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Body mass index and mammographic density in a multiracial and multiethnic population-based study

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Abstract

Background: Mammographic density (MD) is strongly associated with breast cancer risk. We examined whether BMI partially explains racial and ethnic variation in MD.

Methods: We used multivariable Poisson regression to estimate associations between BMI and binary MD (BI-RADS A&B versus BI-RADS C&D) among 160,804 women in the Utah mammography cohort. We estimated associations overall and within racial and ethnic subgroups and calculated population attributable risk percents (PAR%s).

Results: We observed the lowest BMI and highest MD among Asian women, the highest BMI among Native Hawaiian and Pacific Islander women, and the lowest MD among American Indian and Alaska Native (AIAN) and Black women. BMI was inversely associated with MD ($RR_{BMI\geq30\ v<25}$=0.43, 95% CI=0.42-0.44) in the full cohort, and estimates in all racial and ethnic subgroups were consistent with this strong inverse association. For women <45, although there was statistical evidence of heterogeneity in associations between BMI and MD by race and ethnicity (p=0.009), magnitudes of association were similar across groups. PAR%s for BMI and MD among women <45 were considerably higher in White women (PAR% 29.2, 95% CI=28.4-29.9) compared to all other groups with estimates ranging from $PAR\%_{Asain}$=17.2%, 95%CI=8.5-25.8 to $PAR\%_{Hispanic}$=21.5%, 95%CI=19.4-23.6. For women ≥55, PAR%s for BMI and MD were highest among AIAN women (PAR% 37.5, 95% CI=28.1-46.9).

Conclusions: While we observed substantial differences in the distributions of BMI and MD by race and ethnicity, associations between BMI and MD were generally similar across groups.

Impact: Distributions of BMI and MD may be important contributors to breast cancer disparities.

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Keywords

mammographic density; health status disparities; body mass index; hormone therapy; breast cancer

INTRODUCTION

Breast cancer is the second most common cause of cancer-related death among women in the United States (US) (1). Breast cancer incidence is highest among non-Hispanic White women and non-Hispanic Black women, and lowest among the combined Asian and Native Hawaiian/Pacific Islander populations (1). However, data from the Surveillance, Epidemiology and End Results (SEER) cancer registries suggest that when data from Asian and Native Hawaiian/Pacific Islander women are analyzed separately, some of the highest breast cancer incidence and death rates are among Native Hawaiian and Pacific Islander women (2-4).

Mammographic density (MD) is one of the strongest breast cancer risk factors. MD is defined as the extent of fibroglandular versus fatty breast tissue, and can be measured as the percentage of the breast containing fibroglandular tissue, or as a visual estimate by radiologists [Breast Imaging Reporting and Database System (BI-RADS) score] (5). Women with percent MD >75% are estimated to have a risk of breast cancer that is 4-6 times greater than women with percent MD <5% (6, 7), and >30% of breast cancers are attributed to the presence of dense tissue in >50% of the breast (8).

BMI, a metric correlated with measures of body fat, is correlated with the amount of adipose tissue in the breast (9) and, therefore, associated with lower MD (7). While BMI is associated with lower MD in both pre- and postmenopausal women, BMI is inversely associated with breast cancer among premenopausal women, but positively associated with breast cancer among postmenopausal women (7). Hormone therapy (HT) use is also a strong breast cancer risk factor among postmenopausal women (10, 11), and prior studies have reported stronger positive associations between MD and breast cancer among women taking HT (12, 13).

The associations between BMI and MD, and BMI, MD and breast cancer are well-established; however, the extent to which these associations vary by race and ethnicity is still being investigated. Here, we estimated the prevalence of high BMI and high MD within racial and ethnic subgroups in Utah and sought to understand the proportion of MD attributable to low BMI, overall and by race and ethnicity. Then, putting the two together, we estimated the proportion of breast cancer cases that would not have occurred if Utah women had lower MD, and the proportion of breast cancer cases that could have been avoided if postmenopausal Utah women had lower BMI.

MATERIALS AND METHODS

Study Population

The Utah Population Database (UPDB) is a population-based resource that contains information on >11 million individuals who are living or have lived in Utah, or are ancestors of current and former residents. Data are captured from multiple sources, including vital records, US census data, the Utah Cancer Registry (UCR), statewide claims databases and ambulatory surgery records, hospital-level electronic medical records, and Utah Driver License Division data. Within the UPDB, we assembled a mammography cohort including all women who received at least one digital mammogram at Intermountain Healthcare (Intermountain) or University of Utah Health Care (UHEALTH) between 2005 and 2019. As of October 2020, this cohort included 235,520 women ages 18-70 years at baseline mammogram (i.e., first screening mammogram between 2005 and 2019). Data were collected under a waiver of informed consent, and study protocols were approved by the Resource for Genetic Epidemiology ethics committee and the University of Utah IRB, following the guidelines in the Belmont Report.

Covariates

Information on baseline MD was extracted from medical records at Intermountain and UHEALTH, which together, capture >75% of health care in Utah. Radiologists recorded BI-RADS breast density as (A) almost entirely fatty; (B) scattered fibroglandular densities; (C) heterogeneously dense; or (D) extremely dense. Breast cancer cases, defined by ICD-O-2/3 codes of C500-509, were identified through linkage to the UCR, a SEER site since 1973.

Information on race and ethnicity was available through the UPDB demographic dataset which standardizes data from multiple self-reported and observational data sources. We cross-classified the 5 racial categories used by the Federal Office of Management and Budget (OMB)—American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White (14)—with Hispanic ethnicity to get 6 racial-ethnic categories: non-Hispanic American Indian or Alaska Native; non-Hispanic Asian; non-Hispanic Black or African American; non-Hispanic Native Hawaiian or other Pacific Islander; non-Hispanic White, and Hispanic. We also evaluated Native Hawaiian/Pacific Islander, and Asian subgroups. For Native Hawaiian and Pacific Islander women, these included Native Hawaiian and “Other Pacific Islander” (i.e., Samoan, Guamanian, Micronesian, Tahitian, Tongan or “Pacific Islander not otherwise specified”.) For Asian women, subgroupings included Chinese, Japanese, Filipino, and “Other Asian” (i.e., from Korea, Vietnam, India, and additional countries in Asia). Recognizing that all of the above are social constructs, we followed reporting guidelines to encourage clear, consistent, and equitable consideration of race and ethnicity (15).

BMI (in kg/m^2) was calculated using height and weight as self-reported on issuance or renewal of a Utah driver license, a method that systematically underestimates true BMI but effectively ranks people by BMI and consistently identifies those who are obese (BMI ≥ 30) (16). To generate a single value for use in analyses, we dropped unrealistic BMI values (BMI<14 or BMI>100) then averaged each participant’s first and most recent BMI. First

BMI often reflected height and weight many years prior to the baseline mammogram, while the most recent BMI was calculated using height and weight information reported around the time of, or many years after, the baseline mammogram. When only one measurement was recorded we used the single, available value in place of an average.

Consistent with studies of metabolic health and breast cancer risk, we categorized BMI using National Institutes of Health (NIH) and World Health Organization (WHO) cutoffs: underweight (BMI ≤18.5 kg/m^2); normal (18.6-24.9 kg/m^2); overweight (25-29.9 kg/m^2); and obese (≥30 kg/m^2) (17-19). Due to the very small number of women in the underweight category, especially within subgroups, we collapsed underweight and normal weight into a single reference category. In sensitivity analyses, we included categorizations for Asian individuals as 23 (overweight) and 27.5 (obese); and 26 (overweight) and 32 (obese) for NHPI women.

Data on menopausal status were not available, so, consistent with other cohorts, we used age ≥55 years as a proxy for postmenopausal status (20). We also considered age <45 as a proxy for premenopausal status, though prior data suggest that 11-22% of women experience menopause prior to age 45 (21). Data on past and current (within 3 years of baseline mammogram) use of tamoxifen, aromatase inhibitors, and HT were collected from inpatient and outpatient orders and the All-Payer Claims Database. Information on parity, including age at first birth and number of children prior to 2018, was gathered from multiple sources including UPDB ancestry data and birth certificates. Utah birth certificates capture both the current birth and the mother's prior births, so, when combined with ancestry data, parity in Utah is captured very well and out-of-state births are partially captured. Urbanicity was calculated using Rural-Urban Commuting Area (RUCA) coding of the home address in closest temporal proximity to the baseline mammogram (codes <7 were considered urban), and educational status was estimated from the UPDB demographic dataset, also using data in close temporal proximity to the baseline mammogram.

Given our interest in MD as observed on screening mammograms, we excluded women whose initial mammograms within the study period were diagnostic (n=17,619), women with a UCR breast cancer diagnosis before baseline (n=5,374), women with a history of tamoxifen or aromatase inhibitor use (n=238), and women with breast implants (n=17,285). We further excluded women under age 30 (n=408), women missing race or ethnicity data (n=29,355), and women without BMI data (n=4,437). This left 160,804 women (1,962,299 person-years) eligible for analyses.

Statistical Analysis

To estimate multivariable-adjusted relative risks for the association between BMI and high MD we used modified Poisson generalized estimating equations with robust error estimates (22). To estimate multivariable-adjusted relative risks for the associations between BMI and breast cancer, and MD and breast cancer, we used Cox proportional hazards models mutually adjusted for BMI/MD and allowed for differing baseline hazards by increasing age (as individuals contributed person-time). For each analysis, we reported point estimates and 95% confidence intervals (CI) overall and jointly stratified by race and ethnicity and by age (<45, 45-<55, and ≥55 years). Each model accounted for age at mammogram, parity (0, 1,

2+ births in Utah, parous with number of births not known), HT use (current, past, never), and educational status (less than high school, high school, some college, college, missing). Because the distributions of BMI and MD differed across racial and ethnic groups, and these comparisons were central to our research, we created a categorical BMI variable (<25, ≥25-<30, and ≥30 kg/m^2) and binary MD variable ("low MD" defined as "almost entirely fatty or scattered fibroglandular densities" and "high MD" defined as "heterogeneously dense or extremely dense") for our analyses. Tests for trend were conducted using BMI as a continuous variable.

To test for effect modification by race and ethnicity and by HT, we ran models with and without an interaction between MD and the modifier of interest and used likelihood ratio tests to evaluate statistical significance. We were also interested in potential effect modification by urban versus rural residency; however, the vast majority of women resided in urban locations so we were only able to consider an analysis restricted to women in urban neighborhoods.

We calculated population attributable risk percents (PAR%s) to understand the proportion of women with high MD who would have had low MD if they had a BMI ≥25, and we calculated the proportion of breast cancer that would not have occurred if high BMI (BMI≥25) or high MD (BI-RADS C/D) had been removed from our population. PAR%s were calculated using the following formula in which P is the proportion of exposed individuals in the population and RR is the relative risk.

$$PAR\% = \frac{P(RR-1)}{P(RR-1)+1} * 100$$

We estimated adjusted relative risks using the modified Poisson generalized estimating equation modeling approach, as described above, when calculating the percent of high mammographic density explained by low BMI (22), and we estimated adjusted relative risks using pooled conditional regression when calculating the percent of incident breast cancer explained by BMI or MD (23). Analyses were completed using SAS 9.4.1, and statistical tests assumed a two-sided alpha of 0.05. Consistent with UPDB confidentiality policies, we masked all counts and percentages that reflect <11 cases. The data analyzed in this study are available from the Utah Population Database. Utah Population Database data usage is governed by the Utah Resource for Genetic and Epidemiologic Research (RGE). Data are available from the authors upon reasonable request and with approval from the RGE.

RESULTS

Our study included 631 American Indian or Alaska Native women, 1,828 Asian women, 821 Black women, 8,791 Hispanic women, 271 Native Hawaiian or Pacific Islander women, and 148,462 White women. There were dramatic differences in the prevalence of obesity and high MD by race and ethnicity (Table 1). For example, we observed the highest prevalence of obesity among Native Hawaiian and Pacific Islander women (i.e., 39.1% of Native Hawaiian, and 52.2% of "other Pacific Islander" women were obese) and the lowest prevalence of obesity among Asian women (i.e., ranging from 4.6% of "other Asian" women

to 6.8% of Chinese women). We observed the lowest reportable prevalence of "extremely dense" MD among American Indian and Alaska Native women (5.1% categorized as BIRADS-D), and the greatest prevalence of "extremely dense" MD among Chinese (27.5%) and "other Asian" (16.7%) women.

Higher BMI was strongly associated with lower MD (Table 2); the relative risk of high MD among individuals with BMI ≥30 kg/m^2 compared to BMI <25 kg/m^2 ranged from 0.52 (Asian, 95% CI=0.39-0.68) to 0.35 (American Indian or Alaska Native, 95% CI=0.26-0.46). There was statistically significant evidence of heterogeneity (p=0.009) by race and ethnicity among women ages <45 with estimates ranging from 0.56 (Asian, 95% CI=0.34-0.94) to 0.34 (Native Hawaiian or Pacific Islander, 95% CI=0.21-0.54). We did not observe statistically significant evidence of heterogeneity by race and ethnicity among women ages 45-<55 (p=0.14) or ≥55 (p=0.24), though among women ages ≥55, magnitudes of association ranged from $RR_{BMI\geq30 \text{ vs. } BMI<25}$=0.55 (95% CI=0.33-0.91) for Asian women to $RR_{BMI\geq30 \text{ vs. } BMI<25}$=0.24 (95% CI=0.09-0.64) for Native Hawaiian and Pacific Islander women.

We conducted sensitivity analyses to explore the heterogeneity within our study population. First, breast cancer screening is not recommended among average risk women before age 40 (24), so we conducted an analysis restricted to women ages ≥40 years. Results were nearly identical to the main analysis (Supplemental Table 1). Second, to acknowledge the racial diversity within our Hispanic population, we considered alternate cross-classifications of race and ethnicity such that all non-White Hispanic women were moved from the Hispanic category to their racially defined category (Supplemental Table 2). Using this classification, we observed similar associations between BMI and MD (Supplemental Table 3) as were observed in the main analysis (Table 2). Third, as prior studies have suggested that Asian women may experience adverse health effects at lower BMI and Pacific Islander women may experience adverse health effects at higher BMI, we also considered the associations between BMI and MD using racial and ethnic-specific BMI cutoffs (9, 25-28); associations were slightly attenuated, particularly among Asian women (Supplemental Table 4). Fourth, as Utah's urban and rural/frontier populations often have different cultural and lived experiences and different access to health care we ran analyses of BMI and MD that were restricted to women living in more urban areas (RUCA <7; Supplemental Table 5) and observed similar results to the main analysis. Finally, in analyses stratified by HT use, the associations between BMI and MD among never users of HT were similar to the full cohort ($RR_{BMI\geq30 \text{ vs. } BMI<25}$=0.43, 95% CI=0.42-0.44), while results among current HT users were slightly weaker in magnitude ($RR_{BMI\geq30 \text{ vs. } BMI<25}$= 0.50, 95% CI=0.47-0.54; Supplemental Table 6).

The counts of breast cancer cases among American Indian or Alaska Native, Asian, Black, and Native Hawaiian or Pacific Islander women in this cohort were too small to evaluate associations between BMI or MD and breast cancer risk, so we evaluated these associations only among White and Hispanic women (Table 3). Higher BMI was statistically significantly associated with greater breast cancer risk among women ages ≥55 ($HR_{BMI\geq30 \text{ vs. } BMI<25}$=1.41, 95% CI=1.30-1.52), but not among women ages <45 ($HR_{BMI\geq30 \text{ vs. } BMI<25}$=1.09, 95% CI=0.72-1.64), or 45-<55 years

($HR_{BMI\geq30 \text{ vs. } BMI<25}$=1.16, 95% CI=0.99-1.36). There was no evidence of heterogeneity in the magnitude of associations between Hispanic women and White women for the associations between BMI and breast cancer for women ages <45 (p=0.22), 45-<55 (p=0.14), or ≥55 years (p=0.65).

High MD was associated with greater breast cancer risk among women ages <45 (HR=1.73, 95% CI=1.24-2.40), 45-<55 (HR=2.01, 95% CI=1.76-2.31), and ≥55 years (HR=1.71, 95% CI=1.61-1.82; Table 4). There was no statistically significant evidence of heterogeneity comparing Hispanic and White women ages <45 (p=0.98), 45-55 (p=0.98) or ≥55 years (p=0.20).

PAR%s are presented in Table 5. The proportion of high MD explained by low BMI was 28.4% (95% CI=27.7-29.1) among women ages <45, and 22.9% (95% CI=22.2-23.5) among women ages ≥55 (after adjusting for HT). For women ages <45, PAR%s were highest among White women (PAR%=29.2, 95% CI=28.4-29.9) and lowest among Asian (PAR%=17.2, 95% CI=8.5-25.8) and Black (PAR%=17.3, 95% CI=11.6-22.9) women. For women ages ≥55, after additionally adjusting for HT, PAR%s were lowest for Hispanic (PAR%=23.2, 95%CI=19.6-26.7) and White (PAR%=22.5, 95%CI=21.8-23.1) women, and highest for American Indian or Alaska Native women (PAR%=37.5, 95% CI=28.1-46.9).

There was no evidence to suggest that breast cancer was explained by BMI among women ages <45 (PAR%<0), yet 6.2% (95% CI=4.7%-7.7%) of breast cancer was explained by high BMI among women ages ≥55. The percent of breast cancer explained by high MD was 29.2% (95% CI=−17.2%-65.0%) among Hispanic women ages <45, and 28.0% (95% CI=13.3%-41.4%) among White women ages <45, while the percent of breast cancer explained by high MD was 3.5% (95% CI=−3.0%-10.0%) among Hispanic women ages ≥55, and 22.1% (95% CI=19.6%-24.5%) among White women ages ≥55.

DISCUSSION

In this large, population-based study we evaluated distributions of BMI and MD by race and ethnicity and estimated associations between BMI and MD overall and within racial and ethnic subgroups. We observed strong evidence of variation in the distributions of both BMI and MD by race and ethnicity, with the highest BMI among Native Hawaiian and Pacific Islander women and the highest MD among Asian women. Consistent with prior studies, we observed an association between high BMI and low MD among women of all ages (5, 7, 29-31). We noted heterogeneity in the magnitude of this association by race and ethnicity, particularly among women ages <45, with the weakest association among Asian women and the strongest association among Native Hawaiian and Pacific Islander women. Racial and ethnic variation in BMI and MD have been reported previously. Consistent with many of our findings in Utah, the burden of obesity in the US has been described as especially strong among American Indian and Alaska Native, Black, Hispanic, and Native Hawaiian and Pacific Islander populations, and lowest among Asian populations (3, 4, 17, 32). MD is strongly correlated with age, menopausal status, and BMI, and before accounting for these factors many studies observe the greatest prevalence of high MD among Asian women (17,

18, 29, 33), just as we observed. However, after accounting for these factors, the prevalence of high MD is similar across racial and ethnic subgroups (18, 29-31, 33).

More research is needed to understand how menopausal status, BMI, estrogens, and factors associated with race and ethnicity (e.g., cultural practices, experience of racism and psychosocial stressors, genetics) interact to influence MD. Postmenopausal BMI has been positively correlated with estrone and estradiol levels (34, 35), and these estrogens have been inversely associated with MD in some, but not all, studies of postmenopausal women (36). In the Multiethnic Cohort Study, Japanese American, African American and Native Hawaiian women had higher levels of estrogens than non-Hispanic White or Latina women (37), suggesting that, if the inverse association between BMI and MD in postmenopausal women is mediated by estrogen levels, the strength of the association should be greater among Asian, Black, and Native Hawaiian or Pacific Islander women than in White or Hispanic women. This is consistent with our finding of non-statistically significantly stronger magnitudes of association between BMI and MD among Black, Native Hawaiian or Pacific Islander, and American Indian or Alaska Native women (Table 2).

We also evaluated breast cancer PAR%s which reflect the prevalence of the exposure, the cut points used to define exposure levels, and the strength of association between the exposure and outcome within the population of interest (38, 39). Our breast cancer PAR%s for BMI were lower than expected for the percent of breast cancer explained by low BMI among premenopausal women (10, 17), but similar to existing literature for the percent of breast cancer explained by high BMI among postmenopausal women (10, 17, 40, 41). While our study had limited power to consider PAR%s for BMI with breast cancer risk within racial and ethnic subgroups, our finding of similar postmenopausal PAR%s across Hispanic (9.1%, 95% CI −1.5-19.4%) and White (6.1%, 95% CI 4.6-7.7%) groups was generally consistent with data from seven US-based Breast Cancer Surveillance Consortium (BCSC) registries, though BCSC postmenopausal PAR%s were higher than in our report (12.0% Hispanic, and 15.4% White) (17).

Breast cancer PAR%s for MD were also similar to prior US-based studies. Here, we estimated that if women with heterogeneously dense or extremely dense breasts had achieved scattered fibroglandular or fatty breast density, breast cancer incidence would have been reduced by 28.3% (95% CI, 14.3-41.1%) among women ages <45, and by 21.3% (18.9%-23.7%) among women ages ≥55 years. Similar reductions were reported in US-based BCSC registry sites (17, 41). For example, one BCSC study estimated that 29% (95% CI, 25-33%) of premenopausal and 14% (95% CI, 13-16%) of postmenopausal breast cancers could have been avoided if all women with heterogeneously or extremely dense breasts had scattered fibroglandular breast density (41). Interestingly, the PAR%s varied by ethnicity in both our study and the US-based BCSC studies, but the magnitude of variation was not consistent (17).

While racial and ethnic differences in breast cancer incidence can reflect differences in access to mammography, genetic variation, or other factors, findings from the present study suggest that the prevalence of lifestyle and other risk factors should be considered when evaluating the causes of disparities in breast cancer incidence and strategies

for reducing those disparities. For example, most breast cancers are diagnosed among postmenopausal women, so considering the prevalence of high BMI, a modifiable risk factor for postmenopausal breast cancer and many other chronic diseases (e.g., cardiovascular disease, diabetes, chronic kidney disease) (7, 42), may be important when conceptualizing community-based prevention strategies. In this Utah-based study, we observed that BMI is highest in Native Hawaiian and Pacific Islander women and lowest in Asian women. In other US-based studies, the burden of obesity has been described as highest among American Indian and Alaska Native, Black, Hispanic, and Native Hawaiian and Pacific Islander populations, and lowest among Asian populations (3, 4, 17, 32). Given these differences in the distribution of BMI and that sustained weight loss has been associated with lower breast cancer risk (43), weight management interventions that take into consideration structural inequities and the diverse cultural, religious and language preferences of the American Indian and Alaska Native, Black, Hispanic, and Native Hawaiian and Pacific Islander communities are important.

MD is also considered a modifiable breast cancer risk factor, and reductions in MD have been associated with lower breast cancer risk (44). As aromatase inhibitors, tamoxifen and other interventions continue to be assessed as possible modifiers of MD and breast cancer risk, our data suggest that it will be important to consider effect modification by factors that are differentially distributed by race and ethnicity.

Key strengths of our study include the population-based design and the inclusion of granular data on race and ethnicity. The large, population-based design allowed us to consider the importance of obesity and MD to breast cancer risk among NIH-defined racial and ethnic groups, and allowed us to estimate PAR%s for obesity on MD. Important limitations of the study included low power to consider breast cancer incidence, the use of binary BI-RADS scores, limited data on reproductive factors (e.g., age at menarche, menopausal status, parity outside of Utah, oral contraceptive use), and the use of covariate data measured before or after the timing of the baseline mammogram. While we were unable to estimate the associations of BMI and MD with breast cancer risk for Asian, American Indian and Alaska Native, Black, and Native Hawaiian and Pacific Islander women, we were able to estimate the associations between BMI and MD in all of these, often understudied, racial and ethnic groups. As more breast cancer cases accrue within the Utah Mammography Cohort, further evaluation of breast cancer risk may become possible. This study also could have been improved by consideration of percent density; however continuous MD measures are not yet available in this cohort. Evaluation of MD using dichotomized BI-RADS scores resulted in estimates of association that were strong and in the expected direction, but follow-up studies using more granular measures may detect more nuanced differences in the strengths of the associations between BMI and MD, BMI and breast cancer, or MD and breast cancer by race or ethnicity. Measurement error in BMI and residual confounding by unmeasured reproductive factors were also a concern; however, we were able to incorporate BMI and parity data from multiple time points and sources. Further, the median age at menopause in the US is approximately 52.5 years (45), so, by stratifying at ages 45 and 55, we ensured that our younger age group was mostly premenopausal and our older age group almost entirely postmenopausal.

In conclusion, we have reported that BMI ≥25 and high MD account for a large proportion of breast cancers in Utah, and we have generated preliminary data to suggest that the extent to which each of these factors influences breast cancer risk may vary by race and ethnicity. Future efforts to reduce breast cancer risk will need to consider racial and ethnic differences in the contributions of BMI and MD to breast cancer to ensure that any novel prevention strategies reduce breast cancer incidence both successfully and equitably.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Age-standardized mammographic density and other characteristics by racial and ethnic groupings in the Utah mammography cohort (2005-2019)

	AIAN (n=631)	Asian (n=1,828)				Black (n=821)	Hispanic (n=8,791)	NHPI (n=271)		White (n=148,462)
		Chinese (n=244)	Japanese (n=234)	Filipino (n=95)	Other Asian (n=1,255)			Native Hawaiian (n=183)	Other PI (n=88)	
BI-RADS [a]										
Mostly fat, %	12.8	*	*	*	2.1	13.2	8.4	*	*	9.6
Scattered density, %	39.5	*	29.5	18.9	22.9	40.2	38.0	44.8	39.8	42.9
Heterogeneously dense, %	42.6	56.1	56.0	66.3	58.2	39.2	46.9	43.7	46.6	41.4
Extremely dense, %	5.1	27.5	*	*	16.7	7.4	6.7	*	*	6.0
Age at baseline mammogram in years, mean (SD) [a]	51.0 (10.0)	46.5 (7.0)	50.7 (10.6)	45.8 (6.8)	50.4 (9.2)	51.2 (10.9)	48.4 (8.7)	50.0 (9.5)	48.7 (9.8)	54.0 (11.7)
BMI in kg/m^2, mean (SD)	27.4 (6.4)	22.6 (3.3)	23.4 (3.7)	22.4 (3.7)	23.1 (3.8)	28.0 (6.2)	26.8 (5.5)	29.4 (7.2)	31.5 (6.9)	26.6 (5.7)
BMI categories (kg/m^2)										
<25 kg/m^2, %	41.0	86.3	74.4	75.8	76.7	35.6	42.4	32.0	16.7	46.5
≥25-<30 kg/m^2, %	33.0	6.9	19.3	*	18.7	33.1	35.2	28.9	31.1	32.0
≥30 kg/m^2, %	26.0	6.8	6.3	*	4.6	31.3	22.4	39.1	52.2	21.5
Parous in Utah, %	70.1	82.4	84.5	62.2	36.5	46.8	60.8	53.5	61.4	75.3
Number of children, mean (SD) [b]	3.2 (1.7)	2.5 (2.1)	2.5 (1.6)	2.3 (1.0)	2.4 (1.2)	2.8 (1.4)	3.1 (1.6)	3.8(2.0)	3.9(1.5)	3.4 (1.7)
Age at first birth in Utah in years, mean (SD) [c]	24.5 (5.4)	30.3 (5.2)	28.6 (5.5)	31.0 (5.2)	29.4 (6.0)	25.8 (6.2)	25.5 (6.0)	26.2(5.4)	26.5(5.3)	24.4 (5.1)
Ever used HT										
Never, %	89.5	92.5	92.8	85.8	92.8	88.8	89.7	94.1	>87.5	87.1
Past HT, %	4.8	*	*	*	3.0	5.2	4.7	*	*	5.0
Current HT, %	5.7	*	*	*	4.2	6.1	5.6	*	*	7.9
Education										
Less than high school, %	6.7	*	*	*	8.0	6.0	12.4	*	*	5.5
High school, %	23.1	13.4	13.7	*	12.6	18.9	22.4	*	28.0	22.0
Some college, %	24.7	20.7	31.5	33.0	8.2	16.8	18.3	17.5	24.8	26.3
College, %	18.0	49.2	41.2	39.3	12.2	13.8	14.3	17.7	18.5	23.5
Missing, %	27.5	*	*	*	59.0	44.4	32.6	47.1	*	22.8

Abbreviations: AIAN=non-Hispanic American Indian or Alaska Native; Asian=non-Hispanic Asian; Black=non-Hispanic Black; NHPI=non-Hispanic Native Hawaiian or Pacific Islander; White=non-Hispanic White; BI-RADS Breast Imaging-Reporting and Data System; BMI=body mass index; HT=hormone therapy

Values are means (standard deviations) for continuous variables and percentages for categorical variables. All are standardized to the age distribution of the full study population.

[*] Consistent with Utah Population Database confidentiality policies, we have masked percentages that reflect <11 cases by removing prevalence information for the two categories with the smallest percentages.

[a] Value is not age standardized

[b] Number of live births among women parous in Utah

[c] Age at first birth among women parous in Utah

Table 2.

Multivariable-adjusted association between body mass index (BMI) and mammographic density (MD)[a] by race and ethnicity, stratified by age at mammogram

	All (n=160,804)			AIAN (n=631)			Asian (n=1,828)			Black (n=821)			Hispanic (n=8,791)			NHPI (n=271)			White (n=148,462)		
BMI (kg/m^2)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)
Full cohort [b]																					
<25	27,429	47,253	(ref)	88	171	(ref)	268	1,175	(ref)	95	200	(ref)	1,189	2,657	(ref)	17	55	(ref)	25,772	42,995	(ref)
≥25-<30	30,502	21,105	0.68 (0.68, 0.69)	112	92	0.70 (0.59, 0.84)	132	173	0.71 (0.65, 0.79)	156	115	0.64 (0.55, 0.74)	1,558	1,443	0.71 (0.68, 0.74)	38	43	0.70 (0.55, 0.89)	28,506	19,239	0.68 (0.67, 0.69)
≥30	25,461	9,054	0.43 (0.42, 0.44)	130	38	0.35 (0.26, 0.46)	48	32	0.52 (0.39, 0.68)	187	68	0.40 (0.32, 0.50)	1,333	611	0.47 (0.44, 0.50)	85	33	0.38 (0.28, 0.52)	23,678	8,272	0.43 (0.42, 0.44)
p-trend			<0.001			<0.001			<0.001			<0.001			<0.001			<0.001			<0.001
p-heterogeneity[c]																					0.12
Ages <45 [d]																					
<25	5,493	17,652	(ref)	26	65	(ref)	60	488	(ref)	20	79	(ref)	389	1,269	(ref)	*	24	(ref)	4,993	15,727	(ref)
≥25-<30	5,250	5,811	0.69 (0.68, 0.71)	24	30	0.80 (0.61, 1.06)	23	68	0.83 (0.73, 0.94)	32	56	0.80 (0.66, 0.97)	483	625	0.74 (0.69, 0.78)	*	19	0.80 (0.59, 1.07)	4,681	5,013	0.68 (0.67, 0.70)
≥30	4,975	2,388	0.43 (0.41, 0.44)	29	16	0.50 (0.33, 0.76)	*	*	0.56 (0.34, 0.94)	46	27	0.46 (0.33, 0.63)	426	243	0.47 (0.42, 0.52)	29	*	0.34 (0.21, 0.54)	4,438	2,082	0.42 (0.41, 0.44)
p-trend			<0.001			0.016			0.002			<0.001			<0.001			0.004			<0.001
p-heterogeneity[c]																					0.009
Ages 45 to <55 [b]																					
<25	7,730	16,752	(ref)	27	63	(ref)	80	445	(ref)	34	74	(ref)	461	1057	(ref)	*	*	(ref)	7,121	15,091	(ref)
≥25-<30	8,623	7,613	0.70 (0.68, 0.71)	35	44	0.80 (0.63, 1.02)	51	59	0.63 (0.53, 0.75)	62	37	0.56 (0.43, 0.75)	634	611	0.71 (0.66, 0.75)	*	*	0.69 (0.46, 1.03)	7,829	6,846	0.70 (0.68, 0.71)

BMI (kg/m^2)	All (n=160,804)			AIAN (n=631)			Asian (n=1,828)			Black (n=821)			Hispanic (n=8,791)			NHPI (n=271)			White (n=148,462)		
	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)	Low MD (n)	High MD (n)	RR (95% CI)
≥30	8,241	3,460	0.44 (0.43, 0.45)	57	*	0.27 (0.16, 0.45)	22	15	0.47 (0.31, 0.70)	73	27	0.39 (0.28, 0.56)	553	273	0.48 (0.43, 0.53)	29	16	0.44 (0.28, 0.70)	7,507	3,116	0.44 (0.42, 0.45)
p-trend			<0.001			<0.001			<0.001			<0.001			<0.001			0.015			<0.001
p-heterogeneity[c]																					0.14
Ages ≥55 [b]																					
<25	14,206	12,849	(ref)	35	43	(ref)	128	242	(ref)	41	47	(ref)	339	331	(ref)	*	*	(ref)	13,658	12,177	(ref)
≥25-<30	16,629	7,681	0.67 (0.66, 0.69)	53	18	0.44 (0.27, 0.70)	58	46	0.68 (0.55, 0.86)	62	22	0.47 (0.32, 0.70)	441	207	0.64 (0.56, 0.74)	19	*	0.45 (0.21, 0.98)	15,996	7,380	0.67 (0.66, 0.69)
≥30	12,245	3,206	0.44 (0.42, 0.45)	44	*	0.30 (0.16, 0.55)	*	*	0.55 (0.33, 0.91)	68	14	0.30 (0.18, 0.51)	354	95	0.42 (0.35, 0.51)	27	*	0.24 (0.09, 0.64)	11,733	3,074	0.44 (0.42, 0.45)
p-trend			<0.001			<0.001			<0.001			<0.001			<0.001			0.08			<0.001
p-heterogeneity[c]																					0.24

Abbreviations: AIAN=non-Hispanic American Indian or Alaska Native; Asian=non-Hispanic Asian; Black=non-Hispanic Black; NHPI=non-Hispanic Native Hawaiian or Pacific Islander; White=non-Hispanic White

*Consistent with Utah Population Database confidentiality policies, we have masked low counts (n<11) and any counts that could be used to re-create the low counts.

[a]Low MD is defined as BI-RADS A or B, and high MD defined as BI-RADS C or D.

[b]Multivariable models are adjusted for age (continuous), education (less than high school or high school diploma, more than high school, missing), parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known), and hormone therapy (HT) use (never, past, current). The model for the full population, "All," is additionally adjusted for the combined race and ethnicity variable.

[c]The test for heterogeneity is a likelihood ratio test comparing models with and without interaction terms between the combined race and ethnicity variable and BMI.

[d]Multivariable models are adjusted for age (continuous), education (less than high school or high school diploma, more than high school, missing), and parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known). The model for the full population, "All," is additionally adjusted for the combined race and ethnicity variable.

Table 3.

Multivariable-adjusted association between body mass index (BMI) and incident breast cancer by race and ethnicity, stratified by age

	Hispanic (of all racial groups) + non-Hispanic White		Hispanic (of all racial groups)		non-Hispanic White	
BMI (kg/m^2)	**BC (n)**	**HR (95% CI)**	**BC (n)**	**HR (95% CI)**	**BC (n)**	**HR (95% CI)**
Full cohort [a]						
<25	2,409	(ref)	97	(ref)	2,312	(ref)
≥25-<30	1,943	1.16 (1.09, 1.23)	80	1.08 (0.79, 1.48)	1,863	1.16 (1.09, 1.24)
≥30	1,338	1.34 (1.25, 1.43)	58	1.32 (0.92, 1.88)	1,280	1.34 (1.24, 1.43)
p-trend		<0.001		0.14		<0.001
p-heterogeneity[b]						0.95
Ages <45 [c]						
<25	449	(ref)	37	(ref)	412	(ref)
≥25-<30	209	1.10 (0.79, 1.53)	22	0.73 (0.26, 2.04)	187	1.08 (0.76, 1.54)
≥30	137	1.09 (0.72, 1.64)	*	0.24 (0.03, 1.95)	130	1.20 (0.79, 1.84)
p-trend		0.787		0.114		0.510
p-heterogeneity[b]						0.22
Ages 45 to <55 [a]						
<25	770	(ref)	38	(ref)	732	(ref)
≥25-<30	514	1.02 (0.89, 1.17)	34	0.84 (0.50, 1.44)	480	1.02 (0.89, 1.18)
≥30	354	1.16 (0.99, 1.36)	26	1.15 (0.64, 2.10)	328	1.15 (0.97, 1.36)
p-trend		0.022		0.592		0.033
p-heterogeneity[b]						0.14
Ages ≥55 [a]						
<25	1,190	(ref)	22	(ref)	1,168	(ref)
≥25-<30	1,220	1.21 (1.13, 1.30)	24	1.21 (0.77, 1.91)	1,196	1.21 (1.13, 1.30)
≥30	847	1.41 (1.30, 1.52)	*	1.57 (0.96, 2.58)	822	1.40 (1.29, 1.52)
p-trend		<0.001		0.041		<0.001
p-heterogeneity[b]						0.65

Abbreviations: BC=breast cancer

[*] Consistent with Utah Population Database confidentiality policies, we have masked low counts (n<11) and any counts that could be used to re-create the low counts.

[a] Multivariable Cox proportional hazard models are stratified by time-updated age, and adjusted for hormone therapy (HT) use (current, past, never), education (less than high school or high school diploma, more than high school, missing), parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known) and BI-RADS score (low v. high). The model among the combined Hispanic and non-Hispanic White populations is additionally adjusted for ethnicity.

[b] The test for heterogeneity is a likelihood ratio test comparing models with and without interaction terms between ethnicity and BMI.

[c]Multivariable Cox proportional hazard models are stratified by time-updated age, and adjusted for education (less than high school or high school diploma, more than high school, missing), parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known) and BI-RADS score (low v. high). The model among the combined Hispanic and non-Hispanic White populations is additionally adjusted for ethnicity.

Table 4.

Multivariable-adjusted association between baseline mammographic density (MD)[a] and incident breast cancer by race and ethnicity, stratified by age

	Hispanic (of all racial groups) + non-Hispanic White		Hispanic (of all racial groups)		non-Hispanic White	
Mammographic density	**BC (n)**	**HR (95% CI)**	**BC (n)**	**HR (95% CI)**	**BC (n)**	**HR (95% CI)**
Full cohort [b]						
Low MD	2,506	(ref)	99	(ref)	2,407	(ref)
High MD	3,184	1.77 (1.67, 1.87)	136	1.52 (1.13, 2.04)	3,048	1.78 (1.68, 1.88)
p-heterogeneity[c]						0.53
Ages <45 [d]						
Low MD	197	(ref)	*	(ref)	180	(ref)
High MD	598	1.73 (1.24, 2.40)	49	1.50 (0.52, 4.36)	549	1.74 (1.23, 2.47)
p-heterogeneity[c]						0.98
Ages 45 to <55 [b]						
Low MD	543	(ref)	39	(ref)	504	(ref)
High MD	1,095	2.01 (1.76, 2.31)	59	1.64 (0.97, 2.76)	1,036	2.02 (1.76, 2.33)
p-heterogeneity[c]						0.98
Ages ≥55 [b]						
Low MD	1,766	(ref)	43	(ref)	1,723	(ref)
High MD	1,491	1.71 (1.61, 1.82)	*	1.27 (0.85, 1.90)	1,463	1.73 (1.62, 1.84)
p-heterogeneity[c]						0.20

Abbreviations: BC=breast cancer; MD=mammographic density

*Consistent with Utah Population Database confidentiality policies, we have masked low counts (n<11) and any counts that could be used to re-create the low counts.

[a]Low MD is defined as BI-RADS A or B, and high MD is defined as BI-RADS C or D.

[b]Multivariable Cox proportional hazard models are stratified by time-updated age, and adjusted for hormone therapy (HT) use (current, past, never), education (less than high school or high school diploma, more than high school, missing), parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known), and BMI (<25, ≥25-<30, ≥30). The model among the combined Hispanic and non-Hispanic White populations is additionally adjusted for ethnicity.

[c]The test for heterogeneity is a likelihood ratio test comparing models with and without interaction terms between ethnicity and MD.

[d]Multivariable Cox proportional hazard models are stratified by time-updated age, and adjusted for education (less than high school or high school diploma, more than high school, missing), parity (0 births in Utah, 1 birth in Utah, 2+ births in Utah, parous with number of births not known), and BMI (<25, ≥25-<30, ≥30). The model among the combined Hispanic and non-Hispanic White populations is additionally adjusted for ethnicity.

Table 5.

Population attributable risks describing the percent of high mammographic density (MD) explained by body mass index (BMI) and the percent of breast cancer explained by BMI and by MD, stratified by race and ethnicity and by age at mammogram

Model covariates	All PAR% (95% CI)	AIAN PAR% (95% CI)	Asian PAR% (95% CI)	Black PAR% (95% CI)	Hispanic PAR% (95% CI)	NHPI PAR% (95% CI)	White PAR% (95% CI)
All ages							
% of high mammographic density explained by low BMI							
Low BMI only[a]	27.3 (26.9, 27.6)	26.7 (21.8, 31.7)	29.5 (24.1, 34.9)	25.4 (21.6, 29.2)	22.5 (21.2, 23.8)	21.0 (16.4, 25.6)	27.3 (26.9, 27.7)
Low BMI adjusted for age at mammogram[b]	25.9 (25.5, 26.3)	26.4 (21.4, 31.3)	28.1 (22.6, 33.5)	25.2 (21.5, 29.0)	21.9 (20.5, 23.2)	20.0 (15.2, 24.8)	25.9 (25.5, 26.3)
Low BMI adjusted for age at mammogram and HT[c]	25.9 (25.5, 26.3)	26.4 (21.5, 31.3)	28.0 (22.6, 33.5)	25.2 (21.5, 29.0)	21.9 (20.5, 23.2)	*	25.9 (25.5, 26.3)
% of incident breast cancer explained by high BMI							
High BMI only[a]	2.1 (1.4, 2.9)	*	*	*	0.9 (−1.5, 3.3)	*	2.2 (1.4, 3.0)
High BMI adjusted for age[b]	0.6 (0.2, 1.0)	*	*	*	0.3 (−1.1, 1.8)	*	0.6 (0.2, 1.0)
High BMI adjusted for age and HT[c]	0.6 (0.2, 1.0)	*	*	*	0.3 (−1.2, 1.9)	*	0.6 (0.2, 1.0)
High BMI adjusted for age, HT and MD[c]	4.0 (3.0, 5.1)	*	*	*	2.1 (−1.7, 6.0)		4.2 (3.1, 5.3)
% of incident breast cancer explained by high mammographic density							
High MD only[a]	10.0 (8.5, 11.5)	*	*	*	3.4 (−1.3, 8.0)	*	10.5 (8.9, 12.1)
High MD adjusted for age[b]	20.7 (18.7, 22.8)	*	*	*	9.8 (2.1, 17.5)	*	21.3 (19.2, 23.4)
High MD adjusted for age and HT[c]	20.8 (18.7, 22.8)	*	*	*	9.8 (2.1, 17.4)	*	21.3 (19.2, 23.4)
High MD adjusted for age, HT and BMI[d]	24.6 (22.4, 26.8)	*	*	*	12.0 (3.3, 20.5)	*	25.2 (22.9, 27.5)
Ages <45							
% of high mammographic density explained by low BMI							
Low BMI only[a]	28.4 (27.7, 29.1)	20.5 (11.0, 29.9)	17.2 (8.5, 25.8)	17.3 (11.6, 22.9)	21.5 (19.4, 23.6)	18.5 (11.1, 25.8)	29.2 (28.4, 29.9)
% of incident breast cancer explained by low BMI							
Low BMI only[a]	0.6 (−1.5, 2.7)	*	*	*	11.4 (−15.4, 36.7)	*	0.3 (−1.3, 1.8)
Low BMI adjusted for age[b]	0.6 (−1.5, 2.6)	*	*	*	10.9 (−15.4, 35.7)	*	0.3 (−1.3, 1.9)
Low BMI adjusted for age and MD[d]	PAR% < 0	*	*	*	3.3 (−12.6, 19.1)	*	1.4 (−2.2, 5.0)

Model covariates	All PAR% (95% CI)	AIAN PAR% (95% CI)	Asian PAR% (95% CI)	Black PAR% (95% CI)	Hispanic PAR% (95% CI)	NHPI PAR% (95% CI)	White PAR% (95% CI)
% of incident breast cancer explained by high mammographic density							
High MD only[a]	25.6 (12.7, 37.7)	*	*	*	34.3 (−12.7, 68.7)	*	24.6 (11.2, 37.2)
High MD adjusted for age[b]	25.6 (12.7, 37.6)	*	*	*	34.1 (−12.8, 68.5)	*	24.7 (11.2, 37.2)
High MD adjusted for age and BMI[d]	28.3 (14.3, 41.1)	*	*	*	29.2 (−17.2, 65.0)	*	28.0 (13.3, 41.4)
Ages 45 to <55							
% of high mammographic density explained by low BMI							
Low BMI only[a]	25.3 (24.8, 25.9)	23.8 (16.8, 30.8)	34.8 (26.4, 43.2)	28.5 (22.4, 34.5)	21.1 (19.1, 23.1)	17.2 (9.4, 25.0)	25.3 (24.7, 25.9)
Low BMI adjusted for HT[c]	25.3 (24.7, 25.9)	23.8 (16.8, 30.8)	34.9 (26.5, 43.2)	28.5 (22.6, 34.5)	21.1 (19.1, 23.1)	*	25.3 (24.7, 25.9)
% of incident breast cancer explained by low BMI							
Low BMI only[a]	1.6 (0.2, 3.0)	*	*	*	1.8 (−3.9, 7.6)	*	1.5 (0.1, 2.9)
Low BMI adjusted for age[b]	1.7 (0.2, 3.1)	*	*	*	1.8 (−3.9, 7.6)	*	1.6 (0.1, 3.1)
Low BMI adjusted for age and HT[c]	1.6 (0.2, 3.1)	*	*	*	1.8 (−3.9, 7.6)	*	1.6 (0.1, 3.0)
Low BMI adjusted for age, HT and MD[d]	< 0%	*	*	*	< 0%	*	< 0%
% of incident breast cancer explained by high mammographic density							
High MD only[a]	36.3 (30.7, 41.6)	*	*	*	29.9 (8.8, 48.4)	*	36.8 (31.0, 42.4)
High MD adjusted for age[b]	36.7 (31.1, 42.1)	*	*	*	30.0 (8.9, 48.5)	*	37.3 (31.4, 42.8)
High MD adjusted for age and HT[c]	36.6 (30.9, 41.9)	*	*	*	30.3 (9.1, 48.9)	*	37.1 (31.2, 42.6)
High MD adjusted for age, HT, and BMI[d]	38.2 (32.3, 43.8)	*	*	*	30.6 (8.6, 49.7)	*	38.9 (32.8, 44.7)
Ages ≥55							
% of high mammographic density explained by low BMI							
Low BMI only[a]	22.9 (22.3, 23.6)	37.2 (27.7, 46.6)	28.9 (17.8, 40.0)	33.6 (25.6, 41.7)	23.2 (19.6, 26.7)	29.1 (20.3, 37.9)	22.6 (21.9, 23.2)
Low BMI adjusted for HT[c]	22.9 (22.2, 23.5)	37.5 (28.1, 46.9)	29.1 (18.1, 40.1)	33.7 (25.7, 41.7)	23.2 (19.6, 26.7)	*	22.5 (21.8, 23.1)
% of incident breast cancer explained by high BMI							
High BMI only[a]	2.5 (1.5, 3.4)	*	*	*	7.3 (−2.0, 16.4)	*	2.4 (1.4, 3.3)
High BMI adjusted for age[b]	2.0 (1.2, 2.9)	*	*	*	6.5 (−2.3, 15.3)	*	2.0 (1.1, 2.8)

Model covariates	All PAR% (95% CI)	AIAN PAR% (95% CI)	Asian PAR% (95% CI)	Black PAR% (95% CI)	Hispanic PAR% (95% CI)	NHPI PAR% (95% CI)	White PAR% (95% CI)
High BMI adjusted for age and HT[c]	2.1 (1.2, 2.9)	*	*	*	6.7 (−2.3, 15.6)	*	2.0 (1.1, 2.8)
High BMI adjusted for age, HT, and MD[d]	6.2 (4.7, 7.7)	*	*	*	9.1 (−1.5, 19.4)	*	6.1 (4.6, 7.7)
% of incident breast cancer explained by high mammographic density							
High MD only[a]	13.2 (11.3, 15.2)	*	*	*	0.1 (−1.0, 1.2)	*	14.0 (12.0, 16.1)
High MD adjusted for age[b]	17.2 (15.0, 19.4)	*	*	*	1.6 (−2.8, 5.9)	*	17.9 (15.7, 20.2)
High MD adjusted for age and HT[c]	17.2 (15.0, 19.4)	*	*	*	1.4 (−2.7, 5.6)	*	18.0 (15.7, 20.2)
High MD adjusted for age, HT, and BMI[d]	21.3 (18.9, 23.7)	*	*	*	3.5 (−3.0, 10.0)	*	22.1 (19.6, 24.5)

Abbreviations: AIAN=non-Hispanic American Indian or Alaska Native; Asian=non-Hispanic Asian; Black=non-Hispanic Black; NHPI=non-Hispanic Native Hawaiian or Pacific Islander; White=non-Hispanic White; HT=hormone therapy; < 0% implies that, within the given population, the health factor of interest was not positively associated with the outcome of interest

*Breast cancer case counts by explanatory variables are too low for a meaningful estimate.

[a]Model 1 is a univariate model including the explanatory factor only (i.e., low BMI is BMI <25, high BMI is BMI ≥25, high mammographic density is BI-RADS C or D).

[b]Previous model adjusted for age (<55 or ≥55).

[c]Previous model further adjusted for HT use (ever HT versus never HT use).

[d]Previous model further adjusted for BMI (<25 versus ≥25) when MD is the explanatory variable of interest, and further adjusted for MD (BI-RADS C or D versus BI-RADS A or B) when BMI is the explanatory variable of interest.