Published in final edited form as:
Cancer Causes Control. 2008 May ; 19(4): 391–401.

Reproductive history in relation to breast cancer risk among Hispanic and non-Hispanic white women

Carol Sweeney[1], **Kathy B. Baumgartner**[2], **Tim Byers**[3], **Anna R. Giuliano**[4], **Jennifer S. Herrick**[1], **Maureen A. Murtaugh**[1], and **Martha L. Slattery**[1]

1*Division of Epidemiology, University of Utah, 30 N 1900 E, AC230, Salt Lake City, Utah 841032, USA, e-mail: carol.sweeney@hsc.utah.edu*

2*Department of Epidemiology & Population Health, University of Louisville, Louisville, KY, USA*

3*University of Colorado Cancer Center, Denver, CO, USA*

4*Moffitt Cancer Center, Tampa, FL, USA*

Abstract

Objective—To evaluate reproductive history risk factors in breast cancer among Hispanic (HISP) women in the U.S. southwest, a population with approximately 33% lower breast cancer incidence than non-Hispanic whites (NHW).

Methods—Population-based case–control study of HISP (796 cases, 919 controls) and NHW (1,525 cases, 1,596 controls) women.

Results—19.3% of HISP women reported five or more births and had a reduced risk of breast cancer, adjusted odds ratio (OR) 0.70 (95% confidence interval (CI): 0.50, 0.98) compared to those with one or two births. Breast cancer risk for HISP increased with older age at first birth, *p* trend = 0.008. Parity and age at first birth associations were specific to ER positive tumors. HISP women who had given birth within five years had higher breast cancer risk than women with 16–25 years since a birth, OR 2.62 (95% CI: 1.44, 4.78); the tend with years since last birth was stronger than for NHWs, *p* interaction = 0.05.

Conclusions—Reproductive history influences on breast cancer risk among HISP were similar to associations reported for NHWs. Differences in the prevalence of reproductive risk factors would explain an estimated 6.6% lower breast cancer incidence for HISP compared to NHWs.

Keywords

Breast neoplasms; Reproductive history; Hispanic Americans

Hispanic women in the U.S. have a lower incidence of breast cancer than NHW [1]. Racial and ethnic differences in disease incidence may be related to one or more factors: differences in the prevalence of environmental and lifestyle risk factors for the disease, differences in susceptibility to the influence of risk factors, or differences in genetic risk. Possible differences in the role of reproductive and other risk factors in breast cancer among HISP compared to NHW women have been suggested [2–4].

Several aspects of reproductive history, including age at menarche, age at first birth, and parity, have been consistently reported to affect breast cancer risk [5–9] based on studies in predominantly NHW populations. Some reproductive history exposures appear to affect incidence of estrogen receptor (ER) positive tumors specifically [10,11], and the proportion of breast cancers that express the ER differs between HISP and NHW populations [12,13]. Associations of reproductive risk factors with breast cancer, and the pattern of these

associations by ER status, should be evaluated in Hispanics. We have investigated the associations between reproductive factors and breast cancer in the 4 Corners Breast Cancer Study, a case–control study among HISP women and NHW women residing in the U.S. southwest.

Subjects and methods

Study population

Participants were recruited and interviewed for a case–control study of breast cancer in the U.S. states of Arizona, Colorado, New Mexico, and Utah. Methods for identifying, recruiting, and interviewing subjects have been described previously [4,14]. Cases with an incident primary breast cancer diagnosed in December 1999–September 2004 were identified through state-wide cancer registries in each state. HISP ethnicity was initially identified from cancer registry information or by computerized search using the GUESS (Generally Useful Ethnic Search System) [15] algorithm and Census Spanish Surname List [16]. All HISP cases was selected for the study, and a sample of NHW cases, frequency-matched to HISP on age, were selected. Control subjects, frequency-matched to cases on age and ethnicity, were selected from computerized drivers' license lists in New Mexico and Utah, or from commercially available lists in Arizona and Colorado for ages up to 64 years; subjects aged 65 and older were selected from Center for Medicare Studies lists. HISP controls were initially identified using the computerized surname search. Women who, when contacted for the study, self-identified as non-Hispanic white, Hispanic, or American Indian, and were capable of responding to questions in English or Spanish, were eligible to be interviewed. Women with a prior diagnosis of breast cancer were ineligible for this analysis.

Interview

A questionnaire was administered by a trained interviewer using computer-assisted personal interview software. Interviews were audio-recorded for quality assurance [17]. The complete text of the questionnaire is available at https://www.zorro.hrc.utah.edu/breast.html. Information was obtained about diet, medical history, physical activity, menstrual history and use of hormones, pregnancy history, family history of cancer, history of mammograms, and tobacco and alcohol exposures. Exposure histories referred to a reference year one year before diagnosis for cases and one year before selection for the study for controls. Questions about pregnancies included the year, duration, and outcome of each pregnancy and the duration of breastfeeding for each child.

Among eligible subjects contacted for the study, cooperation rates for the four groups were 63% for HISP cases, 36% for HISP controls, 71% for NHW cases, and 47% for NHW Controls [4]. Cases and controls were similar with regard to characteristics influencing participation [18]. The study protocol received human subjects' research approval at each institution, and subjects provided written informed consent.

Tumor characteristics

Data describing clinical characteristics of cases at diagnosis, including tumor stage, grade, histology, and ER expression, were obtained from the cancer registries; categories for these variables were based on standardized definitions [19].

Data analysis

Frequency distributions of characteristics of HISP women were compared to NHW women using chi-square tests with Mantel–Haenszel adjustment for age. We evaluated associations between reproductive history variables and breast cancer using logistic regression models. A

major study goal was to examine breast cancer risk factors among Hispanics, and therefore, our primary analysis considered HISP and NHW women separately. Final classification of ethnicity was based on self-report. There were too few American Indian participants (n = 127) for separate analysis, so American Indian women were grouped with HISP (because the two groups in the U.S. Southwest have shared genetic heritage [20]) for analysis. Subgroup analyses were conducted for pre- and post-menopausal women but are generally not reported if associations were qualitatively similar for the two groups. All models included covariates for age and study center, which were frequency-matching variables, and for education to account for its possible influence on study participation [18]. For exposures of interest for this analysis that were highly correlated with other exposures, e.g., age at first birth, parity, and years since last birth, we examined ORs from two analyses, with and without mutual adjustment. We included other potential confounders in the logistic model if a confounding effect (change of 10% or more in the coefficient for the exposure of interest) was present; variables that met this criterion for any exposure of interest were included in all final analyses. Variables examined as potential confounders that were not included in the final models included: mammography history, height, gestational diabetes, total energy intake from diet, language acculturation, genetic admixture, and characteristics of community of residence (i.e., language, education, and income levels, based on census data). We evaluated trend in associations using a likelihood ratio test of a variable representing the ordered categories of the exposure, treated as a continuous variable. Differences in associations between ethnic groups were tested using a likelihood ratio test for an interaction term representing the product of the exposure trend variable and ethnicity category. We evaluated associations between reproductive risk factors and subgroups of breast cancers according to ER status of tumors, estimating ORs for each group compared to controls in separate logistic regression models. Heterogeneity of associations for risk factors by ER status was evaluated by testing for significance of the exposure trend in a comparison of ER positive cases versus ER negative cases in a logistic regression model. Population attributable risk percents [21] were calculated based on the prevalence of controls in the polytomous exposure categories in this study and the adjusted odds ratios for the entire study population. SAS 9.1 (SAS Institute Inc., Gary, NC) was used for statistical analysis.

Results

A total of 5,012 eligible women were interviewed. After omitting respondents who could not be analyzed for associations between reproductive factors and breast cancer (162 women with incomplete interviews or poor data quality, 12 women who did not provide information about pregnancies, and two who reported never menstruating), there were 796 HISP cases, 919 HISP controls, 1,525 NHW cases, and 1,596 NHW controls available for analysis (Table 1). HISP controls had lower educational attainment than NHW controls ($p < 0.0001$). Participating HISP cases differed from NHW cases on distributions of certain clinical and pathological variables, having higher proportions with regional or distant stage at diagnosis, and with tumors larger than 2 cm in diameter. The difference in distribution of stage at diagnosis by ethnicity was also present when comparisons were made for all eligible cases for whom data were available, including nonparticipants: among all eligible HISP cases, the percentages with in situ, local, and regional/distant disease at diagnosis were 15.1%, 47.8%, and 37.1%, whereas among eligible NHW cases, the corresponding percentages were 16.5%, 53.8%, and 29.7% (p = 0.0003). The two ethnic groups did not differ on tumor histologies, or grade, but, among cases with known ER status, the fraction with ER negative tumors was higher among Hispanics, 26.3%, than non-Hispanic whites. 19.6% (p = 0.03 for difference by ethnicity, age-adjusted).

A trend of lower breast cancer risk with older age at menarche was only weakly apparent among HISP women, with an OR of 0.85 (95% CI: 0.64, 1.13) for women reporting menarche at age 14 or older compared to age 11 or younger (Table 2). The contrast in breast cancer risk between

the oldest and youngest age at menarche categories was stronger among NHW women, with an OR of 0.69 (95% CI: 0.55, 0.86) and a significant trend ($p = 0.003$), but there was no evidence of heterogeneity of effect by ethnicity (p interaction = 0.57). These trends were similar when pre- and peri-menopausal women were considered separately from post-menopausal women.

Hispanic women with a first birth at age 30 or older had an approximately twofold increased risk of breast cancer compared to women with a first birth before age 20 (Table 2). The association was somewhat more apparent in premenopausal women, with an OR of 2.66 (95% CI: 1.41, 5.02), compared to an OR of 1.56 (95% CI: 0.88, 2.75) in the post-menopausal subgroup (Table 3). Nulliparous HISP women had an estimated 30% higher breast cancer risk than women with a first birth before age 20, a non-significant difference. There was little evidence of a trend in breast cancer risk with age at first birth in the NHW study population. NHW in this study included a high proportion who were current users of post-menopausal hormones [4], an exposure that modifies the effects of other breast cancer risk factors. When recent users of estrogen or estrogen plus progestin post-menopausal hormones were excluded, there was some evidence of a trend of increasing breast cancer risk with older age at first birth among the remaining NHW women ($p = 0.07$), with an OR of 1.21 (95% CI: 0.82, 1.79) for a first birth at age 30 or older relative to women with a first birth before age 20. The proportion of HISP controls who did not have a first birth before age 20 was 0.739, whereas for non-Hispanic whites, the proportion was 0.863. The population attributable risk percents associated with not having a first birth before age 20 are estimated to be 7.7% for HISP and 9.9% for non-Hispanic whites, a 2.2% difference between the two ethnic groups.

Hispanic women with five or more births had a reduced risk of breast cancer, OR 0.70 (95% CI: 0.50, 0.98) compared to those with one or two births (Table 2); the protective effect was similar to that observed for the same comparison among NHW women, OR 0.56 (95% CI: 0.41, 0.75). The ORs for five or more births were 0.83 (0.40, 1.72) for pre-menopausal and 0.66 (0.44, 0.97) for post-menopausal HISP women (Table 3). The trend of increasing breast cancer risk with an older age at first birth among HISP women was attenuated when adjusted for number of births and years since last birth (p trend = 0.76). The reduced risks associated with a higher number of births in both ethnic groups were essentially unchanged by adjustment for age at first birth and years since last birth. The proportion of HISP controls with more than two births was 0.567, whereas for non-Hispanic whites, the proportion was 0.449: The population attributable risks percents associated with higher numbers of births are estimated to be −12.7% for HISP and −8.3% for non-Hispanic whites, a 4.4% difference between the two ethnic groups.

Hispanic women who had ever breastfed had a somewhat reduced breast cancer risk compared to those who had given birth but had not breastfed, OR 0.87 (95% CI: 0.70, 1.09), but there was no evidence of a trend with duration of breastfeeding. There was a trend of inverse association between duration of breastfeeding and breast cancer among NHW women, which was attenuated when adjusted for number of births and age at first birth ($p = 0.15$). The trend with duration of breastfeeding was more evident among premenopausal non-Hispanic whites (Table 3), with an OR of 0.59 (95% CI: 0.37, 0.95) for 24 or more months of breastfeeding. Among premenopausal HISP women, the OR for the same duration of breastfeeding was 0.79 (95% CI: 0.46, 1.36).

The number of years that had elapsed between a last birth and the reference year were strong predictors of breast cancer risk among HISP women (p trend = 0.0003). HISP women who had given birth within five years had an approximate doubling of breast cancer risk relative to women with a 16–25 year interval since a birth (Table 2). When pre- and post-menopausal women were considered separately, the trend was present in each group, $p = 0.004$ and $p = 0.01$, respectively (Table 3). There was not a significant trend in breast cancer risk with years

since a birth among NHW women (Table 2), although the comparison of women with more than 35 years since the last birth compared to women with 16–25 years since a birth, OR 0.71 (95% CI: 0.49, 1.02) indicated an almost-significantly reduced risk. There was evidence that there was a difference by ethnicity (p for interaction = 0.05) in the trend of reduced breast cancer risk with years since last birth.

There was no association between induced abortion and breast cancer in HISP or NHW women, nor was there an association in either ethnic group when the comparison was limited to premenopausal women.

We further examined associations between reproductive risk factors and subgroups of ER positive and ER negative breast cancers. Cases with missing ER status (32.5% of HISP cases and 32.4% of NHW cases) did not differ from those with known ER status on associations between reproductive variables and breast cancer risk (data not shown). Among HISP women, trends of lower breast cancer risk with age at menarche, higher risk with older age at first birth, reduced risk with higher parity, and reduced risk with years since last birth were all evident for estrogen receptor positive tumors (Table 4), but not for estrogen receptor negative tumors, with evidence of heterogeneity of effect for age at first birth ($p = 0.001$) and parity ($p = 0.002$). Among NHW women, there were qualitatively similar patterns in that older age at first birth or nulliparity increased the risk of ER positive, but not ER negative breast cancers, and the magnitude of reduced risk for more than two births was stronger for ER positive than for ER negative tumors. Heterogeneity of effects of parity or age at first birth by ER status was not statistically significant among non-Hispanic whites. Results were inconsistent for an association between breastfeeding and breast cancer, which was more evident for ER negative tumors among HISP but for ER positive tumors among non-Hispanic whites. Results were very similar if the subgroups were limited to cases with ER negative/progesterone receptor (PR) negative and ER positive/PR positive tumors (data not shown).

Discussion

Our analysis of reproductive variables in relation to breast cancer among HISP women indicates that several risk factors that are documented in the literature for NHW [5,6,22–24] influence breast cancer risk in HISP in a similar manner. These include younger age at first birth, higher parity, and longer time since last pregnancy, all of which were associated with significant trends of reduced breast cancer risk. The associations with age at menarche and with breastfeeding were not statistically significant in the HISP women studied, but were of comparable magnitude to associations in non-Hispanic whites. Gilliland et al., describing associations between reproductive factors and breast cancer among HISP women diagnosed in New Mexico in 1992–1994 [2], had reported that risk of breast cancer among nulliparous HISP women was more than doubled compared to women with one full-term birth, but that there was no protective effect of higher parity. Differences between the studies in these results may be based on chance, as nulliparous women were a relatively small category of HISP in both studies; Gilliland et al. reported on fewer than 80 nulliparous HISP women. Recent reports considering lifestyle risk factors and breast cancer in prospective studies of multi-ethnic populations include 103 HISP cases in a report by Chlebowski et al. [25] and 276 Latina cases in a report by Pike et al. [26]. These authors did not present estimates of the ethnicity-specific relative risks.

In the present study, the strongest evidence of heterogeneity of effect of a reproductive risk factor between HISP and NHW was for the trend in breast cancer risk with time since a last full-term birth. Studies in majority NHW populations have observed a transient increase in breast cancer risk after a birth, which diminishes with time, trending toward the longer-term reduced risk associated with a birth [27–30]. The doubling of risk for HISP women in the

present study with a birth within five years of the reference date indicates a qualitatively similar, but possibly quantitatively stronger, pattern. We are not aware of any comparable data from other HISP populations (this exposure was not reported on by Gilliland et al. [2]). A biologically based difference between ethnic groups in the influence of pregnancy is possible, perhaps related to differences in hormone exposure during pregnancy [31]. Premenopausal and post-menopausal HISP women had similar patterns of associations between reproductive risk factors and breast cancer, with no indication of a reversed association with parity among young women as has been reported for African-American women [32].

We observed that the higher breast cancer risk associated with older age at first birth, and the reduced breast cancer risk associated with higher parity, were present only for ER positive tumors among Hispanics. Thus results for HISP in the present study display the same tendency of specificity of certain associations to ER positive tumors that was described in a recent meta-analysis of 10 studies [11] of primarily NHW populations.

A potential limitation of this study is that study participation was less than optimal. Low participation rates in a case-control study are always a concern because comparisons may be biased if factors influencing participation differ between case and control populations. When we compared participants and non-participants in the 4 Corners Study [18], we found that age and ethnicity strongly influenced participation. Patterns of association of community characteristics such as income, language, and education, as described by census data, with study participation were generally similar for cases and controls. Thus the potential for bias due to case–control differences in characteristics related to participation should be ameliorated by adjustment for age, ethnicity, and education. However, to the extent that individual characteristics that do not correspond well to age, ethnicity, or community-level census data may have influenced participation differently for cases and controls, the possibility of residual bias must be acknowledged. Among study participants, analyses that included cultural characteristics as represented by mammography history, language acculturation, and community-level census variables, or genetic background represented by a genetic admixture variable [20], did not appreciably change odds ratios. Regarding the transient increase in breast cancer risk after a pregnancy, it has been suggested that the apparent association between case status and a recent birth could be a product of bias if controls with young children differentially refuse participation of a case–control study [28]. However, the association has been observed in registry-linkage studies, a setting in which participation is not an issue [27,29]. In our study population, the reduced risk with time since birth among HISP was significant when women with 36 or more years since a birth were compared to women with 16–25 years since a birth, an association which is unlikely to be explained by issues of participation.

Hispanic women in the U.S. southwest reported a birth before age 20 more frequently than non-Hispanic whites, and HISP women also reported larger family sizes. Reduced breast cancer risk associated with these reproductive patterns could account for some of the difference in breast cancer incidence between the two groups. Based on the New Mexico SEER registry, which has the largest HISP population in the region, HISP women have an age-adjusted breast cancer incidence of 89.9 per 100,000, compared to 134.8 per 100,000 among NHW [1]. Population attributable risk percents based on our data indicate that differences in parity would explain a 4.4% difference, and age at first birth a 2.2% difference. The result of the present analysis, specific to reproductive history, can be seen to be consistent in principal with those from prospective studies which have reported that differences in breast cancer incidence between HISP or Latina and white women were accounted for by differences in the prevalence of reproductive and other risk factors [25,26]. Cohort studies have the advantage of ability to directly estimate incidence rates, which is not possible in case–control studies. Cohort studies are less subject to selection bias, although representativeness can be an issue. Investigators conducting both types of studies have experienced difficulties in accruing population-based

samples of ethnic minority groups in the U.S. Case–control studies can often accrue a larger number of cases in a short time period than cohort studies, which allowed us, in the present study, to calculate ORs for risk factor associations within the Hispanic ethnic group specifically. Environmental, cultural, and biological factors should continue to be examined in relation to the ethnic differences in breast cancer incidence.

Acknowledgements

The authors acknowledge the contributions of Leslie Palmer, Roger Edwards, Karen Curtin, and Betsy Risendal, Tara Patton, Jason Witter, and Kelly May for data collection and management. This study was funded by NIH Grants CA078682, CA078762, CA078552, and CA078802. The Utah Cancer Registry is funded by Contract #N01-PC-67000 from the National Cancer Institute, with additional support from the State of Utah Department of Health.

References

1. National Cancer Institute DCCPS Surveillance Research Program Cancer Statistics Branch. Surveillance, Epidemiology, and End Results (SEER) Program. 2004. (http://www.seer.cancer.gov) SEER*Stat Databases: Incidence - SEER 13 Regs Public-Use. November, 2004 submission
2. Gilliland FD, Hunt WC, Baumgartner KB, Crumley D, Nicholson CS, Fetherolf J, et al. Reproductive risk factors for breast cancer in Hispanic and non-Hispanic white women: the New Mexico Women's Health Study. Am J Epidemiol 1998;148(7):683–692. [PubMed: 9778175]
3. 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(6): 435–434. [PubMed: 12160603]
4. 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. [PubMed: 17080310]
5. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993;15 (1):36–47. [PubMed: 8405211]
6. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002;360(9328):187–195. [PubMed: 12133652]
7. Bernstein L, Ross RK. Endogenous hormones and breast cancer risk. Epidemiol Rev 1993;15(1):48–65. [PubMed: 8405212]
8. Key TJ, Verkasalo PK, Banks E. Epidemiology of breast cancer. Lancet Onool 2001;2(3):133–140.
9. Kelsey JL, Bernstein L. Epidemiology and prevention of breast cancer. Annu Rev Public Health 1996;17:47–67. [PubMed: 8724215]
10. 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):1558–1568. [PubMed: 15466970]
11. 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(4):R43. [PubMed: 16859501]
12. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by race and ethnicity among women 50 years of age and older. Cancer Epidemiol Biomarkers Prev 2002;11(7):601–607. [PubMed: 12101106]
13. Chu KC, Anderson WF, Fritz A, Ries LA, Brawley OW. Frequency distributions of breast cancer characteristics classified by estrogen receptor and progesterone receptor status for eight racial/ethnic groups. Cancer 2001;92(1):37–45. [PubMed: 11443607]
14. Rogers A, Murtaugh MA, Edwards S, Slattery ML. Contacting controls: are we working harder for similar response rates, and does it make a difference? Am J Epidemiol 2004;160(1):85–90. [PubMed: 15229121]
15. Howard CA, Samet JM, Buechley RW, Schrag SD, Key CR. Survey research in New Mexico Hispanics: some methodological issues. Am J Epidemiol 1983;117(1):27–34. [PubMed: 6823950]

16. Word, DL.; Perkins, RC. Population Division Working Paper No. 13. U.S. Bureau of the Census; Washington: 1996. Building a Spanish surname list for the 1990's - A new approach to an old problem. http://www.census.gov/population/documentation/twpno13.pdf

17. Edwards S, Slattery ML, Mori M, Berry TD, Caan BJ, Palmer P, et al. Objective system for interviewer performance evaluation for use in epidemiologic studies. Am J Epidemiol 1994;140(11):1020–1028. [PubMed: 7985650]

18. Sweeney C, Edwards S, Baumgartner KB, Herrick JS, Palmer L, Murtaugh MA, et al. Recruiting Hispanic women for a population-based study: validity of surname search, and characteristics of non-participants. Am J Epidemiol 2007;166(10):1210–1219. [PubMed: 17827445]

19. Division of Cancer Control, Population Sciences. The SEER Program code manual. 3. National Cancer Institute, U.S. Department of Health and Human Services; Washington: 1998.

20. Sweeney C, Wolff RK, Byers T, Baumgartner KB, Giuliano AR, Herrick JS, et al. Genetic admixture among Hispanics and candidate gene polymorphisms: potential for confounding in a breast cancer study? Cancer Epidemiol Biomarkers Prev 2007;16(1):142–150. [PubMed: 17220343]

21. Hanley JA. A heuristic approach to the formulas for population attributable fraction. J Epidemiol Community Health 2001;55(7):508–514. [PubMed: 11413183]

22. Bernstein L. The risk of breast, endometrial and ovarian cancer in users of hormonal preparations. Basic Clin Pharmacol Toxicol 2006;98(3):288–296. [PubMed: 16611204]

23. ESHRE Capri Workshop Group. Hormones and breast cancer. Human Reprod Update 2004;10(4): 281–293.

24. Newcomb PA, Egan KM, Titus-Emstoff L, Trentham-Dietz A, Greenberg ER, Baron JA, et al. Lactation in relation to postmenopausal breast cancer. Am J Epidemiol 1999;150(2):174–182. [PubMed: 10412962]

25. Chlebowski RT, Chen Z, Anderson GL, Rohan T, Aragaki A, Lane D, et al. Ethnicity and breast cancer: factors influencing differences in incidence and outcome. J Natl Cancer Just 2005;97(6):439–448.

26. Pike MC, Kolonel LN, Henderson BE, Wilkens LR, Hankin JH, Feigelson HS, et al. Breast cancer in a multiethnic cohort in Hawaii and Los Angeles: risk factor-adjusted incidence in Japanese equals and in Hawaiians exceeds that in whites. Cancer Epidemiol Biomarkers Prev 2002;11(9):795–800. [PubMed: 12223421]

27. Lambe M, Hsieh C, Trichopoulos D, Ekbom A, Pavia M, Adami HO. Transient increase in the risk of breast cancer after giving birth. N Engl J Med 1994;331(1):5–9. [PubMed: 8202106]

28. Cummings P, Stanford JL, Daling JR, Weiss NS, McKnight B. Risk of breast cancer in relation to the interval since last full term pregnancy. BMJ 1994;308(6945):1672–1674. [PubMed: 8025460]

29. Albrefctsen G, Heuch I, Kvale G. The short-term and long-term effect of a pregnancy on breast cancer risk: a prospective study of 802,457 parous Norwegian women. Br J Cancer 1995;72(2):480–84. [PubMed: 7640236]

30. Chie WC, Hsieh C, Newcomb PA, Longnecker MP, Mittendorf R, Greenberg ER, et al. Age at any full-term pregnancy and breast cancer risk. Am J Epidemiol 2000;151(7):715–722. [PubMed: 10752799]

31. Arslan AA, Zeleniuch-Jacquotte A, Lukanova A, Afanasyeva Y, Katz J, Levitz M, et al. Effects of parity on pregnancy hormonal profiles across ethnic groups with a diverse incidence of breast cancer. Cancer Epidemiol Biomarkers Prev 2006;15(11):2123–2130. [PubMed: 17119037]

32. Palmer JR, Wise LA, Horton NJ, Adams-Campbell LL, Rosenberg L. Dual effect of parity on breast cancer risk in African-American women. J Natl Cancer Inst 2003;95(6):478–483. [PubMed: 12644541]

Table 1

Characteristics of Hispanic and non-Hispanic white breast cancer cases and controls, 4 Corners Study

	Hispanic				Non-Hispanic white				
	Control		Case		Control		Case		
	n	%	*n*	%	*n*	%	*n*	%	*P*
Total	919		796		1,596		1,525		
Study center									
Arizona	207	22.5	168	21.1	305	19.1	231	15.1	
Colorado	198	21.5	164	20.6	298	18.7	318	20.9	
New Mexico	324	35.3	362	45.5	617	38.7	645	42.3	
Utah	190	20.7	102	12.8	376	23.6	331	21.7	
Age*									
25–39	97	10.6	93	11.7	116	7.3	99	6.5	
40–49	250	27.2	266	33.4	418	26.2	433	28.4	
50–59	242	26.3	228	28.6	411	25.8	453	29.7	
60–69	214	23.3	147	18.5	368	23.1	355	23.3	
70–79	116	12.6	62	7.8	283	17.7	185	12.1	
Education*									
Less than high school graduate	267	29.1	242	30.6	73	4.6	64	4.2	
High school graduate	241	26.3	218	27.5	343	21.5	308	20.2	
Some college	255	27.8	218	27.5	596	37.4	559	36.7	
Bachelor's degree or higher	154	16.8	114	14.4	583	36.6	593	38.9	<0.0001**
Stage at Diagnosis									
In situ			129	17.0			258	17:8	
Local			361	47.6			806	55.5	
Regional or distant			269	35.4			387	26.7	
Unknown			37				74		0.003***
Estrogen receptor expression									
Positive			396	73.7			829	80.4	
Negative			141	26.3			202	19.6	
Unknown			259				494		0.03***
Histology									
Ductal			589	75.4			1,100	73.9	
Lobular			58	7.4			117	7.9	
Mixed Ductal/Lobular			59	7.6			123	8.3	
Other types			75	9.6			149	10.0	
Unknown			15				36		0.94***
Grade									
Well or moderately differentiated			398	58.4			838	63.2	
Poorly or un-differentiated			284	41.6			488	36.8	
Unknown			114				199		0.30***
Tumor size									
≤2 cm			408	61.4			912	72.4	
>2 cm			257	38.6			348	27.6	
Unknown			131				265		<0.0001***

*Results of Pearson chi-square tests for case-control differences in distributions were as follows: Among Hispanics, age, $p < 0.01$, education, $p = 0.55$; among non-Hispanic whites, age, $p < 0.01$, education, $p = 0.55$

**p for difference between Hispanic and non-Hispanic white controls, based on a chi-square test with Mantel-Haenszel adjustment for age

*** *p* for difference between Hispanic and non-Hispanic white cases, based on a chi-square test with Mantel-Haenszel adjustment for age; excluding unknown

Table 2

Reproductive history risk factors for breast cancer in Hispanic and non-Hispanic white women, 4 Corners Study

	Hispanic					Non-Hispanic white					*p* interaction[a]
	Controls		Cases		OR (95% CI)*	Controls		Cases		OR (95% CI)*	
	n	%	*n*	%		*n*	%	*n*	%		
Age at menarche[b]											
≤11	187	20.4	181	22.8	1.00 Reference	280	17.6	314	20.7	1.00 Reference	0.57
12	224	24.4	207	26.0	0.93 (0.70, 1.24)	424	26.7	405	26.7	0.82 (0.66, 1.02)	
13	236	25.7	175	22.0	0.73 (0.55, 0.99)	418	26.3	424	27.9	0.87 (0.70, 1.09)	
≥14	271	29.5	232	29.2	0.85 (0.64, 1.13)	468	29.4	375	24.7	0.69 (0.55, 0.86)	
p trend					0.13					0.003	
Age at first birth											
<20	240	26.1	179	22.5	1.00 Reference	218	13.7	200	13.1	1.00 Reference	0.14
20–24	362	39.4	317	39.8	1.16 (0.90, 1.51)	618	38.7	529	34.7	0.92 (0.72, 1.16)	
25–29	167	18.2	135	17.0	1.15 (0.83, 1.58)	368	23.1	354	23.2	1.00 (0.77, 1.31)	
≥30	62	6.7	88	11.1	1.99 (1.32, 3.00)	168	10.5	182	11.9	1.06 (0.77, 1.45)	
Nulliparous	88	9.6	77	9.7	1.30 (0.88, 1.92)	224	14.0	260	17.0	1.18 (0.88, 1.58)	
p trend[c]					0.008					0.35	
Number of births											
Nulliparous	88	9.6	77	9.7	0.96 (0.67, 1.37)	224	14.0	260	17.0	1.11 (0.89, 1.38)	0.52
1–2	310	33.7	324	40.7	1.00 Reference	656	41.1	692	45.4	1.00 Reference	
3–4	344	37.4	281	35.3	0.84 (0.66, 1.06)	544	34.1	478	31.3	0.87 (0.73, 1.03)	
5+	177	19.3	114	14.3	0.70 (0.50, 0.98)	172	10.8	95	6.2	0.56 (0.42, 0.76)	
p trend[c]					0.03					0.0002	
Number of induced abortions[b]											
0	819	89.1	709	89.1	1.00 Reference	1,434	89.8	1,322	86.7	1.00 Reference	0.24
1	65	7.1	69	8.7	1.13 (0.77, 1.64)	116	7.3	148	9.7	1.19 (0.91, 1.56)	
2+	35	3.8	18	2.3	0.64 (0.35, 1.17)	46	2.9	55	3.6	1.06 (0.70, 1.62)	
p trend					0.43					0.35	
Breastfeeding[c]											
Never	292	35.1	278	38.7	1.00 Reference	369	26.9	398	31.5	1.00 Reference	0.37
≤6 months	181	21.8	137	19.1	0.77 (0.58, 1.03)	324	23.6	287	22.7	0.83 (0.66, 1.03)	
> 6 to 12 months	95	11.4	89	12.4	1.04(0.73, 1.48)	236	17.2	191	15.1	0.77 (0.60, 0.98)	
>12 to 24 months	114	13.7	99	13.8	0.97 (0.69, 1.35)	231	16.9	192	15.2	0.74 (0.57, 0.95)	
> 24 months	149	17.9	116	16.1	0.84 (0.61, 1.15)	210	15.3	197	15.6	0.81 (0.62, 1.05)	
p trend					0.55					0.03	
Years since last birth[c,d]											
≤5	45	5.4	64	8.9	2.62 (1.44, 4.78)	81	5.9	66	5.2	1.07 (0.65, 1.75)	0.05
6–15	172	20.7	175	24.3	1.31 (0.93, 1.85)	233	17.0	223	17.6	0.95 (0.71, 1.26)	
16–25	210	25.3	202	28.1	1.00 Reference	288	21.0	317	25.1	1.00 Reference	
26–35	227	27.3	188	26.1	0.82 (0.59, 1.15)	337	24.6	342	27.0	0.88 (0.67, 1.15)	
36+	177	21.3	90	12.5	0.52 (0.31, 0.85)	433	31.6	317	25.1	0.71 (0.49, 1.02)	
p trend					0.0003					0.19	

*Odds ratio and 95% confidence interval from an unconditional logistic regression model, adjusted for age, study center, education, family history of breast cancer, body mass index, alcohol, age at menarche, recent oral contraceptive use, age at menopause, and recent use of hormone replacement therapy

[a]Significance from a test for interaction of the exposure variable and ethnicity

[b]Further adjusted for number of births and years since last birth

[c] Parous women only

[d] Further adjusted for number of births

Table 3

Reproductive history risk factors for breast cancer in Hispanic and non-Hispanic white women by menopausal status, 4 Corners Breast Cancer Study

	Hispanic						Non-Hispanic white					
	Pre- and peri-menopausal			Post-menopausal			Pre- and peri-menopausal			Post-menopausal		
	Controls *n*	Cases *n*	OR (95% CI)*	Controls *n*	Cases *n*	OR (95% CI)*	Controls *n*	Cases *n*	OR (95% CI)*	Controls *n*	Cases *n*	OR (95% CI)*
Age at menarche[a]												
≤1	68	72	1.00	119	109	1.00	73	91	1.00	207	222	1.00
12	88	95	1.08 (0.68, 1.71)	135	111	0.88 (0.60, 1.29)	125	159	1.01 (0.68, 1.50)	299	246	0.75 (0.58, 0.98)
13	75	81	1.05 (0.65, 1.70)	160	94	0.59 (0.40, 0.87)	129	145	0.92 (0.62, 1.38)	289	279	0.88 (0.68, 1.15)
>14	102	85	0.80(0.50, 1.29)	169	146	0.88 (0.61, 1.27)	163	142	0.71 (0.48, 1.06)	305	231	0.70 (0.54, 0.92)
p trend			0.32			0.27			0.05			0.05
Age at first birth												
<20	71	57	1.00	168	120	1.00	38	49	1.00	180	151	1.00
20–24	107	123	1.46 (0.92, 2.32)	254	194	1.07 (0.78, 1.48)	138	107	0.68 (0.41, 1.13)	480	421	0.98 (0.75, 1.29)
25–29	83	64	1.07 (0.64, 1.78)	84	71	1.30 (0.85, 1.99)	130	146	0.94 (0.56, 1.57)	238	207	1.00 (0.73, 1.38)
≥30	27	51	2.66 (1.41, 5.02)	35	37	1.56 (0.88, 2.75)	83	111	1.12 (0.65, 1.95)	85	70	0.88 (0.58, 1.33)
Nulliparous	45	38	1.25 (0.68, 2.29)	43	39	1.38 (0.81, 2.35)	103	125	1.10 (0.64, 1.88)	121	135	1.18 (0.82, 1.68)
p trend[b]			0.03			0.07			0.07			0.82
No. of births												
Nulliparous	45	38	0.87 (0.52, 1.46)	43	39	1.00 (0.60, 1.68)	103	125	1.12 (0.80, 1.57)	121	135	1.09 (0.81, 1.46)
1–2	153	166	1.00	155	156	1.00	235	273	1.00	421	417	1.00
3–4	113	112	0.92 (0.64, 1.32)	231	169	0.78 (0.56, 1.07)	123	119	0.83 (0.60, 1.15)	421	358	0.88 (0.72, 1.09)
5+	22	17	0.83 (0.40, 1.72)	155	97	0.66 (0.44, 0.97)	31	21	0.61 (0.32, 1.16)	141	74	0.56 (0.40, 0.78)
p trend[b]			0.49			0.03			0.03			0.002
No. of induced abortions[a]												
0	282	291	1.00	535	416	1.00	392	409	1.00	1,042	911	1.00
1	35	30	0.75 (0.43, 1.31)	30	39	1.57 (0.93, 2.67)	64	86	1.19 (0.82, 1.73)	52	61	1.20 (0.79, 1.80)
2+	16	12	0.76 (0.34, 1.70)	19	6	0.43 (0.16, 1.14)	36	43	1.01 (0.62, 1.65)	10	12	1.25(0.51,3.04)
p trend			0.28			0.77			0.65			0.34
Breastfeeding[b]												
Never breastfed	72	91	1.00	218	185	1.00	57	87	1.00	312	311	1.00
≤6 months	77	67	0.70 (0.44, 1.13)	104	70	0.81 (0.56, 1.19)	76	74	0.58 (0.36, 0.94)	248	212	0.90 (0.70, 1.16)
>6 to 12 months	40	47	0.96 (0.55, 1.68)	55	42	1.00 (0.62, 1.62)	62	62	0.67 (0.40, 1.12)	174	128	0.79 (0.59, 1.06)
>12 to 24 months	52	41	0.70 (0.41, 1.21)	62	58	1.18 (0.77, 1.81)	93	90	0.60 (0.38, 0.96)	138	102	0.76 (0.55, 1.04)
>24 months	47	49	0.79 (0.46, 1.36)	102	67	0.82 (0.55, 1.22)	101	100	0.59 (0.37, 0.95)	109	96	0.91 (0.65, 1.28)
p trend			0.42			0.72			0.08			0.17
Years since last birth[b,c]												
≤5	43	60	2.81 (1.41, 5.62)	2	4	5.35 (0.63, 45.29)	77	62	1.32 (0.74, 2.37)	4	4	1.33 (0.29, 6.05)
6–15	129	138	1.53 (0.97, 2.42)	43	37	0.96 (0.54, 1.72)	160	187	1.29 (0.89, 1.88)	73	36	0.49 (0.29, 0.81)
16–25	89	77	1.00	120	124	1.00	117	128	1.00	171	187	1.00
26–35	26	19	0.83 (0.38, 1.80)	200	169	0.78 (0.53, 1.15)	35	35	0.73 (0.39, 1.38)	302	306	0.90 (0.66, 1.24)
36+	1	1	0.70 (0.04, 13.18)	176	88	0.47 (0.27, 0.82)	0	1	Undefined	433	316	0.73 (0.48, 1.10)
p trend			0.004			0.014			0.14			0.64

[*] Odds ratio and 95% confidence interval from an unconditional logistic regression model, adjusted for age, study center, education, family history of breast cancer, body mass index, alcohol, age at menarche, recent oral contraceptive use, and, for post-menopausal women, for age at menopause and recent use of hormone replacement therapy. In tests for interaction between the exposure variable and menopausal status, all *p* values were >0.10 and are not shown in table

[a] Further adjusted for number of births and years since last birth

[b] Parous women only

[c] Further adjusted for number of births

Table 4

Reproductive history risk factors for breast cancer by estrogen receptor status of tumors, 4 Corners Study

	Hispanic						Non-Hispanic white					
	Controls	Estrogen receptor +		Estrogen receptor −		*p* heterogeneity[a]	Controls	Estrogen receptor +		Estrogen Receptor −		*p* heterogeneity[a]
	n	*n*	OR 95% CI*	*n*	OR 95% CI*		*n*	*n*	OR 95% CI*	n	OR 95% CI*	
Age at menarche[b]												
≤11	187	100	1.00 Reference	27	1.00 Reference	0.14	280	172	1.00 Reference	51	1.00 Reference	0.20
12	224	102	0.84 (0.59, 1.20)	32	0.84 (0.46, 1.53)		424	225	0.83 (0.64, 1.08)	56	0.74 (0.49, 1.14)	
13	236	80	0.60 (0.41, 0.86)	40	1.14 (0.64, 2.01)		418	210	0.78 (0.60, 1.02)	56	0.78 (0.51, 1.19)	
≥14	271	114	0.74 (0.52, 1.05)	41	0.99 (0.56, 1.75)		468	217	0.73 (0.56, 0.95)	39	0.50 (0.31, 0.79)	
p trend			0.04		0.75				0.02		0.006	
Age at first birth												
<20	240	84	1.00 Reference	38	1.00 Reference	0.001	218	104	1.00 Reference	37	1.00 Reference	0.54
20–24	362	143	1.14 (0.82, 1.58)	55	0.83 (0.50, 1.37)		618	289	0.99 (0.74, 1.31)	62	0.59 (0.37, 0.94)	
25–29	167	68	1.32 (0.89, 1.97)	26	0.82 (0.45, 1.50)		368	193	1.11 (0.80, 1.52)	47	0.67 (0.40, 1.14)	
≥30	62	58	2.98 (1.85, 4.80)	8	0.58 (0.23, 1.44)		168	97	1.16 (0.80, 1.69)	25	0.71 (0.39, 1.32)	
	88	43	1.68 (1.04, 2.71)	14	1.04 (0.49, 2.20)		224	146	1.29 (0.91, 1.83)	31	0.67 (0.37, 1.21)	
Nulliparous												
p trend[c]			< 0.0001		0.29				0.24		0.68	
Number of births												
	88	43	1.00 (0.65, 1.54)	14	1.35 (0.67, 2.69)	0.002	224	146	1.07 (0.83, 1.39)	31	0.94 (0.60, 1.48)	0.73
Nulliparous												
1–2	310	165	1.00 Reference	58	1.00 Reference		656	384	1.00 Reference	96	1.00 Reference	
3–4	344	142	0.74 (0.55, 0.99)	45	1.06 (0.66, 1.69)		544	251	0.78 (0.64, 0.97)	65	0.96 (0.67, 1.38)	
5+	177	46	0.43 (0.28, 0.66)	24	1.59 (0.83, 3.06)		172	48	0.46 (0.31, 0.67)	10	0.49 (0.24, 1.00)	
p trend[c]			0.0002		0.30				< 0.0001		0.05	
Number of Induced Abortions[b]												
0	819	346	1.00 Reference	127	1.00 Reference	0.12	1,434	720	1.00 Reference	168	1.00 Reference	0.22
1	65	38	1.21 (0.78, 1.89)	13	1.03 (0.51, 2.07)		116	80	1.18 (0.85, 1.62)	22	1.27 (0.75, 2.13)	
2+	35	12	0.90 (0.45, 1.80)	1	0.20 (0.03, 1.54)		46	29	0.99 (0.60, 1.64)	12	1.93 (0.95, 3.90)	
p trend			0.81		0.19				0.61		0.06	
Breastfeeding[c]												
Never	292	132	1.00 Reference	48	1.00 Reference	0.34	369	225	1.00 Reference	41	1.00 Reference	0.28
	181	70	0.89 (0.62, 1.27)	30	0.87 (0.50, 1.51)		324	150	0.75 (0.57, 0.98)	50	1.39 (0.88, 2.20)	
≤6 months												
>6 to 12 months	95	52	1.34 (0.88, 2.04)	15	0.88 (0.44, 1.74)		236	109	0.78 (0.58, 1.04)	22	0.85 (0.49, 1.49)	
>12 to 24 months	114	48	1.03 (0.68, 1.56)	15	0.62 (0.32, 1.23)		231	94	0.64 (0.47, 0.87)	29	1.05 (0.62, 1.79)	
	149	51	0.81 (0.54, 1.21)	19	0.63 (0.34, 1.18)		210	105	0.76 (0.56, 1.04)	29	1.21 (0.70, 2.09)	
>24 months												
p trend			0.64		0.09				0.02		0.95	
Years since last birth[c,d]												
≤5	45	19	2.38 (1.07, 5.30)	25	2.88(1.10, 7.54)	0.23	81	33	0.96 (0.52, 1.76)	9	0.54 (0.19, 1.51)	0.30
6–15	172	86	1.47 (0.96, 2.24)	33	0.92 (0.49, 1.70)		233	109	0.80 (0.57, 1.13)	37	0.93 (0.54, 1.62)	
16–25	210	108	1.00 Reference	36	1.00 Reference		288	179	1.00 Reference	44	1.00 Reference	
26–35	227	92	0.63 (0.42, 0.95)	23	0.94 (0.47, 1.88)		337	177	0.82 (0.59, 1.13)	48	1.26 (0.74, 2.15)	
36+	177	48	0.38 (0.21, 0.70)	10	0.81 (0.26, 2.53)		433	185	0.78 (0.50, 1.22)	33	1.14 (0.51, 2.53)	
p trend			0.0001		0.21				0.73		0.36	

[*] Odds ratio and 95% confidence interval from an unconditional logistic regression model, adjusted for age, study center, education, family history of breast cancer, body mass index, alcohol, age at menarche, recent oral contraceptive use, age at menopause, and recent use of hormone replacement therapy

[a] Significance from a test for heterogeneity of the associations for ER+ versus ER− breast cancers

[b] Further adjusted for number of births and years since last birth

[c] Parous women only

[d] Further adjusted for number of births