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Original Contribution

Ethnic Variations in Mammographic Density: A British Multiethnic Longitudinal Study

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It is not known whether the 20–30% lower breast cancer incidence rates in first-generation South Asian and Afro-Caribbean women relative to Caucasian women in the United Kingdom are reflected in mammographic density. The authors conducted a United Kingdom population-based multiethnic study of mammographic density at ages 50–64 years in 645 women. Data on breast cancer risk factors were obtained using a questionnaire/telephone interview. Threshold percent density was assessed on 5,277 digitized mammograms taken in 1995–2004 and was analyzed using multilevel models. Both ethnic minorities were characterized by more protective breast cancer risk factor distributions than Caucasians, such as later menarche, shorter stature, higher parity, earlier age at first birth, and less use of hormone therapy, but they had a higher mean body mass index; the last four factors were associated with lower mammographic density. Age-adjusted percent mammographic densities in Afro-Caribbeans and South Asians were 5.6% (95% confidence interval (CI): 3.5, 7.5) and 5.9% (95% CI: 3.6, 8.0) lower, respectively, than in Caucasians. Lower densities were partly attributed to higher body mass index, less use of hormone therapy, and a protective reproductive history, but these factors did not account entirely for ethnic differences, since fully adjusted mean densities were 1.3% (95% CI: −1.3, 3.7) and 3.8% (95% CI: 1.1, 6.3) lower, respectively. Ethnic differences in mammographic density are consistent with those for breast cancer risk.

breast neoplasms; ethnic groups; mammary glands, human; mammography

Abbreviations: BMI, body mass index; CI, confidence interval.

Breast cancer incidence rates vary sixfold between industrialized and less-developed countries (1), and migrants from low-risk countries to high-risk countries have an intermediate risk (2). Mammographic density, commonly measured as the percentage of breast area that appears as radiodense fibroglandular tissue, is a strong marker of breast cancer risk, as demonstrated by four- to sixfold higher rates in women with over 75 percent density compared with those with lower (<5 percent) density (3). Correlations of country- and ethnic-group-specific mammographic densities with breast cancer incidence rates suggest that mammographic density may underlie international differences (4, 5).

Ethnic variations in density have been studied, predominantly in the United States, but not yet in the United Kingdom, where South Asians and Afro-Caribbeans constitute the largest ethnic minorities. Current breast screenees of these ethnicities are mainly first-generation migrants with lower breast cancer risks; for example, in the Thames Cancer Registry, age-standardized breast cancer incidence rate ratios were 0.68 (95 percent confidence interval (CI): 0.64, 0.73) in Indian women, 0.59 (95 percent CI: 0.51, 0.69) in Pakistani women, 0.80 (95 percent CI: 0.74, 0.86) in Black Caribbean women, and 0.66 (95 percent CI: 0.59, 0.74) in Black African women relative to White women (Ruth H. Jack, King's College

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London, personal communication, 2007). These estimates are consistent with risks that are intermediate between those in the country of origin and those in the United Kingdom. In 2002, age-standardized breast cancer incidence rates (per 100,000 women) were 87.2, 32.9, 27.8, and 19.1 in the United Kingdom, the Caribbean, West Africa, and India, respectively (1).

We conducted a study of differences in mammographic density between Caucasian and first-generation Afro-Caribbean and South Asian migrant women in the United Kingdom. We hypothesized that, akin to ranks of breast cancer incidence rates, mean mammographic density would be lower in the two migrant populations than in Caucasian women. We also investigated the extent to which specific factors contributed to ethnic differences in mammographic density.

MATERIALS AND METHODS

Setting and participants

A multiethnic retrospective longitudinal study of mammographic density was conducted within the Central and East London Breast Screening Service, a National Health Service population-based breast screening center that screens over 12,000 women from an ethnically diverse population each year. At the time of fieldwork (2005–2006), women aged 50–64 years were invited to undergo mammographic screening every 3 years. At each screening, women self-completed a form asking about their ethnicity. We categorized ''White United Kingdom'' as *Caucasian*; ''African,'' ''Afro-Caribbean,'' ''Black African,'' ''Black—other,'' or ''Black Caribbean'' as *Afro-Caribbean*; and ''Indian,'' ''Pakistani,'' or ''Bangladeshi'' as *South Asian* (terms used hereafter). Women of other ethnicities were not included.

From the women in the Caucasian, Afro-Caribbean, and South Asian ethnic groups who had attended their second or later screening in 2004 (totals of 3,925, 969, and 1,117, respectively), we randomly sampled women and invited them to participate by self-completing a questionnaire and optionally providing a blood sample. After excluding women for whom we had the wrong address or who had died ($n = 27$), rates of response to the study invitation were 58.5 percent (278/475) in Caucasians and 40.5 percent (219/540) in Afro-Caribbeans. Despite translation of questionnaires, initial response rates were lower in South Asians, compelling us to change the method of data collection to a telephone interview. Of 597 South Asian women, 168 (28.1 percent) participated (150 by telephone interview). Within each ethnic group, there was no evidence that nonresponders differed from responders in terms of age or area of residence. Radiographic films for 3 percent of the women (20/665) were irretrievable, giving us a total sample size of 645 women.

The study was approved by the East London and The City Local Research Ethics Committee.

Exposure data

Women provided confirmatory information on ethnicity as well as data on country of birth. Both the questionnaire and the telephone interview included questions on breast cancer risk factors: age at menarche, reproductive history (number of livebirths, age at first birth, duration of breastfeeding), education, lifestyle factors (smoking, alcohol), menopausal status and age at menopause, and self-reported height, current weight, and weight 3 years previously, from which current and previous body mass index (BMI; weight (kg)/height (m)^2) were calculated. Women were asked about use of oral contraceptives only on the questionnaire; thus, these data were not available for South Asian women. Information on use of hormone therapy was extracted from screening records. Women who were postmenopausal at the time of questionnaire completion for whom menopausal age was missing (8 percent) were assumed to be postmenopausal at all screenings, since the median age at menopause (50 years) in each ethnic group fell at or before the first screening.

Outcome assessment

We digitized all available radiographs taken between 1995 and 2004 for each woman, typically from three screening rounds held in 1998, 2001, and 2004, on an Array 2905 laser digitizer (optical density 0–4.0, 12 bit, 75 μm) (Array Corporation Europe, Roden, the Netherlands). Mediolateral oblique views were available for all screenings and craniocaudal views were available for the first (prevalent) screening and in 2004. Density was assessed by a single trained observer for 5,277 radiographs using the Cumulus interactive-thresholding method (University of Toronto, Toronto, Ontario, Canada). The breast area was dichotomized into dense and nondense areas, from which percent mammographic density (100 × dense area/total area) was calculated (6). One hundred radiographs were blindly reread, and intrarater reliability for a single radiograph was 0.90.

Statistical analysis

A hierarchical data structure for the primary outcome, percent mammographic density, was modeled using a multilevel linear regression model. Each woman (level 3) attended multiple screening rounds (level 2) (e.g., in 1998, 2001, and 2004), and at each screening up to two views (level 1) were taken (the average of the left and right breasts was the basic unit of analysis). A square-root transformation was used to improve normality. The modeling strategy was to 1) model the age trajectory of density, 2) identify determinants of density, 3) assess age-adjusted differences in density between ethnic groups, and 4) account for ethnic differences by sequentially adjusting for factors identified in step 2, starting with the most proximal exposures.

Explanatory variables were either time-changing or woman-specific variables. Time-changing covariates were age, menopausal status, BMI, and use of hormone therapy, as they may have changed for the same woman between screenings. All other factors (such as parity, age at first birth, ethnicity, and menarche) were specific to each woman, as they did not change between screenings. Current BMI was assumed to apply to the 2004 screening (i.e., the most recent), and BMI calculated from reported weight 3 years previously was assumed to apply to prior screenings (i.e., those occurring in 1998 and 2001).

Regression coefficients (β) refer to differences in square-root values, so more interpretable differences on the original scale were calculated assuming a reference value of 20 percent (the median at age 50–54 years in Caucasians), as

$$(\sqrt{20}+\beta)^2-(\sqrt{20})^2=2\beta\sqrt{20}+\beta^2.$$

Using the same modeling strategy, analysis of the components of mammographic density was also performed, and differences are presented in comparison with reference values of 27 cm^2 (dense), 108 cm^2 (nondense), and 135 cm^2 (total area)—median areas corresponding to a percent density of 20 percent (27/135 = 20 percent). Statistical tests were two-sided.

RESULTS

Characteristics of participants by ethnic group

A total of 645 women with retrievable mammograms participated: 267 Caucasians, 213 Afro-Caribbeans, and 165 South Asians. Almost all Caucasians (95 percent) had been born in the United Kingdom. The mean age at migration to the United Kingdom was the early 20s among Afro-Caribbeans, two thirds of whom had migrated from the Caribbean and one third of whom had migrated from Africa. Migration had occurred later in South Asians, at 28.7 years (table 1).

The average age at the most recent screening was 57.5 years in Caucasians, similar in Afro-Caribbeans, and higher in South Asians. For breast cancer risk factors and other characteristics examined (table 1), there was strong evidence against equal distributions by ethnicity. Compared with Caucasian women, menarche was later in the two ethnic minority groups. South Asians were shorter than women of other ethnicities, but Afro-Caribbean women had the highest mean BMI, being on average 7 kg heavier than their Caucasian counterparts, who were of similar height. Afro-Caribbean and (particularly) South Asian women had greater numbers of livebirths than Caucasians. Caucasians had later first pregnancies and breastfed less, and a higher percentage had used oral contraceptives. They were also more likely than other women to consume alcohol, smoke, or be on hormone therapy at mammography. With the exception of higher BMI (associated with increased postmenopausal breast cancer risk), the distributions of breast cancer risk factors in the two ethnic minority groups were shifted in directions that are associated with lower breast cancer risks and suggested that ethnic-group-specific breast cancer risks in this sample were likely to be consistent with those for the corresponding population subgroup.

Radiographs were available for an average of three screenings per woman, with an average of 2.7 radiographs being read at each screening (72 percent mediolateral oblique views). Although the majority were taken when women were postmenopausal, 44 percent of Caucasian women, 25 percent of Afro-Caribbean women, and 32 percent of South Asian women had at least one screening done at a premenopausal age. Median percent mammographic density and absolute dense area declined with age, whereas the nondense and total breast areas increased (table 2). Within each age category, median percent and absolute mammographic density were highest among Caucasians, much lower among Afro-Caribbeans, and lowest in South Asians (table 2, figure 1). A reversal of ranks was not observed for nondense and total breast areas, for which median values were greatest in Afro-Caribbeans, intermediate in South Asians, and lowest in Caucasians—an ordering that reflects their BMI distributions (correlation of BMI with total area = 0.59).

Determinants of breast density

Associations of breast cancer risk factors with mammographic density, mutually adjusted and also adjusted for ethnic group, showed a decline in density with age, with the menopausal transition, and with increasing BMI (table 3). There was strong evidence that mammographic density was higher among women using hormone therapy. Having an age at first birth under 20 years was associated with lower density, although a linear trend was not observed. Mean mammographic density decreased with more livebirths, although a test for linear trend was not significant. There was some evidence that a positive family history of breast cancer in first-degree relatives might be associated with increased density, but the association was not statistically significant. However, we did not find evidence of associations of mammographic density with age at menarche, adult height, breastfeeding (ever vs. never or duration), smoking status, or, among the ethnic minority women, time since migrating to the United Kingdom. Thus, apart from the latter five factors, other factors may be potential confounders of a mammographic density-ethnicity association, being associated with both outcome (table 3) and exposure (table 1). Furthermore, we found no evidence that determinants of mammographic density differed by ethnic group (no interaction with ethnicity), with the exception of oral contraceptive use, which was associated with higher density in Afro-Caribbeans but not in Caucasians (not investigated in South Asians).

Associations with absolute dense area pointed in similar directions and were of similar magnitudes (in standardized measures) as those for percent mammographic density. The exception to this was BMI, for which there was no evidence against the hypothesis of no association of BMI with dense area (table 3), since the inverse association with percent mammographic density was largely due to a larger nondense area. The factors included in table 3 explained 22.5 percent and 66.9 percent of between-women and between-visit variation in percent mammographic density, respectively, with corresponding values of 5.5 percent and 55.3 percent for dense area.

Ethnicity and mammographic breast density

For both percent density and absolute dense area, there was strong evidence of age-adjusted differences between the three ethnic groups ($p < 0.001$). These differences were present throughout the age range studied, as is illustrated by the BMI-adjusted mean percent and absolute density shown in figure 2. Compared with Caucasians, age-adjusted

TABLE 1. Characteristics of participants in a multiethnic longitudinal study of mammographic density ($n = 645$), by ethnic group, London, United Kingdom, 2005–2006

	Caucasians ($n = 267$)		Afro-Caribbeans ($n = 213$)		South Asians ($n = 165$)		p value*
Mean calendar year of birth	1946 (3.2)†		1946 (3.4)		1944 (3.2)		<0.001
Mean age (years)							
At most recent screening	57.5 (3.2)		57.9 (3.4)		59.8 (2.8)		<0.001
At earliest screening	52.0 (2.2)		52.3 (2.3)		53.0 (2.9)		<0.001
At arrival in United Kingdom	0 (0)		21.2 (8.5)		28.7 (8.4)		<0.001
At menarche	12.8 (1.5)		13.5 (1.9)		14.2 (1.7)		<0.001
At first birth‡	24.9 (6.1)		22.6 (5.2)		23.9 (5.1)		<0.001
At menopause	49.4 (5.6)		48.4 (5.7)		50.2 (5.8)		0.007
Mean adult height (cm)	163.1 (6.3)		162.3 (7.6)		156.0 (8.6)		<0.001
Mean current weight (kg)	68.7 (14.0)		76.2 (15.0)		65.1 (13.8)		<0.001
Mean current body mass index§	25.9 (5.3)		28.9 (5.6)		26.9 (5.9)		<0.001
Median duration (months) of breastfeeding‡	7.3 [3.0–14.8]¶		11 [6.0–22.5]		25 [6.0–56.3]		<0.001
	No.#	%	No.#	%	No.#	%	
Country or region of birth							
United Kingdom	253	94.8	4	1.9	0		<0.001
Caribbean	0		139	65.3	0		
Africa	4	1.5	69	32.4	23	13.9	
India	1	0.4	0		90	54.6	
Pakistan	0		0		27	16.4	
Bangladesh	0		0		21	12.7	
Other	9	3.4	1	0.5	4	2.4	
Education							
None/missing data	10	3.8	13	6.1	47	28.5	<0.001
Primary	15	5.6	35	16.4	36	21.8	
Secondary	146	54.7	126	59.2	64	38.8	
Tertiary	96	36.0	39	18.3	18	10.9	
No. of livebirths							
0	80	30.5	16	7.7	11	6.8	<0.001
1–2	111	42.4	82	39.4	39	24.2	
3	51	19.5	54	26.0	40	24.8	
4–5	17	6.5	47	22.6	53	32.9	
≥6	3	1.2	9	4.3	18	11.2	
Ever breastfeeding‡	116	56.3	166	82.6	110	71.4	<0.001
Ever use of oral contraceptives	197	74.6	93	44.9	—**		<0.001
Use of hormone therapy at any screening	113	42.3	54	25.4	30	18.2	<0.001
Current smoker	43	16.3	9	4.3	1	0.6	<0.001
Current alcohol drinker	221	83.7	120	58.8	—**		<0.001
Family history of breast cancer	50	18.7	16	7.5	8	4.9	<0.001

* p for heterogeneity across ethnic groups (F test or chi-squared test for continuous and categorical outcomes).

† Numbers in parentheses, standard deviation.

‡ Restricted to parous women only.

§ Weight (kg)/height (m)^2.

¶ Numbers in brackets, interquartile range.

Numbers vary because of missing data.

** Data were not collected (missing by study design).

TABLE 2. Mammographic features (mediolateral oblique views) of participants in a multiethnic longitudinal study of mammographic density, by ethnic group and age at mammography, London, United Kingdom, 1995–2004

Age group* (years)	Caucasians ($n = 267$)		Afro-Caribbeans ($n = 213$)		South Asians ($n = 165$)	
	Median	IQR†	Median	IQR	Median	IQR
50–54						
No. of participants‡	231		182		124	
Dense area (cm^2)	25.9	16.4–41.1	22.2	12.5–36.9	19.1	10.1–29.9
Nondense area (cm^2)	107.6	73.7–144.2	142.2	110.1–190.1	128.3	103.0–168.1
Breast area (cm^2)	134.1	105.4–180.7	172.6	134.6–226.5	155.2	125.6–190.0
Percent mammographic density (%)	22.2	10.9–31.1	13.7	7.3–24.0	12.4	6.8–22.3
55–59						
No. of participants	207		162		163	
Dense area (cm^2)	22.6	13.8–35.7	17.5	9.4–34.0	14.2	7.2–24.3
Nondense area (cm^2)	118.8	84.3–158.5	152.8	116.5–202.2	140.2	110.9–176.5
Breast area (cm^2)	140.6	109.1–189.3	176.4	140.8–226.2	159.9	129.1–200.6
Percent mammographic density (%)	17.4	9.7–25.3	10.0	5.2–19.3	8.7	4.4–17.2
60–64						
No. of participants	67		66		79	
Dense area (cm^2)	22.2	13.5–35.7	14.1	7.8–25.0	12.0	6.7–20.9
Nondense area (cm^2)	122.0	93.2–163.8	165.9	129.5–217.4	147.5	110.4–195.8
Breast area (cm^2)	145.6	112.7–203.3	185.5	151.3–231.2	159.0	127.4–208.3
Percent mammographic density (%)	15.3	9.0–24.8	8.1	4.0–15.0	7.7	4.1–14.0

* If a woman was screened twice within an age group, the average of her mediolateral oblique views was used.
† IQR, interquartile range.
‡ Number of women who underwent at least one screening at this age.

mean percent mammographic density was 5.6 percent lower (95 percent CI: 3.5, 7.5) in Afro-Caribbeans (table 4). This difference was accounted for by their higher BMI, since adjustment reduced the difference to 3.6 percent. Although additional adjustments attenuated this difference further, owing to Afro-Caribbeans' having a higher prevalence of factors that were associated with lower density (tables 1 and 4), the adjusted density remained 2.3 percent (95 percent CI: −0.1, 4.4) lower than that in Caucasians, and it was further attenuated upon adjustment for oral contraceptive use (1.3 percent lower; 95 percent CI: −1.3, 3.7). Table 4 shows sequentially adjusted differences for percent mammographic density as well as the three area measures. For absolute dense area, adjustments had an effect similar to that for percent mammographic density; however, there was no evidence, at the 5 percent significance level, of differences between Afro-Caribbeans and Caucasians. Lower percent mammographic density in Afro-Caribbeans was partly driven by a greater nondense area (table 4).

South Asians also had a lower age-adjusted mean percent mammographic density than Caucasians, by 5.9 percent (95 percent CI: 3.6, 8.0) (table 5, figure 2). Higher BMI partly explained the lower density in South Asians (adjusted difference = 5.1 percent; 95 percent CI: 2.9, 7.2), although the confounding effect was less than that in Afro-Caribbeans (table 1). This difference was further explained by less use of hormone therapy (adjusted difference = 4.8 percent) and further by a greater number of livebirths (adjusted difference = 3.7 percent). Additional adjustment for age at first birth and family history of breast cancer led to only a small attenuation, and after full adjustment for all of the factors in table 4, percent mammographic density remained 3.8 percent lower (95 percent CI: 1.1, 6.3) in South Asian women than in Caucasian women. These results were also reflected in absolute dense area and thus inversely in absolute nondense area, as the total breast areas were similar in these two ethnic groups (table 5). There was no evidence of subethnic differences according to country of birth or religion among South Asian women.

DISCUSSION

To our knowledge, this was the first study to investigate differences in mammographic density between ethnic groups in the United Kingdom, a population which includes migrants from the Indian subcontinent who have not been studied previously. We found that, consistent with their relative risks for breast cancer, age-adjusted mean percent and absolute mammographic density were lowest in British South Asian women, intermediate in Afro-Caribbean women, and highest in Caucasian women. A higher mean BMI accounted for lower density among Afro-Caribbeans, and together with earlier menopause, a lower prevalence of hormone therapy, and a greater number of livebirths, these

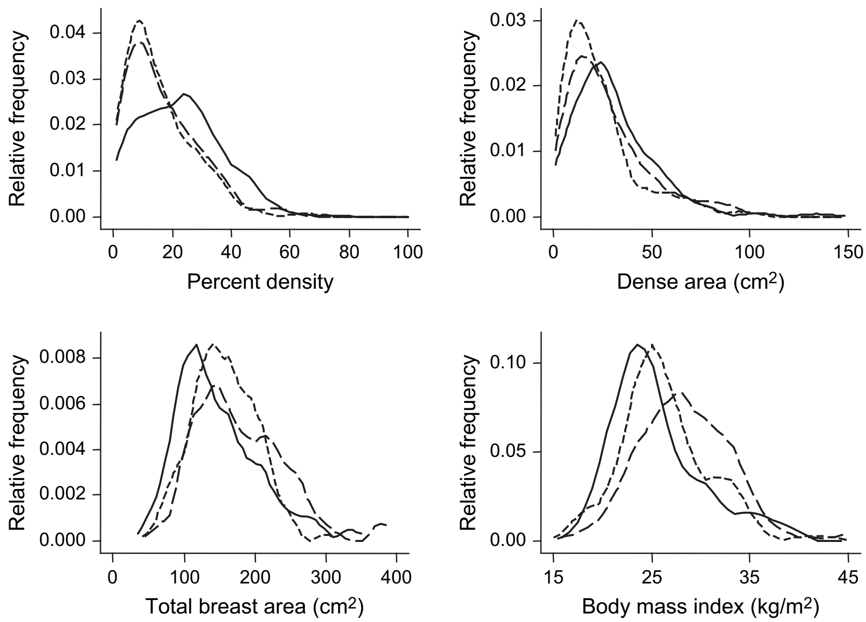

FIGURE 1. Distributions of percent mammographic density, dense area, total breast area (mediolateral oblique views at ages 50–54 years), and body mass index (weight (kg)/height (m)^2), by ethnicity, London, United Kingdom, 1995–2004. ————, Caucasians; – – – –, Afro-Caribbeans; - - - - - - -, South Asians.

factors accounted for almost 60 percent of the mammographic density difference relative to Caucasians. On average, South Asians had a lower percent mammographic density than Caucasians, resulting from much lower absolute dense areas (since their total breast area was only slightly higher than that in Caucasians). BMI and reproductive characteristics explained the reduced density, though not fully, since only one third of the difference was accounted for and the fully adjusted difference remained statistically significant. In both ethnic groups, it was not only contemporary factors that gave rise to differences but also distal reproductive factors, suggesting that ethnic differences may have been present from a much younger age.

Unlike other investigators, we did not observe an association of smoking with mammographic density, but the prevalence of smoking was low, reducing our power to detect an association. In addition, although a longer duration of breastfeeding is associated with lower breast cancer risk (7) and despite our benefitting from a study sample that was heterogeneous in its breastfeeding practices, there was no evidence of an association with mammographic density. We did not find an association with number of years of residence in the United Kingdom, contrary to other findings that a greater degree of acculturation was associated with higher density among foreign-born Chinese women in the United States (4, 5). Use of oral contraceptives was associated with increased mammographic density in Afro-Caribbean women but not in Caucasian women. It is unclear whether this was a false-positive finding, since previous studies found no association. If past use of oral contraceptives results in a permanent long-term increase in mammographic density (unlikely, since it has a transient effect on breast cancer risk), this might account for the unexplained lower densities in South Asian women, as their use is likely to have been lower than that of Caucasians (8).

BMI, a strong determinant of percent mammographic density, and reproductive factors were expected to contribute to variations in mammographic density given the substantial ethnic differences in these factors. However, these factors did not fully account for ethnic differences in mammographic density. Other unexamined factors that may explain ethnic differences include dietary intakes of calcium, vitamin D, fat, and phytoestrogens, which have been found (although not consistently) to be related to mammographic density (9–12). Genetic factors may contribute to differences, as up to 60 percent of variation in mammographic density may be genetically determined (13), but this contribution may be overestimated because of shared environments. Further research into factors that might account for the unexplained ethnic difference is warranted. Volumetric rather than area-based methods of breast density measurement (currently under development) may clarify the extent to which observed differences may be affected by possible ethnic differences in breast compression and thickness.

This study had many strengths. The use of multiple radiographs per woman permitted accurate estimation of a woman's average mammographic density. The validity of mammographic density readings was further confirmed by our observing expected associations with established determinants of mammographic density. However, the study was limited by its sample size, particularly for South Asian women, in whom response rates were low. Difficulties in

TABLE 3. Mutually adjusted associations of breast cancer risk factors with percent mammographic density and absolute dense area, with additional adjustment for ethnic group,* London, United Kingdom, 1995–2004

Factor	Percent mammographic density (%)		Dense area (cm^2)	
	Difference	95% CI†	Difference	95% CI
Age (years) at screening				
50–52	0		0	
53–55	−3.35	−4.04, −2.66	−3.64	−4.66, −2.62
56–58	−5.86	−6.62, −5.10	−6.79	−7.92, −5.66
59–61	−7.92	−8.80, −7.04	−9.47	−10.79, −8.14
62–65	−7.29	−8.50, −6.08	−7.45	−9.32, −5.58
Body mass index‡				
<22	0		0	
22–<24	−3.05	−5.00, −1.10	−0.66	−3.75, 2.44
24–<26	−4.52	−6.50, −2.53	−0.39	−3.74, 2.95
26–<28	−5.55	−7.55, −3.55	−0.45	−3.93, 3.03
28–<30	−7.09	−9.10, −5.08	−2.64	−6.19, 0.91
≥30	−8.10	−10.05, −6.14	−1.53	−5.23, 2.17
Use of hormone therapy at screening (yes vs. no)	2.48	1.42, 3.54	3.22	1.68, 4.76
Menopausal status at screening (postmenopausal vs. premenopausal)	−2.83	−3.80, −1.86	−3.73	−5.14, −2.31
No. of livebirths				
0	0		0	
1–2	−1.13	−5.87, 3.61	1.43	−6.40, 9.26
3	−2.65	−7.51, 2.22	−4.09	−11.61, 3.44
4–5	−3.59	−8.62, 1.43	−4.51	−12.42, 3.41
≥6	−1.21	−8.47, 6.05	−1.93	−13.22, 9.37
Age (years) at first livebirth				
<20	0		0	
20–<25	2.89	−0.24, 6.10	3.13	−1.69, 7.95
25–<30	1.74	−1.76, 5.23	0.58	−4.72, 5.89
≥30	1.21	−2.91, 5.32	−1.79	−7.83, 4.24
Ever having breastfed (yes vs. no)	2.36	−0.52, 5.25	2.42	−2.03, 6.88
Age (years) at menarche (per year)	0.57	−0.03, 1.18	0.49	−0.46, 1.43
Adult height (cm) (per 5 cm)	−0.04	−0.76, 0.67	0.46	−0.66, 1.58
Current smoker (yes vs. no)	0.16	−3.51, 3.83	1.90	−4.01, 7.82
Family history of breast cancer (yes vs. no)	1.50	−1.64, 4.64	2.30	−2.63, 7.24
Past use of oral contraceptives§ (yes vs. no)	4.52	1.82, 7.21	6.95	2.76, 11.13
No. of years of residence in United Kingdom¶ (per 5 years)	−0.46	−1.30, 0.38	−0.57	−1.88, 0.75

* The analysis was conducted on a square-root scale to obtain adjusted regression coefficients. Differences are reported on the original measurement scale, corresponding to reference values of 20% for percent mammographic density and 27 cm^2 for dense area.

† CI, confidence interval.

‡ Weight (kg)/height (m)^2.

§ Assessed in a model that included all of the factors in the table, but excluding South Asian women, for whom this information was not collected.

¶ Restricted to Afro-Caribbean and South Asian women only.

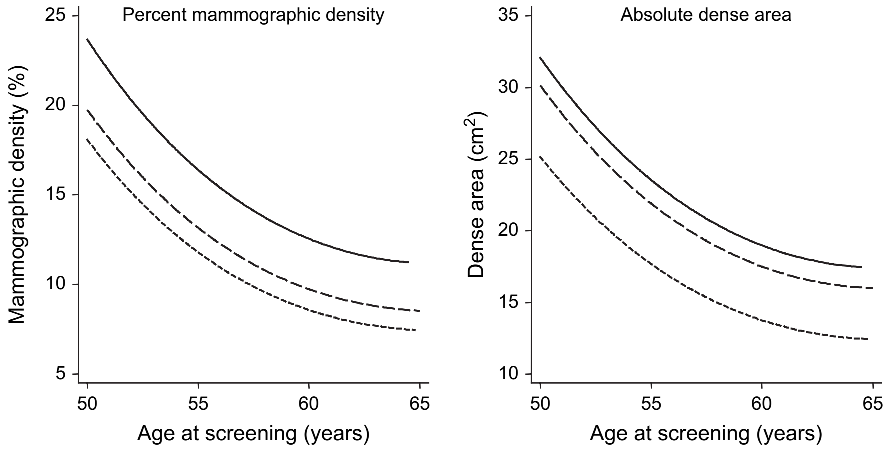

FIGURE 2. Body mass index-adjusted mean percent mammographic density and absolute dense area, by age and ethnic group, London, United Kingdom, 1995–2004. ———, Caucasians; – – – –, Afro-Caribbeans; - - - - - - -, South Asians. Mean values were predicted at a body mass index (weight (kg)/height (m)^2) of 27.

recruitment of this ethnic group meant that we collected fewer exposure variables for these women, so we were not able to assess the impact of factors such as oral contraceptive use. Poor response may have led to selection bias if responders differed from nonresponders with regard to factors that are associated with breast density, but reassuringly, the study sample was representative of the general population, as evidenced by the similarity of ethnic-group-specific mean anthropometric and reproductive factors to those in national surveys (14). Overrepresentation of nulliparous Caucasian women may have led to overestimation of crude mammographic density differences between ethnic groups, but this would not have affected the results once number of livebirths was controlled for. Self-reported exposure data are error-prone, and this may have resulted in residual confounding—a problem that was likely to affect BMI in

TABLE 4. Sequentially adjusted mean differences in percent mammographic density and mammographic area between Afro-Caribbean women and Caucasian women,* London, United Kingdom, 1995–2004

Adjusted for all previously listed factors up to and including:	Percent breast density		Absolute dense area (cm^2)		Nondense area (cm^2)		Total breast area (cm^2)	
	Adjusted mean difference	95% CI†	Adjusted mean difference	95% CI	Adjusted mean difference	95% CI	Adjusted mean difference	95% CI
Immediate time-varying factors								
Age (years)	−5.6	−7.5, −3.5	−2.4	−5.6, 1.0	39.9	28.9, 51.4	38.8	27.5, 50.4
+ body mass index‡	−3.6	−5.6, −1.5	−1.8	−5.1, 1.8	25.5	16.9, 34.4	26.1	16.9, 35.5
+ menopause§	−3.5	−5.4, −1.4	−1.6	−4.9, 1.9	25.3	16.7, 34.1	26.1	16.9, 35.5
+ use of hormone therapy	−3.3	−5.3, −1.2	−1.4	−4.7, 2.1	24.9	16.4, 33.8	25.9	16.8, 35.4
Long-term time-constant factors								
+ no. of livebirths	−2.5	−4.6, −0.3	−0.1	−3.7, 3.7	24.6	15.6, 34.0	27.0	17.2, 37.0
+ age (years) at first birth	−2.4	−4.5, −0.1	−0.1	−3.7, 3.7	23.2	14.2, 32.6	25.6	15.9, 25.7
+ family history of breast cancer	−2.3	−4.4, 0.1	0.1	−3.6, 3.9	22.9	13.8, 32.3	25.4	15.7, 35.5
+ use of oral contraceptives	−1.3	−3.7, 1.3	1.6	−2.5, 5.9	22.8	12.9, 33.0	26.1	15.4, 37.2

* The analysis was conducted using square-root transformations, producing adjusted regression coefficients (β). Differences on the original scale were calculated at reference value *v*, where *v* was 20% for percent mammographic density and 27 cm^2, 108 cm^2, and 135 cm^2 for dense, nondense, and total breast areas, respectively, using the formula $\beta \times \beta + 2\beta \times \text{sqrt}(v)$. Caucasian women formed the reference group.

† CI, confidence interval.

‡ Weight (kg)/height (m)^2.

§ Postmenopausal vs. premenopausal.

TABLE 5. Sequentially adjusted mean differences in percent mammographic density and mammographic area between South Asian women and Caucasian women,* London, United Kingdom, 1995–2004

Adjusted for all previously listed factors up to and including:	Percent breast density		Absolute dense area (cm^2)		Nondense area (cm^2)		Total breast area (cm^2)	
	Adjusted mean difference	95% CI†	Adjusted mean difference	95% CI	Adjusted mean difference	95% CI	Adjusted mean difference	95% CI
Immediate time-varying factors								
Age (years)	−5.9	−8.0, −3.6	−6.6	−9.8, −3.1	15.6	4.3, 27.4	9.4	−2.1, 21.3
+ body mass index‡	−5.1	−7.2, −2.9	−6.3	−9.6, −2.8	10.1	1.3, 19.3	4.6	−4.8, 14.3
+ menopause§	−5.1	−7.1, −2.9	−6.3	−9.5, −2.8	10.1	1.3, 19.3	4.6	−4.8, 14.3
+ use of hormone therapy	−4.8	−6.9, −2.7	−5.9	−9.2, −2.4	9.5	0.7, 18.6	4.4	−5.0, 14.1
Long-term time-constant factors								
+ no. of livebirths	−3.7	−6.0, −1.2	−3.9	−7.6, 0.8	9.2	−0.3, 19.2	6.2	−4.0, 16.8
+ age (years) at first birth	−4.0	−6.3, −1.5	−4.3	−8.0, −0.3	10.4	0.7, 20.5	7.1	−3.3, 17.8
+ family history of breast cancer	−3.8	−6.3, −1.1	−3.4	−7.4, 1.0	13.0	2.6, 23.9	10.3	−0.9, 21.9

* The analysis was conducted using square-root transformations, producing adjusted regression coefficients (β). Differences on the original scale were calculated at reference value *v*, where *v* was 20% for percent mammographic density and 27 cm^2, 108 cm^2, and 135 cm^2 for dense, nondense, and total breast areas, respectively, using the formula $\beta \times \beta + 2\ \beta \times \text{sqrt}(v)$. Caucasian women formed the reference group.
† CI, confidence interval.
‡ Weight (kg)/height (m)^2.
§ Postmenopausal vs. premenopausal.

particular—or to reduced power to detect associations (e.g., if there was large measurement error in the recall of duration of breastfeeding).

Eight previous studies have compared mammographic densities among women of different ethnic groups or have investigated the effect of acculturation (4, 5, 15–21). With the exception of one international study, all of the studies were conducted in the United States. Their findings for African-American women are largely consistent with those observed here: that African-American women have a lower mammographic density than White American women that is either fully or partially accounted for by a higher BMI. Asian Americans have been studied in detail, but they need to be distinguished from British South Asians, since the former are East Asian (mainly of Chinese and Japanese ethnicities). Our results for South Asians are consistent with the sole previous study of this ethnic group (22), but to our knowledge ours is the first to examine factors contributing to ethnic differences. Studies that have included East Asian women have found that their lower BMIs and smaller breast sizes as compared with Caucasians lead to conflicting results for relative and absolute measures of density (18, 20). In contrast, South Asian women are characterized by breast sizes similar to those of Caucasians, and thus findings for both the relative and absolute measures of density were broadly similar.

A 1-percentage-point difference in mammographic density is associated with a 2 percent increase in breast cancer risk (23); thus, age and BMI-adjusted mean mammographic densities that are lower by 3.6 percent in Afro-Caribbeans and 5.1 percent in South Asians would correspond to 6.9 percent and 9.6 percent lower breast cancer risks, respectively, in comparison with Caucasians ($100 - 100 \times [1.02^{\text{difference}}]$). However, mammographic density at ages 50–65 years may not entirely capture breast cancer risk differences attributed to breast density. Boyd et al. (24) pointed out that the age decline in mammographic density parallels that for the rate of breast tissue aging, as described in Pike's model, proposed to explain the age-incidence curve for breast cancer. In this model, the cumulative rate of breast tissue aging determines breast cancer incidence; thus, analogous to this, a woman's cumulative mammographic density may be a more pertinent marker. If mammographic density reflects the rate of stromal and epithelial cell proliferation or some other underlying biologic process, and if some factors (such as pregnancy, through epithelial cell differentiation) have a long-term effect on proliferation rates whereas others have only transient effects that act at the time of exposure, this study would only have been able to detect factors that have a permanent effect on mammographic density or concurrent factors that have transient effects. Factors (such as breastfeeding) that are associated with breast cancer risk but were not found to affect mammographic density at ages 50–65 years may still affect mammographic density at other ages.

In the next few decades, a rising proportion of British South Asian and Afro-Caribbean breast screenees will be second-generation migrants with increasingly Westernized lifestyles. Monitoring of trends in mammographic density in these women may provide early indications of changes in breast cancer incidence. Screening programs provide a unique but underutilized research setting in which to conduct studies of this marker of breast cancer.

Although mammographic density, as measured using current tools, provides only a small improvement in individual-level risk assessment (25), at a population level it remains a powerful tool with which to study breast cancer etiology. This study was the first to demonstrate that differences in mammographic density between ethnic groups in the United Kingdom are consistent with those for breast cancer risk, giving further weight to the importance of this intermediate phenotype. If mammographic density distributions resemble breast cancer risk profiles, factors that explain differences in distributions, if modifiable, may provide clues to ways in which high mammographic density distributions could be shifted downward. The ultimate aim of such a shift would be population risk reduction. These consequences do not necessarily follow but are worth investigating.

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