A Prospective Study of Body Size and Breast Cancer in Black Women

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Abstract

The relation of body mass index (BMI) and weight gain to breast cancer risk is complex, and little information is available on Black women, among whom the prevalence of obesity is high. We assessed BMI and weight gain in relation to breast cancer risk in prospective data from the Black Women's Health Study. In 1995, 59,000 African American women enrolled in the Black Women's Health Study by completing mailed questionnaires. Data on anthropometric factors were obtained at baseline and every 2 years afterwards. In 10 years of follow-up, 1,062 incident cases of breast cancer occurred. Incidence rate ratios (IRR) were computed in multivariable Cox proportional hazards regression. BMI at age 18 years of ≥25 relative to <20 was associated with a reduced risk of breast cancer among both premenopausal women (IRR, 0.68; 95% confidence interval, 0.46-0.98) and postmenopausal women (IRR, 0.53; 95% confidence interval, 0.35-0.81). There was an inverse association of current BMI with premenopausal breast cancer but no association with postmenopausal breast cancer, either overall or among never-users of hormone therapy. Weight gain was not associated with postmenopausal breast cancer risk. In analyses restricted to breast cancers that were estrogen and progesterone receptor positive, IRRs for current BMI and weight gain were elevated but not statistically significant. The findings indicate that being overweight at age 18 years is associated with a reduced risk of both premenopausal and postmenopausal breast cancer in African American women. Understanding the reasons for the association may help elucidate the pathways through which adolescent exposures influence breast cancer risk. The lack of association of obesity with receptor-negative tumors in postmenopausal African American women may partially explain why breast cancer incidence in older Black women is not high relative to other ethnic groups in spite of the high prevalence of obesity in Black women. (Cancer Epidemiol Biomarkers Prev 2007;16(9):1795–802)

Introduction

Numerous studies, largely of White women, have assessed the relation of overall obesity, central adiposity, and weight gain to risk of breast cancer. The relation differs by menopausal status: among postmenopausal women, those who are overweight or obese have an increased breast cancer risk compared with women of normal weight (1-4), whereas among premenopausal women, overweight women have a reduced risk (1, 2, 4). The increased risk in overweight postmenopausal women can be explained by the fact that adipose tissue is the major source of estrogenic hormones after the menopause (5, 6). The mechanism for the inverse association in premenopausal women is less clear. One hypothesis is that overweight young women are more likely to have anovulatory cycles, with less cumulative exposure to endogenous estrogens (7, 8); another is that there is greater clearance of estrogens by the liver in young women who are overweight (9).

Several case-control studies have reported on the relation of obesity to breast cancer risk in African American women separately by menopausal status, with inconsistent results (10-14). There was little evidence of an association of current body mass index (BMI) with risk of breast cancer in premenopausal women (10-14). Among postmenopausal women, high BMI was associated with an increased risk (11, 14), a reduced risk (12, 13), or there was no association (10). In addition, the Cancer Prevention Study II (15) provided data on BMI and death from breast cancer during 20 years of follow-up, with a total of 257 breast cancer deaths among Black women; there was not a statistically significant association of BMI with risk of breast cancer mortality.

African American women as a group differ from European Americans in that they have a higher incidence of breast cancer before age 40 years, a lower incidence at older ages, and a considerably higher prevalence of overweight and obesity (16, 17). It is therefore of interest to conduct further study of the relation of measures of obesity to risk of breast cancer. The current study is the largest study of body size and breast cancer incidence in African American women and the first to use prospective data.

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Materials and Methods

The study protocol was approved by the Institutional Review Boards of Boston University and Howard University. The Black Women's Health Study is an ongoing prospective cohort study of African American women from all regions of the United States. The study was begun in 1995 when women were enrolled by responding to questionnaires mailed to subscribers of Essence magazine (a popular magazine targeted to Black women), members of several Black professional organizations, and friends or relatives of early respondents. After exclusion of women who were outside the ages of 21 through 69 years, who did not fill out the questionnaire satisfactorily, or whose addresses were judged to be invalid, 59,000 women of ages 21 to 69 years composed the study cohort.

The baseline questionnaire obtained information on adult height, current weight, waist circumference, hip circumference, demographic characteristics, reproductive history, medical history, use of medications, use of cigarettes and alcohol, and usual diet. Follow-up questionnaires that update information on reproductive history and other exposures and identify new occurrences of cancers and other serious illnesses are mailed to participants every 2 years. Follow-up has been complete for ~80% of the baseline cohort for each questionnaire cycle. The analysis reported here is based on data from the first 10 years of follow-up, from 1995 through 2005.

New cases of breast cancer were identified from 1997-2005 biennial questionnaire responses. Death certificates were obtained for deaths reported by family members or the U.S. Postal Service. In addition, the National Death Index was searched for all nonrespondents, and death certificate data was obtained for all matches. Pathology reports were obtained for 635 self-reported incident cases of breast cancer, and 36 additional incident cases were identified through death certificate data. In addition, 134 women refused permission to release their records but confirmed the breast cancer diagnosis in a phone conversation with study staff, 119 did not respond to requests for medical record release, 20 signed a release form but the records were not available, and 150 cases are still in progress. Many women cited confidentiality concerns as the reason for the decision not to allow review of their medical records. The diagnosis of breast cancer was confirmed for 99.4% of potential cases whose pathology reports were reviewed. Because the rate of confirmation was so high, we included as cases all self-reported breast cancers except the four that were disconfirmed by records. Thus, there were 1,090 incident breast cancer cases. Eleven of the cases were excluded due to missing data on height or weight at baseline and 17 were censored before they became cases because they had an earlier diagnosis of another cancer, leaving a total of 1,062 breast cancers for the present analysis.

Information on estrogen receptor (ER) status and progesterone receptor (PR) status was abstracted from the medical records. Cases were classified as positive or negative for ERs and PRs according to classification on the original reports. Among the 392 breast cancer cases for whom receptor status information was available, 64.9% were classified as ER^+, 50.7% as PR^+, and 48.4% as both ER^+ and PR^+. A comparison of characteristics of those cases with known receptor status and those with unknown status indicated that the two groups were similar with regard to levels of BMI, education, parity, age at first birth, and age at diagnosis (data not shown).

Baseline BMI was calculated as kilogram per square meter based on weight and height in 1995. We updated BMI for each 2-year period using weight reported on subsequent questionnaires. Self-reports of waist and hip circumference from the 1995 questionnaire were used to calculate a baseline ratio of waist to hip circumference. As part of a physical activity validation study carried out at the Howard University Cancer Center, the questionnaire self-reports of anthropometric variables were compared with measurements in 115 participants (18). Self-reports of weight, height, waist circumference, and hip circumference were significantly correlated with values measured in the validation study, with Spearman correlation coefficients of 0.97, 0.93, 0.75, and 0.74, respectively.

Statistical Analysis. Analyses were carried out separately among premenopausal and postmenopausal women. Women who had had a hysterectomy but had retained one or both ovaries were classified as premenopausal if their current age was less than the 10th percentile of age at natural menopause in the Black Women's Health Study (age 43 years), as postmenopausal if their age was greater than the 90th percentile of age at natural menopause in the cohort (age 56 years), and as unknown menopausal status if age was 43 to 56 years. Waist circumference and waist-to-hip ratio were categorized by quintile. A categorical variable for current BMI was used as a measure of overweight and obesity, with cutoff points of <25, 25-29, 30-34, and ≥35. ''Current'' BMI represented BMI calculated from weight reported on the questionnaire before the questionnaire cycle during which the breast cancer occurred or the questionnaire before the last follow-up (for noncases). BMI at age 18 years was categorized as <20, 20-24, and ≥25. A weight gain variable represented gain in weight from age 18 years to last follow-up, with categories of <10, 10-14, 15-19, 20-24, and ≥25 kg. Participants were excluded from all analyses if they had reported a cancer other than nonmelanoma skin cancer at baseline (n = 1,372), if they were pregnant at baseline (n = 1,003), or if they had missing information on height or weight at baseline (n = 603).

Age-stratified Cox proportional hazards regression models were used to derive incidence rate ratios (IRR) for breast cancer in relation to each of the anthropometric measures (19). Each participant contributed follow-up time from baseline in 1995 until the occurrence of any cancer other than nonmelanoma skin cancer, death, loss to follow-up, or end of follow-up, whichever occurred first. Multivariable models controlled for age, age at menopause (as a time-dependent variable), age at menarche, parity (time-dependent), age at first birth, hours per week of vigorous exercise (time-dependent), years of education, and family history of breast cancer (mother or sister). Control for adult height, age at attainment of adult height, and birthweight did not materially change the estimates and were not included in the multivariate models. Analyses of current BMI, weight gain, and weight distribution were further controlled for BMI at age 18 years. Similarly, analyses of the relation of BMI at age 18 years to breast cancer risk were further controlled for current BMI.

Departures from the proportional hazards assumption were tested by a likelihood ratio test comparing models with and without age by covariate interaction terms (19). No violations of this assumption were found. All 95% confidence intervals (95% CI) were two sided. SAS statistical software (version 9.1; SAS Institute, Inc.) was used for the analyses.

We repeated the analyses of BMI, weight gain, and weight distribution separately among postmenopausal women who had never used hormone supplements. We also carried out analyses in which breast cancer cases were grouped according to hormone receptor status. To test the hypothesis that overweight young women may have a reduced risk of breast cancer due to a higher prevalence of anovulatory menstrual cycles, we carried out several additional analyses of BMI at age 18 years and current BMI in premenopausal women: (*a*) with adjustment for self-report of infertility due to ovulatory problems; (*a*) with exclusion of any women who reported infertility due to ovulatory problems; and (*a*) with exclusion any women who reported infertility, regardless of cause.

Results

After the exclusions noted above, there were 1,062 cases diagnosed with breast cancer during the 10 years of follow-up, with age at diagnosis ranging from 25 to 79 years (median, 51 years). Four hundred ninety-six cases were diagnosed before menopause had taken place, 455 were diagnosed after the menopause, and 111 could not be classified as to menopausal status. The relation of known risk factors for breast cancer to baseline BMI is given in Table 1. The prevalence of obesity (BMI ≥ 30) increased with age among premenopausal women and decreased slightly with age among postmenopausal women. Among both premenopausal and postmenopausal women, the prevalence of obesity was positively associated with number of births; inversely associated with years of education, age at menarche, age at first birth, and number of hours per week of vigorous exercise; and not associated with family history of breast cancer.

Among premenopausal women, both BMI at age 18 years and current BMI were inversely associated with breast cancer risk (Table 2): the multivariable IRR for a BMI at age 18 years of ≥25 relative to <25 was 0.63 (95% CI, 0.46-0.87), and the IRR for current BMI ≥35 relative to <25 was 0.72 (95% CI, 0.54-0.96). The IRR for BMI at age 18 years did not change appreciably with further control for current BMI, but the IRR for current BMI ≥35 moved closer to 1.0 (IRR, 0.87; 95% CI, 0.62-1.21) after control for BMI at age 18 years. Weight gains of 10 to 19 kg were associated with an increased risk relative to a gain of <10 kg, but larger gains in weight were not. The results were unchanged when a term for ovulatory infertility was included in the model and when the analyses excluded women who reported a history of infertility

Table 1. Baseline characteristics according to BMI by menopausal status in the Black Women's Health Study, 1995

	Premenopausal (*N* = 42,538)		Postmenopausal (*N* = 9,542)	
	Total *N* in strata of each characteristic	With baseline BMI ≥30 (%)	Total *N* in strata of each characteristic	With baseline BMI ≥30 (%)
Age (y)				
<30	12,100	22.1	46	
30-39	18,234	28.2	406	44.1
40-49	11,049	32.5	2,436	38.0
50-59	1,115	37.7	4,124	37.7
≥60	40		2,530	35.3
Education				
≤12	6,212	35.6	2,562	42.3
13-15	16,031	29.8	3,019	38.2
16	10,879	24.1	1,424	34.4
≥17	9,120	23.6	2,459	33.2
Age at menarche (y)				
≤11	11,996	36.9	2,620	46.1
12-13	22,430	25.4	4,794	35.4
≥14	7,926	21.0	2,068	31.3
Parity				
Nulliparous	17,617	24.8	1,541	35.1
1	9,511	27.6	1,835	34.8
2	9,097	28.6	2,460	35.5
≥3	6,249	35.5	3,667	41.2
Age at first birth (y)				
<20	8,164	33.6	2,924	41.4
20-24	8,588	30.0	3,151	37.6
25-29	5,287	26.7	1,267	34.6
≥30	2,592	25.3	559	30.2
Vigorous activity (h/wk)				
None	11,799	37.5	4,513	43.6
<5	23,220	25.7	3,584	32.7
≥5	6,222	17.2	7,98	26.1
Family history of breast cancer				
Yes	2,426	28.9	909	38.5
No	40,112	27.8	8,633	37.4

Table 2. Risk of breast cancer in relation to body size among premenopausal women

	Cases	Person-years	Age-adjusted IRR	Multivariable IRR*	Multivariable IRR
BMI at age 18 y					
<20	216	121,508	1.00 (reference)	1.00 (reference)	1.00 (reference) †
20-24	230	143,205	1.00 (0.83-1.20)	0.98 (0.82-1.19)	1.01 (0.83-1.23)
≥25	45	50,111	0.63 (0.46-0.87)	0.63 (0.46-0.87)	0.68 (0.46-0.98)
Current BMI					
<25	157	103,732	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
25-29	169	101,399	0.89 (0.71-1.10)	0.88 (0.71-1.10)	0.92 (0.74-1.15)
30-34	98	57,997	0.88 (0.68-1.13)	0.89 (0.68-1.15)	0.97 (0.74-1.28)
≥35	71	53,509	0.71 (0.53-0.93)	0.72 (0.54-0.96)	0.87 (0.62-1.21)
Weight gain since age 18 y (kg)					
<10	101	97,838	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
10-14	88	49,277	1.36 (1.02-1.82)	1.37 (1.03-1.83)	1.31 (0.99-1.75)
15-19	86	43,621	1.40 (1.05-1.88)	1.41 (1.05-1.88)	1.35 (1.01-1.81)
20-25	68	41,778	1.09 (0.80-1.49)	1.11 (0.81-1.51)	1.07 (0.78-1.46)
≥25	147	82,126	1.14 (0.88-1.47)	1.18 (0.91-1.53)	1.17 (0.90-1.52)
Waist circumference (in.)					
<28	81	63,604	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
28-30	113	70,669	1.10 (0.83-1.47)	1.09 (0.82-1.46)	1.13 (0.85-1.50)
31-32	74	37,287	1.26 (0.92-1.73)	1.28 (0.93-1.75)	1.34 (0.98-1.85)
33-36	104	57,608	1.09 (0.81-1.46)	1.11 (0.83-1.49)	1.20 (0.89-1.62)
≥37	65	45,500	0.86 (0.62-1.19)	0.88 (0.63-1.23)	1.04 (0.73-1.48)
Waist-to-hip ratio					
<0.71	82	57,146	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
0.71-0.75	88	52,113	1.16 (0.86-1.58)	1.18 (0.87-1.59)	1.17 (0.87-1.58)
0.76-0.80	87	52,132	1.11 (0.82-1.51)	1.15 (0.85-1.55)	1.15 (0.85-1.56)
0.81-0.86	93	52,218	1.20 (0.89-1.62)	1.25 (0.93-1.69)	1.27 (0.94-1.72)
≥0.87	79	53,574	1.08 (0.80-1.48)	1.16 (0.85-1.59)	1.19 (0.87-1.64)

*Adjusted for age, age at menarche, parity, age at first birth, vigorous activity, education, and family history of breast cancer.
†Further adjusted for current BMI.
‡Further adjusted for BMI at age 18 y.

(data not shown). Results were also unchanged when analyses were repeated using invasive cases only (data not shown). Waist circumference and waist-to-hip ratio were not associated with breast cancer risk.

Among postmenopausal women, BMI at age 18 years was also inversely associated with risk of breast cancer (Table 3): the IRR for BMI ≥25 relative to BMI <20 was 0.53 (95% CI, 0.35-0.81). Current BMI was not associated with risk, with an IRR of 0.99 (95% CI, 0.72-1.36) for BMI ≥35 relative to BMI <25, controlling for BMI at age 18 years and other variables. Weight gain, waist circumference, and waist-to-hip ratio also were not associated with risk. Results were unchanged when analyses were restricted to invasive cases only (data not shown).

When we repeated the analyses in the subset of postmenopausal women who had never used hormone supplements, the inverse association with BMI at age 18 years persisted (Table 4). For current BMI ≥35 relative to <25, the IRR was 1.12 (95% CI, 0.66-1.90), and for weight gain ≥25 kg relative to <10 kg, it was 1.40 (95% CI, 0.84-2.32). There was not a statistically significant interaction of hormone supplement use with current BMI ($P = 0.70$) or weight gain ($P = 0.14$).

We carried out further analyses of current BMI and weight gain in relation to postmenopausal breast cancer within strata of age, family history of breast cancer, parity, and waist-to-hip ratio. None of the stratum-specific estimates showed statistically significant elevations for higher levels of BMI, nor were there any significant interactions (data not shown).

Because BMI at age 18 years was the factor most strongly related to breast cancer risk, we assessed the combined effects of BMI at age 18 years and weight gain and of BMI at age 18 years and current BMI (Table 5). Risk increased with increasing weight gain when BMI at age 18 years was ≥20, but not when BMI at age 18 was <20. Risk increased slightly with increasing current BMI when BMI at age 18 years was ≥20, but not when BMI at age 18 was <20. A similar pattern was seen when users of hormone supplements were excluded from the analysis (data not shown).

Previous studies suggest that the association of obesity or weight gain with risk of breast cancer in postmenopausal women may occur only for tumors that have ERs and PRs (20-22). To test this hypothesis, we stratified breast cancer cases according to receptor status (Table 6). For breast cancers that had both ER and PR, the IRRs for weight gain ≥25 kg relative to <15 kg and for current BMI ≥30 relative to <25 exceeded 1.0 (1.29 and 1.66) but were not statistically significant. In analyses that excluded users of hormone supplements, the IRRs were higher, but numbers were small (data not shown). Weight gain and current BMI were not associated with an increased risk of receptor-negative breast cancers or of those with mixed ER/PR status. There was a statistically significant inverse association of weight gain ≥25 kg with risk of cancers with mixed ER/PR status, but this was based on only eight cases who gained ≥25 kg.

Discussion

The most striking finding from this prospective study of Black women is that being overweight at age 18 years is associated with a reduced risk of breast cancer, one that persists through both the premenopausal and postmenopausal periods.

Findings on the relation of weight during adolescence or young adulthood to risk of either premenopausal or postmenopausal breast cancer have received little attention. A few studies, including recent reports from the Women's Health Initiative (23) and the Nurses Health Study II (24), indicate that overweight at ages 18 to 20 years reduces risk (23-27); in other studies, weight at ages 18 to 20 years was not associated with risk (28-30). An inverse association with breast cancer has also been reported for being overweight at age 10 years and during adolescence (31-35). Only one previous study, a case-control study with 304 breast cancer cases, assessed weight at a young age and risk of breast cancer in U.S. Black women: BMI at age 18 years was not associated with a reduction in breast cancer risk (14). However, that study was limited by very low participation rates and the inclusion of BMIs up to 25 in the reference category of ''low'' BMI (14).

The reasons for the inverse association of BMI at age 18 years and breast cancer risk are unknown. The hypothesis that overweight young women have a lower risk due to a lower cumulative exposure to estrogens stemming from having a greater number of anovulatory cycles (7, 8) is not supported by our analyses that controlled for history of ovulatory infertility and that excluded any woman who reported infertility. Nor was it substantiated in a study of premenopausal women from the Nurses' Health Study II that also took into account ovulatory problems (24). In addition, whereas anovulation can result from extreme overweight, it should not be associated with moderate overweight. There may be other mechanisms by which estrogen levels are decreased in overweight premenopausal women. For example, there is evidence that free estradiol is cleared by the liver at a faster rate in overweight women than in thin women (36).

Alternatively, it is possible that thin women may, because of their leanness, have a greater biologically effective exposure to carcinogenic substances. Several studies have found that BMI is inversely associated with levels of environmental contaminants or with levels of DNA adducts, which are indicators of the biologically effective dose of a carcinogen (37, 38). As explained by Wolff and Anderson (39), obese women, who have a larger adipose reservoir, will have lower serum levels of environmental toxins close to the time of exposure because the toxins will be sequestered in the adipose tissue. Thin women will have higher serum levels and thus a higher body burden close to the time of exposure. Undifferentiated breast epithelial cells are at particularly high risk of cancer initiation in the years closely following puberty; as a result, exposures to toxins during those years may have a relatively greater effect on thin women.

The majority of previous epidemiologic studies have found that current BMI is inversely associated with risk of premenopausal breast cancer (1, 2, 4). A similar association was observed in our study. Although further control for BMI at age 18 years reduced the magnitude of the association, this may be due to correlation between BMI at age 18 years and current BMI during the premenopausal years.

Neither current BMI nor adult weight gain was associated with an increased risk of postmenopausal breast cancer in the present study; nor was there evidence of an association among the subset of women who had never used female hormone supplements.

Table 3. Risk of breast cancer in relation to body size among postmenopausal women

	Cases	Person-years	Age-adjusted IRR	Multivariable IRR*	Multivariable IRR
BMI at age 18 y					
<20	241	51,789	1.00 (reference)	1.00 (reference)	1.00 (reference) †
20-24	173	48,226	0.79 (0.65-0.96)	0.76 (0.63-0.93)	0.75 (0.62-0.92)
≥25	28	10,839	0.61 (0.41-0.90)	0.55 (0.37-0.82)	0.53 (0.35-0.81)
Current BMI					
<25	101	20,952	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
25-29	151	41,507	0.73 (0.56-0.93)	0.72 (0.56-0.92)	0.75 (0.58-0.97)
30-34	117	28,075	0.85 (0.65-1.11)	0.82 (0.62-1.07)	0.92 (0.69-1.21)
≥35	85	21,729	0.84 (0.63-1.12)	0.78 (0.58-1.05)	0.99 (0.72-1.36)
Weight gain since age 18 y (kg)					
<10	57	16,389	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
10-14	62	13,618	1.25 (0.87-1.80)	1.27 (0.88-1.82)	1.19 (0.83-1.71)
15-19	64	16,420	1.08 (0.75-1.54)	1.09 (0.76-1.55)	1.01 (0.70-1.45)
20-25	65	18,396	0.99 (0.69-1.41)	0.99 (0.69-1.41)	0.90 (0.63-1.30)
≥25	195	45,946	1.20 (0.89-1.62)	1.19 (0.88-1.61)	1.09 (0.81-1.48)
Waist circumference (in.)					
<28	48	12,303	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
28-30	84	20,788	0.98 (0.69-1.40)	0.97 (0.68-1.39)	1.00 (0.70-1.42)
31-32	58	15,632	0.86 (0.59-1.27)	0.84 (0.57-1.24)	0.88 (0.60-1.29)
33-36	112	26,730	0.99 (0.70-1.39)	0.95 (0.67-1.33)	1.00 (0.71-1.42)
≥37	91	21,946	0.98 (0.69-1.39)	0.93 (0.65-1.33)	1.05 (0.73-1.51)
Waist-to-hip ratio					
<0.71	78	19,073	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
0.71-0.75	57	18,346	0.74 (0.53-1.04)	0.74 (0.52-1.04)	0.73 (0.52-1.03)
0.76-0.80	84	19,559	1.01 (0.74-1.38)	0.99 (0.73-1.35)	0.98 (0.72-1.34)
0.81-0.86	88	20,483	1.04 (0.77-1.42)	1.03 (0.76-1.40)	1.01 (0.74-1.38)
≥0.87	75	17,763	1.03 (0.75-1.42)	1.01 (0.74-1.40)	0.99 (0.72-1.37)

*Adjusted for age, age at menarche, parity, age at first birth, age at menopause, vigorous activity, education, and family history of breast cancer.
†Further adjusted for current BMI.
‡Further adjusted for BMI at age 18 y.

Table 4. Risk of breast cancer in relation to body size among postmenopausal women who had never used hormone therapy

	Cases	Person-years	Age-adjusted IRR	Multivariable IRR*	Multivariable IRR
BMI at age 18 y					
<20	84	17,938	1.00 (reference)	1.00 (reference)	1.00 (reference) †
20-24	60	17,531	0.74 (0.53-1.03)	0.71 (0.51-0.99)	0.67 (0.48-0.95)
≥25	16	4,445	0.81 (0.47-1.39)	0.74 (0.43-1.27)	0.63 (0.34-1.16)
Current BMI					
<25	32	7,405	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
25-29	53	14,540	0.84 (0.54-1.30)	0.80 (0.51-1.24)	0.82 (0.52-1.28)
30-34	42	10,025	0.95 (0.60-1.51)	0.88 (0.55-1.42)	0.95 (0.59-1.54)
≥35	38	8,494	1.06 (0.66-1.70)	0.94 (0.58-1.54)	1.12 (0.66-1.90)
Weight gain since age 18 y (kg)					
<10	20	6,004	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
10-14	23	4,920	1.42 (0.78-2.59)	1.44 (0.79-2.63)	1.42 (0.77-2.62)
15-19	21	5,584	1.09 (0.59-2.02)	1.09 (0.59-2.02)	1.07 (0.57-2.00)
20-25	14	6,613	0.63 (0.32-1.25)	0.62 (0.31-1.23)	0.60 (0.30-1.21)
≥25	82	16,700	1.46 (0.90-2.39)	1.42 (0.86-2.34)	1.40 (0.84-2.32)
Waist circumference (in.)					
<28	15	4,300	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
28-30	25	6,689	1.00 (0.53-1.91)	0.98 (0.52-1.87)	1.00 (0.52-1.90)
31-32	25	5,570	1.24 (0.65-2.36)	1.17 (0.61-2.24)	1.21 (0.63-2.32)
33-36	43	9,776	1.23 (0.68-2.22)	1.15 (0.64-2.09)	1.19 (0.66-2.17)
≥37	34	8,572	1.06 (0.58-1.96)	0.98 (0.53-1.83)	1.07 (0.57-2.01)
Waist-to-hip ratio					
<0.71	27	6,596	1.00 (reference)	1.00 (reference)	1.00 (reference) ‡
0.71-0.75	21	6,202	0.83 (0.47-1.47)	0.82 (0.46-1.45)	0.82 (0.46-1.45)
0.76-0.80	30	7,076	1.00 (0.60-1.69)	0.99 (0.58-1.67)	0.99 (0.58-1.67)
0.81-0.86	25	7,349	0.82 (0.48-1.42)	0.80 (0.46-1.38)	0.80 (0.46-1.39)
≥0.87	33	6,777	1.19 (0.71-1.99)	1.17 (0.70-1.97)	1.15 (0.69-1.94)

*Adjusted for age, age at menarche, parity, age at first birth, age at menopause, vigorous activity, education, and family history of breast cancer.
†Further adjusted for current BMI.
‡Further adjusted for BMI at age 18 y.

However, when we restricted our case group to cancers that were ER^+/PR^+, IRRs were elevated for the highest categories of current BMI and weight gain. These finding suggest that overweight in postmenopausal Black women may be associated with an increased risk of hormone receptor–positive breast cancers, but not of other types.

With regard to current BMI and risk of postmenopausal breast cancer in White women, there is a large body of literature, including a recent pooled analysis of data from cohort studies, indicating that risk increases with increasing BMI up to a BMI of ~28 kg/m^2, after which there is no further increase (2, 4). The magnitude of the association in cohort studies is modest, with a RR of ~1.3 for the highest categories relative to lowest. Adult weight gain has also been associated with increased risk of postmenopausal breast cancer in White women (40-44). Recent studies have indicated that the associations with BMI and weight gain are present primarily among women who are not taking hormone supplements (23, 45). Furthermore, there is some evidence that the associations are present only for tumors that are positive for both ERs and PRs (20-22).

Limited data are available on Black women. A population-based case-control study that included 350 Black breast cancer cases (Carolina Breast Cancer Study) did not observe an increased risk of postmenopausal breast cancer in women who were overweight or obese; nor did a cohort study of breast cancer mortality (Cancer Prevention Study II; ref. 13). Hospital-based case-control studies yielded conflicting results (10-12). None of the studies of Black women reported results stratified by receptor status.

A likely contributor to the discrepancy in findings between Black and White women with regard to current BMI, weight gain, and postmenopausal breast cancer risk is the difference in distributions of ER and PR status. African American women have a considerably lower proportion of breast carcinomas that are ER^+, PR^+, or both, than do White women. SEER data from 1990-1997 indicate the following distributions for African American and Caucasian women, respectively: ER^+, 60.6% and 77.4%; PR^+, 53.8% and 68.0%; and ER^+/PR^+, 48.0% and

Table 5. Weight gain and current BMI in relation to postmenopausal breast cancer, according to BMI at age 18 y

	BMI ≥20 at age 18 y		BMI <20 at age 18 y	
	Cases	IRR*	Cases	IRR*
Weight gain since age 18 y (kg)				
<10	27	1.00 (reference)	30	2.38 (1.41-4.02)
10-14	25	1.34 (0.78-2.31)	36	2.44 (1.48-4.02)
15-19	28	1.31 (0.77-2.23)	36	1.84 (1.11-3.03)
20-25	28	1.25 (0.73-2.12)	37	1.58 (0.96-2.60)
≥25	93	1.63 (1.06-2.51)	102	1.79 (1.17-2.74)
Current BMI				
<25	17	1.00 (reference)	81	1.95 (1.16-3.30)
25-29	62	1.12 (0.66-1.92)	87	1.31 (0.78-2.21)
30-34	63	1.23 (0.72-2.11)	50	1.59 (0.92-2.77)
≥35	59	1.16 (0.67-1.99)	23	1.86 (0.99-3.50)

*Adjusted for age, age at menarche, parity, age at first birth, age at menopause, vigorous activity, education, and family history of breast cancer.

Table 6. Weight gain and current BMI in relation to postmenopausal breast cancer, according to ER/PR status

	ER^+/PR^+		ER^+/PR^- or ER^-/PR^+		ER^-/PR^-	
	Cases	IRR*	Cases	IRR*	Cases	IRR*
Weight gain since age 18 y (kg)						
<15	19	1.00	14	1.00	13	1.00
15-24	25	1.12 (0.61-2.06)	14	0.69 (0.33-1.52)	13	0.76 (0.35-1.65)
≥25	38	1.29 (0.73-2.28)	8	0.31 (0.13-0.77)	26	1.03 (0.52-2.05)
Current BMI						
<25	13	1.00	10	1.00	10	1.00
25-29	25	0.99 (0.50-1.94)	18	0.88 (0.40-1.94)	21	1.02 (0.47-2.18)
≥30	46	1.66 (0.86-3.21)	8	0.39 (0.14-1.07)	21	0.88 (0.39-1.97)

*Adjusted for age, age at menarche, parity, age at first birth, age at menopause, vigorous activity, education, family history of breast cancer, and BMI at age 18 y.

64.2% (46). The distributions within the Black Women's Health Study were very similar to SEER data on African American women. If obesity conveys an increased risk only of postmenopausal ER^+/PR^+ breast cancers, it would be more difficult to detect the association in an overall sample of African American women in which relatively fewer cases are ER^+/PR^+.

Another possibility for the lack of association of obesity and weight gain with overall risk of postmenopausal breast cancer is that the strong and lasting effect of body size at age 18 years makes it difficult to detect an effect of weight gain and high BMI at later ages. In our study, breast cancer risk in postmenopausal women increased with increasing weight gain among those who had a BMI at age 18 years of 20 or higher (i.e., lower-risk women) but not among those who were thin at age 18 years (i.e., higher-risk women).

In a recent analysis from the Multiethnic Cohort Study, postmenopausal African American women had relatively high levels of serum estrogens but a low incidence of breast cancer, whereas estrogen levels and breast cancer risk were positively correlated across other ethnic groups (47). This finding suggests that increases in postmenopausal estrogen levels, as occurs with increasing BMI, may not have as much effect on breast cancer incidence in Black women. In the same cohort, levels of plasma insulin-like growth factor I, which is part of the pathway for negative feedback on growth hormone secretion, declined with increasing BMI in Latinas, Japanese, and White women, but increased with increasing BMI in African American women (48). Insofar as growth hormone plays a role in the etiology of breast cancer, the differing relation of obesity to insulin-like growth factor-I levels by ethnic group may explain the relative lack of association of obesity with breast cancer risk in postmenopausal Black women.

Waist circumference and waist-to-hip ratio were not associated with breast cancer risk in the present study. Findings from previous studies are inconsistent (4, 49-51).

Anthropometric measures in the present study were obtained by self-report, but a validation study indicated good agreement between self-reports and measurements by study personnel (18). In addition, we have assessed the relation of BMI to both type 2 diabetes (52) and hypertension (53) and have found, in agreement with the literature, a strong increase in risk of each condition with increasing increments of BMI. These findings support the validity of Black Women's Health Study data on height and weight. A study strength is the collection of data on weight, waist circumference, and other anthropometric measures before occurrence of the cancer, obviating reporting bias, and before treatment, which can affect weight. Nevertheless, it is likely that there was some nondifferential misclassification of the measures, which could have influenced the results. We were able to control for most known breast cancer risk factors in multivariable analyses. Follow-up rates were high, reducing concern about selective losses.

The study was limited by missing hormone receptor data for an appreciable number of the breast cancer cases because participants would not consent to release of medical records, records were not available, or receptor assays had not been done. This reduced the statistical power available for analysis of receptor-positive or receptor-negative tumors. However, among the cases for whom we did have receptor data, the distributions of ER^+, PR^+, and ER^+/PR^+ were almost identical to those from SEER data on African American women.

In summary, the present study of a large cohort of U.S. Black women provides several important findings. First, the results indicate that being overweight at age 18 years, close to the time of puberty, reduces risk of breast cancer, even up to 50 years later. This factor was the strongest anthropometric predictor of breast cancer risk among both premenopausal and postmenopausal women. Second, the results suggest an explanation for the previous findings of no association of obesity or weight gain with risk of postmenopausal breast cancer in Black women. Whereas we, too, found no association overall, a positive association with current BMI and with adult weight gain was observed for the subgroup of breast cancers that had both ERs and PRs. The lack of an association in receptor-negative cases, which make up ~50% of breast cancer cases in postmenopausal African American women, may explain, in part, why there is not an excess of breast cancer in postmenopausal Black women relative to White women even though the prevalence of obesity is considerably higher in Black women.

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