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Brief Communication: Reproductive and lifestyle risk factors and mammographic density in Mexican women

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Abstract

Purpose—Several breast cancer risk factors have been consistently associated with mammographic density (MD); however, data are limited for Hispanic women.

Methods—We examined data from 1007 premenopausal and 600 postmenopausal women in the Mexican Teachers' Cohort (MTC). Multivariable linear regression was used to estimate associations between risk factors and MD.

Results—Among premenopausal women, age, current body mass index (BMI), BMI at age 18, and weight change since age 18 were inversely associated with percent MD, whereas benign breast disease (BBD), alcohol intake, and breastfeeding 12 months were associated with higher percent MD. Among postmenopausal women, age, current BMI, BMI at age 18, weight change since age 18, and speaking/having parents who speak an indigenous language were inversely associated with percent MD, while BBD and greater age at natural menopause, were positively associated with percent MD. Other breast cancer risk factors, such as age at menarche, parity, and age at first pregnancy, were not significantly associated with density in either premenopausal or postmenopausal women.

Conclusion—Results from the MTC are generally consistent with predictors of mammographic density observed in primarily non-Hispanic white populations; however, certain risk factors (e.g., parity) were not significantly associated with MD.

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COMPETING INTERESTS

The authors have no competing interests to declare.

INTRODUCTION

Percent mammographic density, the proportion of radio-dense epithelial and stromal breast tissue visible on a mammogram, is a strong independent breast cancer risk factor [1]. While the distribution of absolute and percent breast density varies across racial and ethnic groups [2], the positive association with breast cancer has been observed in diverse populations of women [3, 4].

Several established breast cancer risk factors, such as age [5, 6], body mass index (BMI) [7–9], menopausal status [5, 7, 10], and parity [6, 7], have been consistently associated with mammographic density; however, data are limited for Hispanic and Mexican women [11, 12]. Given rapidly increasing breast cancer incidence and mortality rates in Mexico [13], understanding predictors of mammographic density in this population has important public health and clinical implications. Therefore, we examined the associations between reproductive and lifestyle factors and mammographic density among pre- and postmenopausal women residing in Mexico.

METHODS

Study population

Briefly, the Mexican Teachers' Cohort (MTC) was established in 2006 when 28,345 female teachers aged 35 years in the Mexican states of Jalisco and Veracruz responded to a baseline questionnaire. The cohort was subsequently expanded to include 115,315 women in 12 states. In 2007, 2,349 women in Jalisco and Veracruz aged 35 or older were randomly selected within strata of menopausal status (~50% premenopausal and ~50% postmenopausal) and area of residence (~70% urban, ~30% rural) and invited to participate in a clinical evaluation at their local clinic that included an interview, anthropometry, and mammography conducted on the same day [14, 15]. A total of 1,942 women who were invited from the two states participated in the clinical subcohort. Further, an additional 91 MTC participants from Jalisco learned about the clinical subcohort from fellow participants and volunteered to participate in the subcohort. Mammographic density measurements were available for 1,707 women. The following exclusions were made: unknown menopausal status (n=83), prior breast cancer diagnosis (n=11), or unknown BMI (n=6). Our final analytic sample included 1007 premenopausal and 600 postmenopausal women. Informed consent was obtained from all participants and the study was approved by the human research committee at the National Institute of Public Health in Mexico.

Selected reproductive and lifestyle risk factors

From the 2006 self-administered questionnaire, we obtained information on year of birth, age at menarche, parity, age at first pregnancy, breastfeeding, family history of breast cancer (defined as history of breast cancer in the participant's mother, father, siblings, or children), personal history of benign breast disease (BBD), height, weight at age 18, current weight, hormonal contraceptive use, alcohol consumption (average consumption over the last year), and menopausal hormone therapy (HT) use. Current height and weight was measured by trained technicians at clinic visit. For 99 women missing data on height and weight from the

clinic visit, we used self-reported height and weight from the 2006 questionnaire. Current BMI and BMI at age 18 were calculated as weight (kg)/height(m)². Age was calculated as age at mammogram. In addition, as indigenous genetic ancestry has been associated with lower risk of breast cancer in Mexican women, we also examined whether women who reported on the 2006 questionnaire that they spoke, or their parents spoke, an indigenous language had lower mammographic density.[16]

Menopausal status

On the 2006 questionnaire, participants were asked whether they had undergone menopause (defined as the permanent cessation of periods for more than 12 months). Women who responded no were classified as premenopausal and women who did not respond were classified as unknown. Women who responded yes were then asked the reason why their periods stopped with the following as options: 1) natural menopause, 2) oophorectomy, 3) hysterectomy, 4) radiation, or 5) chemotherapy. Women who responded that they underwent natural menopause or had an oophorectomy were classified as postmenopausal; women who reported other reasons (or did not provide a reason) were classified as unknown. Lastly, women who were of unknown menopausal status, but under the age of 40 were classified as premenopausal as over 90% of women in the cohort had not reached menopause by that age. Similarly, women who were of unknown menopausal status, but over the age of 51 were classified as postmenopausal as over 90% of women in the cohort had reached menopause by that age.

Mammographic density

Mammography methods were reported previously[17–19]. Briefly, a single reader measured breast density from digitized film mammograms of the craniocaudal view of the left breast using Mamgr (developed at the Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine), a computer-assisted thresholding technique [20–22]. As previously reported, the intraclass correlation coefficient (ICC) between percent MD assessed using Mamgr software versus the Cumulus program (developed at the University of Toronto) was 0.87 in a reliability study of 100 mammograms.[18] Percent mammographic density was calculated by dividing dense area by total breast area; non-dense area represents the difference between total and dense area.

Statistical analysis

Multivariable linear regression was used to estimate cross-sectional associations between selected factors and percent mammographic density, adjusting for age (continuous), state (Veracruz, Jalisco), BMI (continuous), BMI at age 18 (continuous), age at menarche (<12, 12, 13, 14+, unknown), nulliparity (yes, no, unknown), number of children among parous women (continuous), age at first pregnancy (<25, 25+, unknown), breastfeeding among parous women (never, <12 months, 12+ months, unknown), family history of breast cancer (no, yes), BBD history (never, ever), hormonal contraceptive use (never, past, current, unknown), alcohol consumption (none, any, unknown), speaking, or having parents who speak, an indigenous language/dialect (no, yes), and HT use (never, past, current; postmenopausal women only) among pre- and postmenopausal women separately. Dense and non-dense breast areas were natural log-transformed and modeled as secondary

outcomes. In a sensitivity analysis, we stratified all analyses by state. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Means and frequencies of selected risk factors stratified by menopausal status are presented in Table 1. Dense area and non-dense area of the breast were positively correlated (Pearson correlation coefficient= 0.049, $p=0.05$). Overall, women in Jalisco had a 6 percentage point higher mean percent density compared to women in Veracruz, after adjustment for the selected lifestyle and reproductive risk factors (data not shown). In multivariable models, greater age, current BMI, BMI at age 18, and weight change since age 18 were associated with significantly lower percent density among premenopausal women, while history of BBD and 12 months breastfeeding among parous women (vs. never) were associated with significantly higher percent density (Table 2). In addition, percent density was higher among women who reported that they drank alcohol. Similar patterns of associations were observed for dense breast area, with the exception of current BMI and weight change since age 18 which were positively associated with absolute dense area as well as strongly positively associated with non-dense breast area. Associations between the selected factors and percent density in premenopausal women did not vary significantly by state except for nulliparity. Nulliparous women in Veracruz had lower percent density compared to parous women in Veracruz (difference=−5.03 percentage points, 95%CI: −9.62, −0.44) whereas there was no difference in percent density by nulliparity in Jalisco (difference= 1.92 percentage points, 95%CI: −1.56, 5.39; p -heterogeneity = 0.01).

Among postmenopausal women, greater age, current BMI, BMI at age 18, weight change since age 18, and speaking (or having parents who speak) an indigenous language were associated with significantly lower percent density, while history of BBD and greater age at natural menopause was associated with higher percent density (Table 3). Similar patterns of associations were observed for absolute dense breast area, except for current BMI and weight change since age 18, which were positively associated with dense area. Age, current BMI, BMI at age 18, and weight change since age 18 were both significantly positively associated with non-dense breast area. Family history of breast cancer was not significantly associated with percent mammographic density, but a significant positive association was observed for dense area. While the association between number of children (among parous) and percent density in postmenopausal women did vary by state (p -heterogeneity=0.04), the associations were not significant in either state (difference=1.55, 95%CI: −0.11, 3.22; difference= −1.21, 95%CI: −2.83, 0.42 for Jalisco and Veracruz, respectively). In multivariable-adjusted models, there were no apparent associations between mammographic density and age at menarche, age at first pregnancy, hormonal contraceptive use, or number of births among parous women in either pre- or postmenopausal women (Tables 2 and 3).

DISCUSSION

We observed inverse associations for age, current BMI, BMI at age 18, and weight change since age 18 as well as a positive association for history of BBD with percent mammographic density in this population of Mexican women. We previously reported the

association between current adult BMI and percent density in the MTC [17], which has been observed in other studies including Hispanic women [11, 12]. The positive association between percent mammographic density and history of BBD that we observed is consistent with the published literature on this topic [23].

There is fairly consistent evidence that nulliparity is associated with higher mammographic density, however we did not observe an association in this population [7, 24]. Consistent with our findings, Gapstur et al. [11] found no association for nulliparity among Hispanic women, but were limited by few nulliparous women (n=10). Our observation that parous premenopausal women in the MTC who breastfed 12 months had significantly higher mammographic density was unexpected: prior studies have suggested either no association or an inverse association [24, 25]. In contrast to Gapstur et al. [11], we observed a significant positive association between age at natural menopause and percent density. Most prior studies have found a positive association between alcohol intake and mammographic density [7, 26]; among Hispanic women, Gapstur et al. [11] reported a non-significant positive association with alcohol. Our findings among premenopausal women are consistent with this evidence, however the difference was modest potentially due to low consumption of alcohol among drinkers.

A novel finding in these analyses was that postmenopausal Mexican women who reported speaking (or having parents who speak) an indigenous language/dialect had significantly lower mean percent density and lower dense area than those who did not. This is consistent with a prior study in Mexican women which observed that proportion of indigenous genetic ancestry was inversely associated with risk of breast cancer.[16] Similarly, indigenous genetic ancestry was associated with a lower risk of breast cancer in US Latinas.[27] While this difference in percent MD was not observed among premenopausal women, this observation suggests possible influences of genetic variation or cultural factors (e.g., socioeconomic, lifestyle, or dietary factors) on mammographic density. While we believe these findings warrant further investigation, only 4% of the women in this analysis reported speaking an indigenous language; therefore these results should be interpreted with caution.

Differences in breast cancer risk by race/ethnicity may reflect, in part, differences in the distribution of known epidemiologic risk factors, such as mammographic density, yet most studies have evaluated predictors of mammographic density among non-Hispanic white women [11, 12]. Heterogeneity likely also exists within Hispanic populations [11, 25]. In this study of Mexican women, a population experiencing a rapid epidemiologic transition and increasing breast cancer incidence rates [13], we found risk factors for high mammographic density that were generally consistent with those identified in primarily non-Hispanic white populations (e.g., age, BMI, and history of BBD). Differences in the distributions of risk factors in different study populations could explain some of the differences in study findings; alternatively, some risk factors for mammographic density (e.g., indigenous language) may be unique to this population.

Our study has some limitations. Because of the cross-sectional study design, temporality could not be established for many of the factors evaluated. While mammographic density measurements are highly reproducible (intrareader ICC=0.84; [17]), there may be some

random error. Importantly, with some exceptions (i.e., BMI), participant characteristics were mainly based on self-report and therefore there may be non-differential misclassification of the selected risk factors. While missingness was less than 10% for each variable included in the models, there may be a small amount of residual confounding in our analyses. To our knowledge, ours is the first comprehensive study of breast cancer risk factors and mammographic density in a large population of Mexican women. Additional strengths of our study include the centralized administration of mammograms, availability of detailed information on demographic and risk factor information (reducing the potential for unmeasured confounding), and relatively large sample size, which allowed us to evaluate associations for pre- and postmenopausal women separately.

In conclusion, among premenopausal Mexican women, age, current BMI, BMI at age 18, and weight change since age 18 were inversely associated with percent density, whereas history of BBD, alcohol intake, and breastfeeding 12 months among parous women were associated with higher percent density. Among postmenopausal women, age, current BMI, BMI at age 18, and weight change since age 18, and speaking (or having parents who speak) an indigenous language/dialect were inversely associated with percent density, while a positive association between age at natural menopause, history of BBD, and percent mammographic density was observed. Other breast cancer risk factors, such as age at menarche as well as age at first pregnancy and number of births among parous women, were not associated with mammographic density in either premenopausal or postmenopausal women.

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ABBREVIATIONS

BMI	body mass index
BBD	benign breast disease
HT	hormone therapy

References

1. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2006; 15(6):1159–1169. [PubMed: 16775176]
2. El-Bastawissi AY, White E, Mandelson MT, Taplin S. Variation in mammographic breast density by race. *Ann Epidemiol*. 2001; 11(4):257–263. [PubMed: 11306344]

3. Maskarinec G, Pagano I, Lurie G, Wilkens LR, Kolonel LN. Mammographic density and breast cancer risk: the multiethnic cohort study. *Am J Epidemiol*. 2005; 162(8):743–752. [PubMed: 16150892]
4. Ursin G, Ma H, Wu AH, Bernstein L, Salane M, Parisky YR, Astrahan M, Siozon CC, Pike MC. Mammographic density and breast cancer in three ethnic groups. *Cancer Epidemiol Biomarkers Prev*. 2003; 12(4):332–338. [PubMed: 12692108]
5. Byrne C, Schairer C, Wolfe J, Parekh N, Salane M, Brinton LA, Hoover R, Haile R. Mammographic features and breast cancer risk: effects with time, age, and menopause status. *Journal of the National Cancer Institute*. 1995; 87(21):1622–1629. [PubMed: 7563205]
6. Martin LJ, Boyd NF. Mammographic density. Potential mechanisms of breast cancer risk associated with mammographic density: hypotheses based on epidemiological evidence. *Breast cancer research: BCR*. 2008; 10(1):201. [PubMed: 18226174]
7. Vachon CM, Kuni CC, Anderson K, Anderson VE, Sellers TA. Association of mammographically defined percent breast density with epidemiologic risk factors for breast cancer (United States). *Cancer Causes Control*. 2000; 11(7):653–662. [PubMed: 10977110]
8. Boyd NF, Lockwood GA, Byng JW, Little LE, Yaffe MJ, Tritchler DL. The relationship of anthropometric measures to radiological features of the breast in premenopausal women. *Br J Cancer*. 1998; 78(9):1233–1238. [PubMed: 9820186]
9. McCormack VA, dos Santos Silva I, De Stavola BL, Perry N, Vinnicombe S, Swerdlow AJ, Hardy R, Kuh D. Life-course body size and perimenopausal mammographic parenchymal patterns in the MRC 1946 British birth cohort. *Br J Cancer*. 2003; 89(5):852–859. [PubMed: 12942117]
10. Boyd N, Martin L, Stone J, Little L, Minkin S, Yaffe M. A longitudinal study of the effects of menopause on mammographic features. *Cancer Epidemiol Biomarkers Prev*. 2002; 11(10 Pt 1):1048–1053. [PubMed: 12376506]
11. Gapstur SM, Lopez P, Colangelo LA, Wolfman J, Van Horn L, Hendrick RE. Associations of breast cancer risk factors with breast density in Hispanic women. *Cancer Epidemiol Biomarkers Prev*. 2003; 12(10):1074–1080. [PubMed: 14578145]
12. Caire-Juvera G, Arendell LA, Maskarinec G, Thomson CA, Chen Z. Associations between mammographic density and body composition in Hispanic and non-Hispanic white women by menopause status. *Menopause*. 2008; 15(2):319–325. [PubMed: 18090034]
13. Chavarri-Guerra Y, Villarreal-Garza C, Liedke PE, Knaul F, Mohar A, Finkelstein DM, Goss PE. Breast cancer in Mexico: a growing challenge to health and the health system. *Lancet Oncol*. 2012; 13(8):e335–343. [PubMed: 22846838]
14. Lajous ML-RR, Santoyo-Vistrain R, Garcia-Anaya A, Ortiz-Panozo E, Yunes-Diaz E, Sanchez-Zamorano LM, Torres-Mejia G, Lazcano-Ponce E, Hernandez-Avila M, Willet WC, Romeieu I. Cohort Profile: The Mexican Teachers' Health Study (ESMaestras). *Int J Epidemiol*. Accepted.
15. Romeieu I, Escamilla-Nunez MC, Sanchez-Zamorano LM, Lopez-Ridaura R, Torres-Mejia G, Yunes EM, Lajous M, Rivera-Dommarco JA, Lazcano-Ponce E. The association between body shape silhouette and dietary pattern among Mexican women. *Public Health Nutr*. 2011:1–10. [PubMed: 21211099]
16. Fejerman L, Romeieu I, John EM, Lazcano-Ponce E, Huntsman S, Beckman KB, Perez-Stable EJ, Gonzalez Burchard E, Ziv E, Torres-Mejia G. European ancestry is positively associated with breast cancer risk in Mexican women. *Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2010; 19(4):1074–1082.
17. Rice MS, Bertrand KA, Lajous M, Tamimi RM, Torres-Mejia G, Biessy C, Lopez-Ridaura R, Romeieu I. Body size throughout the life course and mammographic density in Mexican women. *Breast Cancer Res Treat*. 2013; 138(2):601–610. [PubMed: 23460247]
18. Rice MS, Biessy C, Lajous M, Bertrand KA, Tamimi RM, Torres-Mejia G, Lopez-Ridaura R, Romeieu I, Rinaldi S, Hernandez M, et al. Metabolic syndrome and mammographic density in Mexican women. Circulating concentrations of insulin-like growth factor-I, insulin-like growth factor-binding protein-3, genetic polymorphisms and mammographic density in premenopausal Mexican women: results from the ESMaestras cohort. *Cancer Prev Res (Phila)*. 2013; 6(7):701–710. doi:10.1158/1940-6207.CAPR-1112-0475. Epub 2013 May 11. [PubMed: 23682074]

19. Rinaldi S, Biessy C, Hernandez M, Lesueur F, dos-Santos-Silva I, Rice MS, Lajous M, Lopez-Ridaura R, Torres-Mejia G, Romieu I. Circulating concentrations of insulin-like growth factor-I, insulin-like growth factor-binding protein-3, genetic polymorphisms and mammographic density in premenopausal Mexican women: results from the ESMAestras cohort. *Int J Cancer*. 2014; 134(6):1436–1444. doi:1410.1002/ijc.28469. Epub 22013 Oct 28465. [PubMed: 24037648]
20. Byng JW, Boyd NF, Fishell E, Jong RA, Yaffe MJ. The quantitative analysis of mammographic densities. *Phys Med Biol*. 1994; 39(10):1629–1638. [PubMed: 15551535]
21. Ursin G, Astrahan MA, Salane M, Parisky YR, Pearce JG, Daniels JR, Pike MC, Spicer DV. The detection of changes in mammographic densities. *Cancer Epidemiol Biomarkers Prev*. 1998; 7(1): 43–47. [PubMed: 9456242]
22. Torres-Mejia G, De Stavola B, Allen DS, Perez-Gavilan JJ, Ferreira JM, Fentiman IS, Dos Santos Silva I. Mammographic features and subsequent risk of breast cancer: a comparison of qualitative and quantitative evaluations in the Guernsey prospective studies. *Cancer Epidemiol Biomarkers Prev*. 2005; 14(5):1052–1059. [PubMed: 15894652]
23. Boyd NF, Jensen HM, Cooke G, Han HL, Lockwood GA, Miller AB. Mammographic densities and the prevalence and incidence of histological types of benign breast disease. Reference Pathologists of the Canadian National Breast Screening Study. *Eur J Cancer Prev*. 2000; 9(1):15–24. [PubMed: 10777006]
24. Butler LM, Gold EB, Greendale GA, Crandall CJ, Modugno F, Oestreicher N, Quesenberry CP Jr, Habel LA. Menstrual and reproductive factors in relation to mammographic density: the Study of Women's Health Across the Nation (SWAN). *Breast Cancer Res Treat*. 2008; 112(1):165–174. [PubMed: 18066689]
25. Tehranifar P, Reynolds D, Flom J, Fulton L, Liao Y, Kudadjie-Gyamfi E, Terry MB. Reproductive and menstrual factors and mammographic density in African American, Caribbean, and white women. *Cancer Causes Control*. 2011
26. Cabanes A, Pastor-Barriuso R, Garcia-Lopez M, Pedraz-Pingarron C, Sanchez-Contador C, Vazquez Carrete JA, Moreno MP, Vidal C, Salas D, Miranda-Garcia J, et al. Alcohol, tobacco, and mammographic density: a population-based study. *Breast Cancer Res Treat*. 2011
27. Fejerman L, John EM, Huntsman S, Beckman K, Choudhry S, Perez-Stable E, Burchard EG, Ziv E. Genetic ancestry and risk of breast cancer among U.S. Latinas. *Cancer research*. 2008; 68(23): 9723–9728. [PubMed: 19047150]

Table 1

Selected risk factors and mammographic density measures by menopausal status (MTC, 2006)

	Premenopausal N=1007	Postmenopausal N=600
Mean (SD)		
Age (years)	43.3 (4.1)	53.4 (5.3)
BMI (kg/m ²)	28.4 (5.2)	29.2 (5.1)
BMI at age18 (kg/m ²)	21.2 (2.9)	21.2 (3.0)
Weight change since age 18 (lbs)	17.5 (11.5)	19.2 (12.1)
Parity (among parous)	2.4 (1.0)	2.6 (1.2)
Percent Density	37.1 (14.7)	28.0 (13.6)
Dense Area (cm ²)	48.6 (29.1)	39.9 (27.2)
Non-dense Area (cm ²)	81.6 (36.5)	102.2 (42.7)
N (Percent)		
Nulliparous	124 (12.9%)	80 (14.1%)
Family history of breast cancer	50 (5.0%)	40 (6.7%)
History of BBD	140 (13.9%)	67 (11.2%)
Indigenous language/dialect	41 (4.1%)	24 (4.1%)
Age at menarche		
<12	234 (23.5%)	147 (25.1%)
12	284 (28.5%)	158 (27.0%)
13	235 (23.6%)	106 (18.1%)
14+	242 (24.3%)	175 (29.9%)
Age at first pregnancy (among parous)		
<25	423 (51.3%)	236 (49.0%)
25+	401 (48.7%)	246 (51.0%)
Breastfeeding (among parous)		
Never breastfed	95 (11.5%)	77 (16.3%)
<12 months	359 (43.6%)	203 (42.9%)
12+ months	369 (44.8%)	193 (40.8%)
Hormonal contraceptives		
Never	461 (47.5%)	284 (49.8%)
Past use	402 (41.4%)	286 (50.2%)
Current use	25 (2.6%)	--
Ever use – current status unknown	83 (8.5%)	--
Alcohol		
None	265 (28.8%)	167 (30.8%)
Any	656 (71.2%)	375 (69.2%)
Age at natural menopause		
<45	--	142 (26.4%)

	Premenopausal N=1007	Postmenopausal N=600
45–49	--	234 (43.4%)
50+	--	163 (30.2%)
HT use		
Never	--	390 (67.2%)
Past		102 (17.6%)
Current		41 (7.1%)
Ever use – current status unknown	--	47 (8.1%)
State		
Jalisco	574 (57.0%)	217 (36.2%)
Veracruz	433 (43.0%)	383 (63.8%)

BMI=body mass index; BBD=benign breast disease; HT=hormone therapy use

Number missing for each of the selected risk factors (none missing unless otherwise indicated): BMI at age 18 (N=100), weight change since age 18 (N=100), parity (N=74), indigenous language/dialect (n=21), age at menarche (N=26), age at first pregnancy among parous (N=23), breastfeeding among parous (N=33), hormonal contraceptive use (N=66), alcohol use (N=144), PMH use (N=20), age at natural menopause (N=61)

Table 2

Differences in mammographic density by selected risk factors among premenopausal women (MTC, 2006)

	Percent density ^a	Ln dense area (cm ²) ^{a,b}	Ln non-dense area (cm ²) ^{a,c}
Age (years)	-0.38 (-0.60,-0.16)	-0.017 (-0.027,-0.007)	0.004 (-0.002,0.009)
BMI (kg/m ²)	-0.40 (-0.58,-0.21)	0.028 (0.018,0.038)	0.048 (0.043,0.052)
BMI at age 18 (kg/m ²) [^] [✓]	-0.68 (-0.99,-0.37)	0.014 (-0.001,0.029)	0.054 (0.047,0.062)
Weight change since age 18 (lbs) [^]	-0.13 (-0.21,-0.05)	0.012 (0.008,0.016)	0.019 (0.017,0.021)
Nulliparity	-0.23 (-2.99,2.53)	-0.119 (-0.237,-0.001)	-0.098 (-0.168,-0.029)
Number of children among parous [*]	-0.62 (-1.72,0.48)	-0.018 (-0.065,0.029)	0.005 (-0.022,0.032)
Family history of breast cancer	-0.02 (-4.00,3.96)	0.041 (-0.131,0.214)	0.029 (-0.070,0.128)
History of BBD	4.56 (2.03,7.08)	0.152 (0.042,0.261)	-0.062 (-0.125,0.001)
Indigenous language/dialect	-0.91 (-5.40,3.58)	-0.018 (-0.212,0.177)	-0.015 (-0.127,0.098)
Age at menarche			
<12	Ref	Ref	Ref
12	1.63 (-0.79,4.05)	0.052 (-0.053,0.157)	-0.022 (-0.083,0.038)
13	-0.63 (-3.17,1.90)	-0.077 (-0.187,0.033)	-0.010 (-0.073,0.054)
14+	0.87 (-1.68,3.42)	-0.011 (-0.121,0.100)	-0.018 (-0.082,0.045)
Age at first pregnancy [*]			
<25	Ref	Ref	Ref
25+	-0.84 (-2.88,1.20)	0.014 (-0.074,0.101)	0.042 (-0.009,0.093)
Breastfeeding [*]			
Never	Ref	Ref	Ref
<12 months	1.37 (-1.81,4.56)	0.082 (-0.053,0.218)	0.014 (-0.065,0.092)
12+ months	3.78 (0.51,7.05)	0.122 (-0.017,0.262)	-0.030 (-0.111,0.050)
Hormonal contraceptives			
Never	Ref	Ref	Ref
Past	-0.52 (-2.56,1.52)	-0.034 (-0.123,0.054)	-0.007 (-0.057,0.044)
Current	1.46 (-4.27,7.20)	0.121 (-0.128,0.369)	0.062 (-0.080,0.204)
Alcohol use			
No	Ref	Ref	Ref
Yes	2.26 (0.25,4.26)	0.141 (0.054,0.229)	0.021 (-0.029,0.072)

^a Adjusted for age (continuous), state (Jalisco, Veracruz), BMI (continuous), BMI at age 18 (continuous), nulliparity (yes, no), parity among parous (continuous), family history of breast cancer (yes, no), history of BBD (yes, no), indigenous language/dialect (yes, no), age at menarche (<12, 12, 13, 14+), age at first pregnancy (<25, 25+, unknown), breastfeeding among parous (never, <12 months, 12+ months, unknown), hormonal contraceptives (never, past, current, ever – current status unknown, unknown), alcohol (no, yes)

^b Further adjusted for non-dense area

^c Further adjusted for dense area

^{*} among parous

[^] not adjusted for current BMI

[✓] further adjusted for weight change since age 18

Table 3

Differences in mammographic density by selected risk factors among postmenopausal women (MTC, 2006)

	Percent density ^a	Ln dense area (cm ²) ^{a,b}	Ln non-dense area (cm ²) ^{a,c}
Age (years)	-0.25 (-0.48,-0.02)	-0.001 (-0.013,0.011)	0.010 (0.004,0.016)
BMI (kg/m ²)	-0.43 (-0.65,-0.21)	0.017 (0.004,0.030)	0.042 (0.036,0.048)
BMI at age 18 (kg/m ²) ^{^v}	-0.47 (-0.85,-0.09)	0.020 (-0.001,0.041)	0.050 (0.040,0.060)
Weight change since age 18 (lbs) [^]	-0.17 (-0.27,-0.08)	0.007 (0.002,0.013)	0.017 (0.015,0.020)
Nulliparity	0.39 (-2.77,3.56)	-0.016 (-0.177,0.144)	-0.012 (-0.095,0.070)
Parity [*]	-0.02 (-1.13,1.10)	-0.007 (-0.063,0.049)	-0.006 (-0.035,0.024)
Family history of breast cancer	2.07 (-2.06,6.20)	0.229 (0.018,0.441)	0.075 (-0.034,0.183)
History of BBD	3.68 (0.38,6.98)	0.223 (0.055,0.392)	0.024 (-0.063,0.111)
Indigenous language/dialect	-6.41 (-11.79,-1.02)	-0.279 (-0.554,-0.005)	0.050 (-0.093,0.192)
Age at menarche			
<12	Ref	Ref	Ref
12	-1.28 (-4.25,1.68)	-0.052 (-0.203,0.100)	0.022 (-0.056,0.099)
13	1.11 (-2.17,4.39)	0.078 (-0.09,0.245)	0.034 (-0.052,0.120)
14+	0.89 (-2.04,3.82)	0.079 (-0.070,0.229)	0.045 (-0.031,0.122)
Age at first pregnancy [*]			
<25	Ref	Ref	Ref
25+	-0.16 (-2.59,2.27)	-0.016 (-0.138,0.105)	-0.011 (-0.076,0.054)
Breastfeeding [*]			
Never	Ref	Ref	Ref
<12 months	-0.77 (-4.16,2.62)	-0.047 (-0.216,0.123)	-0.004 (-0.094,0.086)
12+ months	-1.22 (-4.81,2.37)	-0.023 (-0.203,0.157)	0.040 (-0.056,0.135)
Hormonal contraceptives			
Never	Ref	Ref	Ref
Past	-1.91 (-4.17,0.36)	-0.114 (-0.230,0.002)	0.001 (-0.059,0.060)
Alcohol use			
No	Ref	Ref	Ref
Yes	-0.16 (-2.53,2.21)	-0.020 (-0.140,0.101)	-0.027 (-0.090,0.035)
Age at natural menopause			
<45	Ref	Ref	Ref
45-49	3.38 (0.57,6.19)	0.172 (0.032,0.312)	-0.027 (-0.100,0.045)
50+	3.45 (0.06,6.85)	0.183 (0.014,0.352)	-0.002 (-0.090,0.086)
HT Use			
Never	Ref	Ref	Ref
Past	0.44 (-2.41,3.29)	0.051 (-0.093,0.194)	0.024 (-0.051,0.099)
Current	-0.73 (-5.01,3.54)	-0.139 (-0.354,0.076)	-0.010 (-0.122,0.102)

^a Adjusted for age (continuous), state (Jalisco, Veracruz), BMI (continuous), BMI at age 18 (continuous), parity (continuous), family history of breast cancer (yes, no), history of BBD (yes, no), other dialect (yes, no), nulliparity (yes, no), age at menarche (<12, 12, 13, 14+, unknown), age at

first pregnancy(<25, 25+, unknown), breastfeeding (<12 months, 12+ months, unknown), hormonal contraceptives (never, ever, unknown), alcohol (none, any), HT use (never, past, current, ever – current status unknown, unknown), and age at natural menopause (<45, 45–49, 50+, unknown).

^b Further adjusted for non-dense area

^c Further adjusted for dense area

* among parous

[^] not adjusted for current BMI

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