51	68	$P_{\rm trend}^{-1.30}$ 0	$1.30\ 0.75-2.27$ $P_{\rm trend}=0.41$	61	111	$1.54 \ 0.84-2.84$ $P_{\rm trend} = 0.14$	-2.84 .14				
Waist-to-height ratio 5												
T1: <0.54	78	107	1.0		35	64	1.0					
T2: 0.55-0.61	55	80	1.240	1.24 0.73-2.12	52	95	1.87 0.97-3.64	-3.64				
T3: >0.61	50	LL	1.80~0 $P_{ m trend}$	$P_{\rm trend} = 0.11$	52	104	$2.14\ 0.98-4.68$ $P_{\rm trend} = 0.07$	-4.68 .07				
									I			

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Based on median percent genetic admixture among premenopausal Hispanic controls.

² Information on genetic admixture was available for a subset of 444 Hispanic cases and 586 Hispanic controls for whom a blood or mouthwash sample was collected.

nulliparous), lifetime number of months of breast-feeding (nulliparous, 0, 1-6, 7-12, 13-24, >24), hormonal contraception use (never, former, current), and alcohol consumption in reference year (g/day; 0, 20). Height, young-adult BMI, current BMI, and weight gain additionally adjusted for waist circumference (continuous) and abdominal obesity measures additionally adjusted for ³Odds ratios and 95% confidence intervals, adjusted for age (years, continuous), study (4-CBCS, SFBCS), acculturation (low, moderate, high), education (some high school or less, high school graduate, 30. 5), age at first birth (<20, 20-24, 25-29, 14), parity (nulliparous, 1-2, 3-4, some college or higher), family history of breast cancer in first-degree relatives (no, yes), age at menarche (<12, 12, 13, current BMI (continuous). 0.1-4.9, 5-9.9, 10-19.9,

⁴Odds ratios and 95% confidence intervals, adjusted for age (years, continuous), study (4-CBCS, SFBCS), acculturation (low, moderate, high), and alcohol consumption in reference year (g/day; 0, 0.1-4.9, 5-9.9, 10-19.9, 20). Height, young-adult BMI, current BMI, and weight gain additionally adjusted for waist circumference (continuous) and abdominal obesity measures additionally

5 adjusted for current BMI (continuous). Based on tertiles among premenopausal Hispanic controls.

6 Based on measured height at interview (for SFBCS participants, self-reported adult height was used when measured height was not available).

April 1995 to April 1998 and matched controls and between ages 20-29 for cases diagnosed from May 1998 to April 2002 and matched controls), and measured height at interview (for SFBCS participants, 7 Pased on self-reported averaged weight at age 15 and age 30 for 4-CBCS cases and controls, self-reported weight in the 20's for SFBCS cases and controls (between ages 25-30 for cases diagnosed from self-reported adult height was used when measured height was not available). 8 Based on self-reported weight in reference year (or measured weight at interview if self-reported weight in reference year was not available) and measured height at interview (or self-reported adult height for SFBCS participants for whom measured height was not available).

⁷Adjusted additionally for young-adult BMI (continuous).

10 Based on self-reported weight in reference year (or measured weight at interview when self-reported weight was not available) minus self-reported young-adult weight; excludes 53 premenopausal Hispanic cases and 65 premenopausal Hispanic controls who lost weight.