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Pre-diagnostic breastfeeding, adiposity and mortality among parous Hispanic and non-Hispanic white women with invasive breast cancer: the Breast Cancer Health Disparities Study

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Abstract

Background—U.S. Hispanic women have high rates of parity, breastfeeding and obesity. It is unclear whether these reproductive factors are associated with breast cancer (BC) mortality. We examined the associations between breastfeeding, parity, adiposity and BC-specific and overall mortality in Hispanic and non-Hispanic white (NHW) BC cases.

Methods—The study population included 2,921 parous women (1,477 Hispanics, 1,444 NHWs) from the Breast Cancer Health Disparities Study with invasive BC diagnosed between 1995 and 2004. Information on reproductive history and lifestyle factors was collected by in-person interview. Overall and stratified Cox proportional hazard regression models by ethnicity, parity, and body mass index (BMI) at age 30 years were used to calculate hazard ratios (HR) and 95% confidence intervals (CI).

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Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Results—After a median follow-up time of 11.2 years, a total of 679 deaths occurred. Pre-diagnostic breastfeeding was associated with a 16% reduction in mortality (HR, 0.84; 95% 0.72-0.99) irrespective of ethnicity. Parity significantly modified the association between breastfeeding duration and mortality (p-interaction= 0.05), with longer breastfeeding duration associated with lower risk among women who had ≤ 2 births (p-trend= 0.02). Breastfeeding duration was associated with reduced risk of both BC-specific and overall mortality among women with BMI < 25 kg/m^2, while positive associations were observed among women with BMI ≥ 25 kg/m^2 (p-interactions < 0.01).

Conclusion—Pre-diagnostic breastfeeding was inversely associated with risk of mortality after BC, particularly in women of low parity or normal BMI. These results provide another reason to encourage breastfeeding and weight management among young women.

Keywords

Breast cancer mortality; Hispanic Americans; Breastfeeding; Obesity

Introduction

Hispanics are the largest and fastest growing minority group in the United States (U.S.) [1,2].While heart disease is the leading cause of death among all U.S. women, breast cancer (BC) is the leading cause of death among U.S. Hispanic women [3,4]. Compared to non-Hispanic white (NHW) women, Hispanic women are more likely to be diagnosed with higher BC stage and with larger breast tumors [5]. They are also more likely to be diagnosed with estrogen receptor negative (ER-) tumors which have poor prognosis [6,7]. These BC disparities exist even after taking into consideration differences in demographic factors and breast cancer screening [5]. While BC risk factors have been extensively researched, our current understanding of factors that might influence BC prognosis is limited, especially for Hispanic women.

Parity and breastfeeding are well-established protective factors for BC development [8]. It is less clear whether these reproductive factors have the same impact on BC prognosis. Hispanic women have high parity and some studies reported that they are more likely to breastfeed compared to NHW women [9,10]. To date, only one prospective study has included Hispanic women in the evaluation of the association between reproductive factors and mortality among women diagnosed with BC [11]. Overall, results for the association between higher parity and BC-specific mortality have varied, with some studies reporting positive associations [12,13], inverse associations [14], or no association [15-17]. Findings from the few studies that have evaluated the relationship between breastfeeding and mortality among women diagnosed with BC have been inconsistent, with both inverse [11] and null [16,13,18,19] associations reported. The majority of women included in these studies were NHW cases.

Obesity has been found to be associated with lower survival of women diagnosed with BC [20-22]. Few studies have examined the impact of obesity during the reproductive years on BC-specific and overall mortality among BC survivors and neither of these studies found significant associations [23,24]. These studies did not include Hispanic women who have a

high prevalence of obesity [25]. We previously examined the associations between body mass index (BMI) at age 30 years and BC-specific and all-cause mortality among Hispanic and NHW invasive BC cases [26]. Among all women, obesity at age 30 years significantly increased risk of all-cause mortality [26]. However, when stratifying the analysis by ethnicity, obesity at age 30 was associated with increased risk of BC-specific mortality only among NHW women, with a significant interaction by ethnicity ($p = 0.045$) [26]. Parity has been found to be associated with increased maternal weight gain, however the strength of this association may vary by other factors such as pre-pregnancy body weight and race/ethnicity [27]. Additionally, obese mothers have lower rates of breastfeeding initiation [28]. The higher rates of obesity during the reproductive years among parous women could have an impact on BC prognosis.

We hypothesized that breastfeeding and adiposity could be important modifiable prognostic factors among parous Hispanic and NHW women diagnosed with BC. We examined the associations between breastfeeding, parity and BC-specific and overall mortality in Hispanic and NHW parous women with invasive BC from the Breast Cancer Health Disparities Study (BCHDS). We also evaluated if the associations differed by ethnicity, obesity measures at various ages, and tumor estrogen receptor (ER) status.

Methods

This analysis includes BC cases from two population-based case-control studies that were pooled for the BCHDS and had survival data available, the 4-Corners Breast Cancer Study (4-CBCS) and the San Francisco Bay Area Breast Cancer Study (SFBCS) (20). All participants signed informed written consent prior to participation. The study was approved by the Institutional Review Board for Human Subjects at each institution.

The 4-CBCS consists of NHW and Hispanic/Native American (NA) women aged 25 to 79 years residing in Arizona, Colorado, New Mexico, and Utah at the time of diagnosis. Cases newly diagnosed with in situ or invasive BC between October 1999 and May 2004 were identified through the state-wide cancer registries [29]. A total of 852 Hispanic, 22 NA, and 1,683 NHW BC cases completed an in-person interview in English or Spanish on BC risk factors and participated in the measurement of body size (height, weight, waist, and hip circumferences). The sample size of NA cases was too small for separate analysis; therefore, these women were combined with Hispanics. A total of 1,544 (560 Hispanics, 984 NHWs) parous, first primary invasive BC cases (stages I-IV) were included from the 4-CBCS with data on parity, breastfeeding history, survival status, and BC stage. The SFBCS included Hispanic, African American, and NHW women between the ages of 35 and 79 years from the San Francisco Bay Area [30,31]. Cases newly diagnosed with invasive BC (stages I-IV) between April 1995 and April 2002 were identified through the Greater Bay Area Cancer Registry. A total of 2,258 cases completed an in-person interview in English or Spanish on BC risk factors and body size measurements. A total of 1,377 (917 Hispanics, 460 NHWs) parous Hispanic or NHW cases were included from the SFBCS with data on parity, breastfeeding history, survival status, and BC stage.

Information on estrogen and progesterone receptor (ER/PR) status and stage at diagnosis (Surveillance, Epidemiology, and End Results (SEER) summary stage) was obtained from the New Mexico, Utah, Colorado, Arizona, and California cancer registries. ER/PR status was available for 979 (68%) NHW cases and 958 (75%) Hispanic cases. Through linkage with the cancer registries we obtained information on vital status as of November 2013, including date of death or last follow-up (month and year). Survival (in months) was calculated as the difference between diagnosis date and date of death or last follow-up. The cause of death was classified as BC if either the primary or contributing cause of death noted on the death certificate was BC.

Interview data were harmonized across the studies [32]. The referent year was defined as the calendar year prior to BC diagnosis. Parity was defined as the number of live births and was categorized as 1 to 2, 3 to 4, 5 or more. Parity was also categorized as 1 to 2 vs 3 or more to conserve statistical power in stratified models. Nulliparous women were excluded from all analyses. History of breastfeeding was recorded in weeks for each live birth and was evaluated by weeks of lifetime breastfeeding duration, categorized as tertiles based upon the distribution among all cases, and was also categorized as ever vs. never.

Potentially confounding variables evaluated included age at BC diagnosis, self-reported ethnicity, study site, highest level of education (less than high school, high school graduate, and post high school), caloric intake per day in referent year, age at first and last birth, pregnancy duration in years (age at first birth subtracted from age at last birth), BMI at age 30 years and in the referent year, waist circumference (WC), and waist-hip ratio (WHR). BMI in the referent year was calculated as self-reported weight (in kg) during the referent year (or more distantly recalled weight if referent year weight was not available or measured weight if neither were available) divided by measured height (in m) squared. The 4-CBCS asked about weight at age 30 years. Phase 1 of the SFBCS collected self-reported weight for the age range of 25 to 30 years, and for Phases 2 and 3, participants were asked about their weight for the age ranges of 20-29 years and 30-39 years. The weight reported for 25 to 30 years in Phase 1 and the mean of the weights for Phases 2 and 3 for each age range were then harmonized with weight at age 30 from the 4-CBCS. BMI at age 30 was calculated as self-reported weight at age 30 (in kg) divided by measured height (in m) squared. Waist and hip circumference were measured post-diagnosis at the time of interview and converted to centimeters (cm); WHR was calculated as WC divided by hip circumference. All body size measures were modeled as continuous variables.

Descriptive statistics were calculated by ethnicity for parity, history of breastfeeding, and all potential confounders and chi-square tests and t-tests were used to compare distributions between ethnic groups. HRs and 95% CIs were calculated by Cox proportional hazards regression models for associations with mortality overall and BC-specific mortality, and by ethnicity, ER status, parity, and BMI at age 30. Interactions between parity and breastfeeding with ethnicity, ER status, BMI at age 30 and at referent year, WC and WHR were assessed using the likelihood-ratio test comparing the model including an interaction term with a reduced model without the term.

The proportional hazards assumption was tested statistically using an interaction of main effects and covariates with the log of survival time. To correct these violations, we stratified models using the "STRATA" statement in SAS on variables that were found to be time dependent which included BC stage and age (only for the association between breastfeeding and all-cause mortality among all women by ER status). Strata-specific results are presented for those associations. Covariates included in multivariable models for BC-specific and all-cause mortality were known prognostic factors that changed the point estimate for the main effect of parity or history of breastfeeding by ≥10% [33]. Final parity-mortality models were adjusted for age at diagnosis, ethnicity, stage, and study site and final breastfeeding-mortality models were adjusted for these same covariates in addition to parity. A two-tailed probability value of ≤ 0.05 was considered statistically significant. All data analyses were performed using SAS version 9.4 (SAS Institute, Cary NC).

Results

After a median follow-up time of 11.2 years since BC diagnosis, a total of 679 deaths occurred, of which 352 deaths were due to BC. Table 1 presents the baseline characteristics of all parous BC cases (N=2,921) by ethnicity. A history of breastfeeding was reported by 62.4% of Hispanic cases and 64.8% of NHW cases, with Hispanic women reporting longer duration of breastfeeding compared to NHW cases ($p< 0.001$). Hispanic cases were younger at first birth (mean= 23.3 years) compared to NHW cases (mean= 24.6 years); and were older at last birth (mean=30.5 years) compared to NHW cases (mean= 29.3 years). More Hispanic cases (17.4%) compared to NHW cases (7.7%) reported five or more births. Compared to NHW cases, Hispanic cases were younger at diagnosis ($p=0.002$) and more likely to be diagnosed with ER-/PR- tumors ($p<0.001$) (Table 1).

Overall, parity was not significantly associated with BC-specific or all-cause mortality in our study population (Table 2). However, among women with 5 or more births, our results were suggestive of positive associations among all women (HR, 1.25; 95% CI 0.99-1.57) and among Hispanic cases (HR, 1.35; 95% CI 0.99-1.85) for risk of all-cause mortality (Table 2). No significant associations were observed between parity and mortality outcomes by ER status, WC, WHR, BMI during referent year, or BMI at age 30 (data not shown).

Breastfeeding was associated with reduced risk of overall mortality (HR, 0.84; 95% CI 0.72-0.99) (Table 3); however, breastfeeding was not significantly associated with BC-specific mortality (HR, 0.91; 95 % CI 0.77-1.14). When stratified by ethnicity, no significant associations were observed for either all-cause or BC-specific mortality (p-interaction > 0.05) (Table 3). The statistical interaction between breastfeeding dichotomized as ever/never and parity was not statistically significant for BC-specific ($p= 0.23$) or all-cause ($p= 0.11$) mortality.

We observed significant reductions in risk of all-cause mortality among women who reported breastfeeding for 1 to 24 weeks (HR, 0.80; 95% CI 0.65-0.99) or for 24 to 69.9 weeks (HR, 0.76; 95% CI 0.62-0.95), compared to women who never breastfed (Table 4). In stratified analysis by parity, we observed a significant reduction in risk of all-cause mortality among women that reported 1 to 2 births and that breastfed for ≥ 69.6 weeks (HR, 0.62; 95%

CI 0.40-0.97) with a significant trend (p=0.02). In contrast, breastfeeding among women that reported 3 or more births was only protective for women that breastfed for 1 to 24 weeks (HR, 0.72; 95% CI 0.53-0.98) or for 24 to 69.9 weeks (HR, 0.72; 95% CI 0.52-0.99). Breastfeeding for 69.6 weeks or longer was not associated with a reduction in mortality among all women or among women that reported 3 or more births. Parity was found to be a significant effect modifier for both BC-specific (p-interaction= 0.04) and all-cause (p-interaction=0.05) mortality. Breastfeeding duration in weeks was not significantly associated with BC-specific mortality (Table 4).

Table 5 presents associations between breastfeeding, BC-specific and all-cause mortality by ER status. There were no significant associations between breastfeeding, BC-specific and all-cause mortality among women with ER+ breast tumors. However, borderline inverse associations with history of breastfeeding were found for both BC-specific (HR, 0.66; 95 % CI 0.41-1.05) and all-cause (HR, 0.72; 95% CI 0.50-1.04) mortality among women with ER- breast tumors.

BMI at age 30 years was the only obesity measure to result in significant statistical interactions with a history of breastfeeding for BC-specific (p interaction = 0.01) and all-cause (p interaction=0.001) mortality (Table 6). Breastfeeding was significantly associated with reduced risk of BC-specific (HR, 0.70; 95 % CI 0.53-0.92) and all-cause (HR, 0.68; 95% CI 0.56-0.83) mortality among women with normal BMI (< 25 kg/m^2); while we did not observe significant statistical trends between breastfeeding duration and BC-specific (p-trend=0.29) and all-cause (p-trend=0.98) mortality (Table 6). Among cases with BMI ≥ 30 kg/m^2 at age 30, we observed nonsignificant positive associations between breastfeeding and BC-specific (HR, 1.67; 95% CI 1.00-2.80) and all-cause (HR, 1.38; 95% CI 0.97-1.97) mortality. Furthermore, breastfeeding for 69.6 weeks or longer was associated with increased risk of BC-specific (HR, 2.02; 95% CI 1.10-3.70; p-trend= 0.04) and all-cause (HR, 1.79; 95% CI 1.18-2.73; p-trend= 0.002) mortality among overweight/obese women at age 30 years, with significant dose responses. We observed a statistically significant interaction between breastfeeding duration and BMI at age 30 for all-cause mortality (p interaction= 0.003); while the interaction between breastfeeding duration and BMI at age 30 was not significant for BC-specific mortality (p interaction= 0.055).

Discussion

In this study population, Hispanic women had higher parity and a higher prevalence of obesity at age 30 years, compared to NHW women. The prevalence of breastfeeding for all women was 63.6% and was not significantly different by ethnicity; however, Hispanic cases did report breastfeeding for a longer duration compared to NHW cases. Breastfeeding was associated with reduced risk of overall mortality, but was not associated with BC-specific mortality. We observed a statistically significant interaction between breastfeeding and BMI at age 30 for BC-specific and all-cause mortality. We did not observe a significant association between parity and mortality outcomes; however parity significantly modified the association between breastfeeding duration and mortality. Breastfeeding among women with normal BMI at age 30 was associated with a 30% reduction in BC-specific mortality, while being overweight or obese at age 30 and breastfeeding for 69.6 weeks or longer was

associated with increased risk of both BC-specific and all-cause mortality. Associations between breastfeeding and mortality outcomes by ER status were not statistically significant, although results for women with ER- tumors were suggestive of inverse associations. Lastly, ethnicity did not modify the associations between parity, breastfeeding and mortality in our study population.

A recent analysis from two prospective BC cohorts by Kwan and colleagues found an inverse association between ever breastfeeding and BC-specific mortality (HR, 0.72; 95% CI 0.53 – 0.98) [11]; this study did include Hispanics (8.7% of the study population), however, results were not reported by race/ethnicity. Our overall results for a history of breastfeeding were similar to the results from Kwan et al. Other studies that evaluated the relationship between breastfeeding and all-cause mortality among women diagnosed with BC have reported null associations [16,13,18,19]. Unlike those previous studies, we explored the modifying effect of parity on the association between breastfeeding and mortality, and found a significant statistical interaction between breastfeeding duration and parity. Therefore, it is possible that in prior studies the inverse associations between breastfeeding duration and mortality could have been indiscernible due to the complex relationship between BMI, parity, and breastfeeding duration, resulting in null associations. We believe the parity interaction results in our study are driven by the Hispanic women who have high parity (17% with 5 or more births), long breastfeeding duration (mean= 71 weeks), and high BMI at age 30.

The biological mechanisms of how breastfeeding prior to BC diagnosis affects survival are uncertain. Proliferative expansion of progenitor cells in the breasts occurs during pregnancy, and breastfeeding reduces this expansion by terminal differentiation of epithelial cells in the lobules with reducing the mammary epithelium proliferative activity [11,34]. The malignant transformation of the differentiated progenitor cells might lead to tumor subtypes that are more differentiated (i.e., ER+/PR+) instead of those that are undifferentiated (i.e., ER-/PR- tumors). Lack of breastfeeding could preserve the progenitor cells in their undifferentiated state inside the breast lobules, then the malignant transformation of these progenitor cells would result in undifferentiated ER- breast tumors which have poorer prognosis versus the differentiated ER+ tumors [11,35]. It is therefore plausible that breastfeeding initiation could either promote or prevent specific types of BC. The findings from our study support this mechanism, particularly for women diagnosed with ER- BC.

Reportedly, obese mothers are less likely to breastfeed [28]. Interestingly, in our study population with a high prevalence of breastfeeding, we did not observe any differences in breastfeeding duration by obesity status at age 30 years, which is close to the average age of last birth for parous women in our study. We did detect a statistical interaction between BMI at age 30 and breastfeeding with associations for both BC-specific and all-cause mortality. To the best of our knowledge, no other study has reported on this interaction. From our findings, we postulate that normal weight women at age 30 receive the benefits of breastfeeding by stimulating breast progenitor cells to reach their differentiated state, while the increased mortality risk associated with being overweight may provide a hormonal environment conducive for promoting tumor initiation among these actively dividing cells. These interesting observations should be further evaluated in larger study populations.

Our findings for the associations between parity and mortality outcomes that were not significant are similar to results that have been observed in other epidemiological studies [15-17]. However, these same studies and others have found that a recent pregnancy or birth prior to BC diagnosis was associated with increased mortality. In a study conducted by Kroman et al., a recent pregnancy that occurred 2 years or less prior to BC diagnosis was associated with increased risk of all-cause mortality (relative risk, 1.58; 95% CI 1.24-2.02) [36]. Whiteman et al. found that among women aged 20-45 years whose last birth was 12 months or less prior to their BC diagnosis were at increased risk of overall mortality (HR, 1.62; 95 % CI 1.10-2.37) compared with nulliparous women [16]. We were unable to examine the association between recent birth and mortality outcomes due to the older age of the study population, with a mean age at diagnosis of 55 years. Moreover, only 39 women in our analytical study population had their last birth 2 years prior to their BC diagnosis and exclusion of these cases did not alter our findings.

Our study has several strengths and limitations. This is one of the first studies to evaluate the effects of reproductive factors on BC mortality in a large sample of Hispanics (51% of study population). We examined the interaction effects of multiple obesity measures, including BMI at age 30, BMI one year prior to diagnosis, WC, and WHR with parity and breastfeeding history. Additionally, our study has over 10 years of follow-up since BC diagnosis. We were also able to evaluate the effects of other reproductive factors as covariates, including age at menarche, menopausal status, age at first and last birth, and overall pregnancy duration. Also, BC cases from our study population that reported ever breastfeeding were not significantly different from cases that did not breastfeed based on clinical prognostic markers, including ER/PR and BC stage. As mentioned, one factor of interest that we were unable to examine was recent pregnancy. We were unable to further stratify the association between breastfeeding duration, parity, and mortality outcomes by ethnicity due to sample size constraints. As with past survival analyses using the BCHDS data, we were unable to adjust for BC treatment and mammography as those data were not available. In a recent report, we conducted sensitivity analyses in an effort to adjust for these factors, and concluded that adjustment for these factors did not alter the associations between BMI at age 30 years and mortality [26].

Our study results support the hypothesis that breastfeeding prior to the development of BC may be associated with lower risk of mortality. However, the association between breastfeeding duration and mortality is complex, and both parity and BMI should be considered when evaluating this relationship. In this study, inverse associations with ever breastfeeding were limited to women with normal BMI during their reproductive years. With the increasing rates of obesity, these results provide another reason to encourage breastfeeding and weight management among young women.

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Table 1

Baseline characteristics of parous breast cancer cases (stage I-IV), stratified by ethnicity: The Breast Cancer Health Disparities Study (n=2,921)

	Non-Hispanic White		Hispanic		
	No.	**%**	**No.**	**%**	**P value** [a]
Total Subjects	*1,444*		*1,477*		
Study site					< 0.0001
4-CBCS	984	68.1	560	37.9	
SFBCS	460	31.9	917	62.1	
Age at diagnosis, y					< 0.0001
<40	72	5.0	133	9.0	
40-49	337	23.3	457	30.9	
50-59	429	29.7	412	27.9	
60-69	358	24.8	319	21.6	
≥ 70	248	17.2	156	10.6	
Parity					< 0.0001
1 to 2	814	56.4	636	43.1	
3 to 4	519	35.9	584	39.5	
5 or more	111	7.7	257	17.4	
Age at first birth, y					< 0.0001
Less than 20	218	12.3	366	21.9	
20 to 24	586	33.1	610	36.6	
25 to 29	408	23.0	306	18.4	
30 or more	231	13.0	194	11.6	
Missing	1		1		
Age at last birth, y					< 0.0001
Less than 20	322	18.2	333	20.0	
26 to 30	469	26.5	429	25.8	
31 to 35	413	23.4	400	24.0	
35 or more	236	13.3	311	18.7	
Missing	4		4		

	Non-Hispanic White		Hispanic		
	No.	%	No.	%	P value [a]
Breastfeeding					0.18
Never	508	35.2	555	37.6	
Ever	936	64.8	922	62.4	
Menopausal status					< 0.0001
Premenopausal	422	30.0	541	38.5	
Postmenopausal	986	70.0	863	61.5	
Missing	36		73		
Body mass index, referent year (kg/m^2)					< 0.0001
< 25	633	44.0	362	24.6	
25-30	430	29.9	514	34.9	
≥ 30	376	26.1	595	40.5	
Missing	5		6		
Education					< 0.0001
Less than high school	78	5.4	546	37.7	
High school graduate	328	22.8	374	25.8	
Post high school	1,036	71.8	529	36.5	
Missing	2		28		
Body mass index, age 30 years (kg/m^2)					< 0.0001
Normal (< 25)	1,166	85.0	985	71.1	
Overweight/obese (≥ 25)	206	15.0	401	28.9	
Missing	72		91		
Estrogen/Progesterone Receptor (ER/PR) status					< 0.0001
ER+/PR+	802	68.8	731	60.4	
ER+/PR-	135	11.6	144	11.9	
ER-/PR+	23	2.0	38	3.1	
ER-/PR-	205	17.6	298	24.6	
Missing	279		266		
Stage at diagnosis					< 0.0001
Localized	990	68.6	892	60.4	
Regional	435	30.1	567	38.4	

	Non-Hispanic White		Hispanic		
	No.	**%**	**No.**	**%**	**P value** [a]
Distant	19	1.3	18	1.2	
Vital status					0.027
Alive	1,083	75.0	1,159	78.5	
Deceased	361	25.0	318	21.5	
Cause of death among deceased					0.013
Breast Cancer	171	47.4	181	56.9	
Other Cancer	63	17.5	49	15.4	
Non-Cancer	127	35.2	88	27.7	
	Mean	**SD**	**Mean**	**SD**	**P value** [b]
Duration of breastfeeding, weeks	59.6	55.5	77.3	71.0	< 0.001
Age at first birth, y	24.5	5.1	23.3	5.3	< 0.001
Age at last birth, y	29.9	5.5	30.5	6.0	0.01
Pregnancy duration, years	5.4	5.1	7.1	6.9	< 0.001
Calories consumed/day, referent yr.	2,100	925.0	2,491	1261.7	< 0.001
Waist circumference, cm	87.0	14.0	91.4	13.9	< 0.001

[a] Ethnic group comparison, chi-square p value

[b] Ethnic group comparison, t-test p value

Table 2

Associations between parity and breast cancer-specific and all-cause mortality, by ethnicity

	All Women (N=2,921)					Hispanic (n=1,477)					Non-Hispanic white (n=1,444)				
Parity	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**
Breast cancer-specific mortality															
1 to 2	1450	175	1.00	referent		636	78	1.00	referent		814	97	1.00	referent	
3 to 4	1103	135	1.17	0.93-1.47	0.19	584	71	1.15	0.82-1.59	0.42	519	64	1.24	0.90-1.71	0.20
5 or more	368	42	1.08	0.75-1.54	0.68	257	32	1.20	0.76-1.87	0.44	111	10	0.86	0.44-1.68	0.67
All-cause mortality															
1 to 2	1450	302	1.00	referent		636	115	1.00	referent		814	187	1.00	referent	
3 to 4	1103	264	1.16	0.98-1.37	0.09	584	125	1.16	0.90-1.51	0.26	519	139	1.18	0.94-1.48	0.1 5
5 or more	368	113	1.25	0.99-1.57	0.06	257	78	1.35	0.99-1.85	0.06	111	35	1.11	0.76-1.62	0.58

Models adjusted for age, SEER summary stage, study site, and ethnicity (among all women)

Table 3

Associations between history of breastfeeding and breast cancer-specific and all-cause mortality, by ethnicity

	All Women (n=2,921)					Hispanic (n=1,477)					Non-Hispanic white (n=1,444)				
Breastfeeding History	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**
Breast cancer-specific mortality															
Never	1063	126	1.00	referent		555	66	1.00	referent		508	60	1.00	referent	
Ever	1858	226	0.91	0.77-1.14	0.40	922	115	0.94	0.68-1.29	0.70	936	111	0.88	0.63-1.15	0.44
All-cause mortality															
Never	1063	273	1.00	referent		555	123	1.00	referent		508	150	1.00	referent	
Ever	1858	406	0.84	0.72-0.99	0.03	922	195	0.87	0.69-1.10	0.23	936	211	0.83	0.67-1.04	0.10

Models adjusted for age, SEER summary stage, study site, ethnicity (among all women), and parity

Table 4

Associations between lifetime breastfeeding duration in weeks (categorized as tertiles) and breast cancer-specific and all-cause mortality, overall and stratified by parity

	All Women (n=2,921)					1 to 2 births (n=1450)					3 or more births (n=1471)					
Lifetime Breastfeeding Duration (weeks)	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**P-int.**
Breast cancer-specific mortality																
Never	1063	126	1.00	referent		617	74	1.00	referent		446	52	1.00	referent		0.04
< 24	609	69	0.90	0.57-1.21	0.49	313	39	1.06	0.71-1.58	0.77	296	30	0.72	0.46-1.14	0.16	
24 -< 69.6	629	71	0.84	0.62-1.13	0.25	356	46	1.00	0.68-1.46	0.98	273	25	0.62	0.38-1.01	0.06	
≥ 69.6	620	86	0.98	0.74-1.32	0.91	164	16	0.67	0.38-1.16	0.15	456	70	1.03	0.72-1.50	0.86	
P trend								0.29					0.78			
All-cause mortality																
Never	1063	273	1.00	referent		617	150	1.00	referent		446	123	1.00	referent		0.05
< 24	609	127	0.80	0.65-0.99	0.04	313	63	0.90	0.67-1.21	0.48	296	64	0.72	0.53-0.98	0.04	
24 -< 69.6	629	122	0.76	0.62-0.95	0.01	356	65	0.81	0.61-1.09	0.21	273	57	0.72	0.52-0.99	0.04	
≥ 69.6	620	157	0.95	0.77-1.17	0.62	164	24	0.62	0.40-0.97	0.04	456	133	1.06	0.82-1.36	0.66	
P trend								0.02					0.62			

Models adjusted for age, SEER summary stage, study site, ethnicity, and parity (among all women)

Table 5

Associations between history of breastfeeding and breast cancer-specific and all-cause mortality, by tumor estrogen receptor status

	Estrogen Receptor Positive*					Estrogen Receptor Negative*				
Breastfeeding History	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**
Breast cancer-specific mortality										
Never	670	78	1.00	referent		191	30	1.00	referent	
Ever	1142	135	0.99	0.74-1.32	0.92	373	58	0.66	0.41-1.05	0.08
All-cause mortality										
Never	670	166	1.00	referent		191	53	1.00	referent	
Ever	1142	247	0.92	0.75-1.12	0.40	373	91	0.72	0.50-1.04	0.08

Models adjusted for age, SEER summary stage, study site, ethnicity, and parity

*N=545 missing estrogen receptor status

Table 6

Associations between breastfeeding history, lifetime duration of breastfeeding and breast cancer-specific and all-cause mortality, by body mass index at age 30 years

	Normal BMI at age 30 y (< 25 kg/m^2)					Overweight BMI at age 30 y (≥ 25 kg/m^2)					
Breastfeeding history and lifetime duration (weeks)	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**N**	**No. of Events**	**Hazard Ratio**	**95 % Confidence Interval**	**P value**	**P-int.**
Breast cancer-specific mortality											
Never	796	99	1.00	referent		213	20	1.00	referent		0.01
Ever	1355	135	0.70	0.53-0.92	0.01	394	69	1.67	1.00-2.80	0.05	
< 24	451	42	0.70	0.49-1.02	0.06	131	22	1.44	0.76-2.72	0.26	0.055
24 - < 69.6	471	42	0.64	0.44-0.93	0.02	122	21	1.46	0.77-2.76	0.24	
≥ 69.6	433	51	0.74	0.51-1.07	0.1	141	26	2.02	1.10-3.70	0.02	
P trend			0.29					0.04			
All-cause mortality											
Never	796	208	1.00	referent		213	45	1.00	referent		0.001
Ever	1355	244	0.68	0.56-0.83	<0.001	394	117	1.38	0.97-1.97	0.08	
< 24	451	85	0.71	0.55-0.92	0.01	131	31	1.04	0.65-1.70	0.86	0.003
24 - < 69.6	471	75	0.64	0.49-0.84	0.001	122	35	1.32	0.83-2.08	0.24	
≥ 69.6	433	84	0.70	0.53-0.91	0.01	141	51	1.79	1.18-2.73	0.01	
P trend			0.98					0.002			

Models adjusted for age, SEER summary stage, study site, ethnicity, and parity