

# Body mass index and serum leptin concentration independently estimate percentage body fat in older adults<sup>1-3</sup>

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## ABSTRACT

**Background:** Because serum concentrations of leptin, a hormone produced by adipocytes, can be relatively reliably and inexpensively measured, it may be considered complementary to, or even a substitute for, body mass index (BMI) as a measure of adiposity.

**Objective:** We examined the ability of BMI and leptin concentrations, separately and together, to estimate total percentage fat in older adults.

**Design:** Total percentage fat measured by dual-energy X-ray absorptiometry and fasting serum leptin concentrations were measured in 2911 well-functioning 70–79-y-old participants (42% black, 51% women) in the Health, Aging, and Body Composition Study.

**Results:** Mean ( $\pm$ SD) total percentage fat was 29.2  $\pm$  5.0% in men and 40.5  $\pm$  5.7% in women, and the geometric mean ( $\pm$ SD) serum leptin concentration was 5.6  $\pm$  2.5 ng/mL in the men and 16.4  $\pm$  2.3 ng/mL in the women. Among men, total percentage fat was strongly associated with both BMI ( $R^2 = 0.56$ ) and leptin ( $R^2 = 0.57$ ) in separate linear regression analyses and in a combined linear regression analysis ( $R^2 = 0.68$ ). Similarly, among women, total percentage fat was associated with both BMI ( $R^2 = 0.65$ ) and leptin ( $R^2 = 0.54$ ) separately and in combination (model  $R^2 = 0.71$ ). Independent relations of BMI and leptin with total percentage fat were also found among both black and white participants. With the population divided into quintiles according to percentage fat, BMI and serum leptin correctly classified 49% of men and 50% of women in the correct quintile.

**Conclusions:** Among older adults, total percentage fat was better estimated by using both serum leptin concentrations and BMI than by using either alone. However, their performance does not suggest that they can substitute for more accurate measures. *Am J Clin Nutr* 2007;85:1121–6.

**KEY WORDS** Leptin, body composition, anthropometry, dual-energy X-ray absorptiometry, race, epidemiology, Health, Aging, and Body Composition Study, Health ABC

## INTRODUCTION

Obesity is defined as excess body fat. Body mass index (BMI) is nearly universally used as a measure for obesity in large studies that examine the association of obesity with morbidity and mortality—yet it does not discriminate between fat and lean body mass. The percentage variation of percentage body fat, as measured by hydrodensitometry, that can be explained by BMI ( $R^2$ ) has ranged from 0.50 to 0.68 in men and from 0.58 to 0.74 in

women (1–7). Because techniques that can discriminate between fat mass and fat-free mass, such as dual-energy X-ray absorptiometry (DXA), are generally not feasible among large populations, an accurate, reliable measure of total body fat that can be easily determined in clinical care and population studies is needed. One such possible measure is leptin, which is produced by adipocytes and whose serum concentration appears to reflect total body fat (8–10). Because leptin can be relatively reliably and inexpensively measured, it may be considered complementary to, or even a substitute for, BMI as a measure of adiposity. However, we are unaware of any full-scale studies of the relative value of BMI and leptin in estimating body fat. We examined these issues in a large cohort of healthy, elderly blacks and whites from the Health, Aging, and Body Composition (Health ABC) Study.

## SUBJECTS AND METHODS

The Health ABC study is a population-based, longitudinal study of 3075 community-dwelling, nondisabled white and black men and women aged 70–79 y that was begun in 1997. The main goal was to investigate changes in weight and body composition,

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**TABLE 1**

Characteristics of the study subjects by sex and race

Characteristic	Men		Women		<i>P</i> <sup>1</sup>		
	White ( <i>n</i> = 889)	Black ( <i>n</i> = 528)	White ( <i>n</i> = 807)	Black ( <i>n</i> = 687)	Sex	Race	Sex × race
Total percentage fat (%) <sup>2</sup>	29.9 ± 4.7	28.0 ± 5.3	40.0 ± 5.5	40.9 ± 6.0	< 0.001	0.016	< 0.001
Serum leptin concentration (ng/mL) <sup>3</sup>	5.7 ± 2.2	5.5 ± 2.8	13.9 ± 2.3	19.7 ± 2.2	< 0.001	< 0.001	< 0.001
BMI (kg/m <sup>2</sup> ) <sup>2</sup>	26.9 ± 3.7	27.1 ± 4.3	26.0 ± 4.5	29.5 ± 5.7	< 0.001	< 0.001	< 0.001
Age (y) <sup>2</sup>	73.9 ± 2.9	73.5 ± 2.8	73.6 ± 2.8	73.3 ± 3.0	0.029	0.005	0.41
Examination site (%)					0.95	0.025	0.059
Memphis	51	50	55	47			
Pittsburgh	49	50	45	53			

<sup>1</sup> From 2-factor ANOVA.<sup>2</sup> Values are  $\bar{x} \pm$  SD.<sup>3</sup> Values are geometric  $\bar{x} \pm$  SD.

weight-related health conditions, and incident functional limitations (11). Participants were recruited from a random sample of white Medicare beneficiaries and all age-eligible black community residents residing in designated zip codes in the metropolitan areas of Pittsburgh, PA, and Memphis, TN. The sample was selected to represent well-functioning older persons. Eligible participants reported no difficulty walking one-fourth mile, walking up 10 steps, or performing basic activities of daily living. The study was approved by the Institutional Review Boards at the Universities of Pittsburgh and Tennessee, and all participants provided written, informed consent to participate. The present analysis used cross-sectional data from the baseline examination conducted between 1997 and 1998 on all 2911 participants with data on serum leptin concentration, total percentage fat, and BMI.

Serum leptin concentrations were measured in duplicate by radioimmunoassay on a morning fasting venous blood sample [Sensitive Human Leptin RIA Kit (product no. SHL-81K); Linco Research Inc, St Charles, MO] (12). The minimum detectable concentration of the assay is 0.05 ng/mL. The mean intraassay CV is 5.8% (range: 3.7–7.5%) and the mean interassay CV is 7.4% (range: 3.2–8.9%). The linear range of leptin concentration was 0–99 ng/mL. Six participants with leptin concentrations >99 ng/mL, for whom an accurate value could not be determined by the laboratory, were excluded from analysis.

Total body fat was estimated from DXA (QDR 4500A, with Software Version 8.21 for analysis; Hologic Inc, Waltham, MA) (13). Height was measured to the nearest mm by using a Harpenden stadiometer (Holtain Ltd, Crosswell, Wales, United Kingdom) with the participant barefoot, and weight was measured to the nearest 0.1 kg by using a standard balance beam scale with the participant wearing lightweight clothing. BMI [weight (in kg)/height<sup>2</sup> (in m)] was calculated.

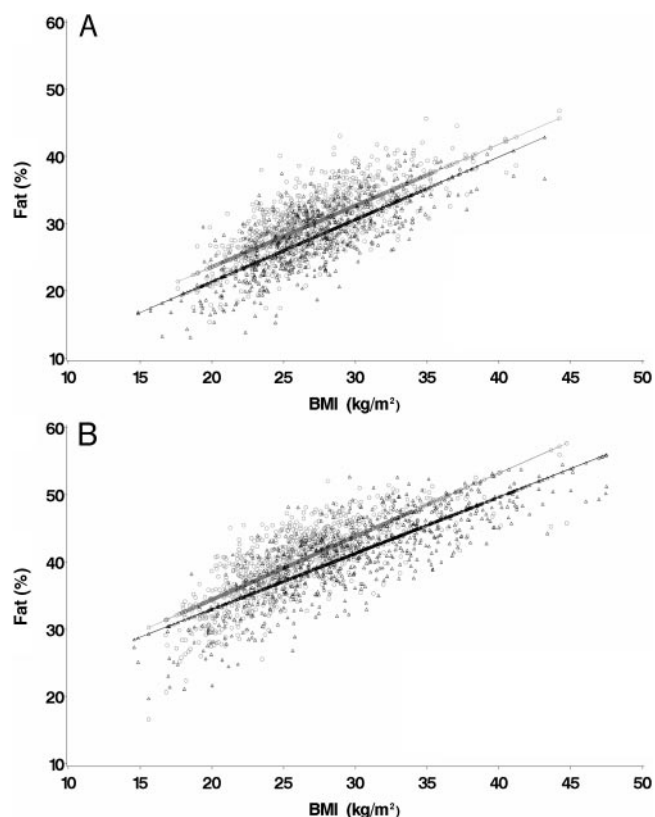
Leptin concentration was log<sub>10</sub> transformed to normalize its distribution. Means and SDs for total percentage fat, serum leptin concentration, and BMI were calculated, and means were compared between sex and race subgroups by using analysis of variance. A *P* value < 0.05 indicated statistical significance. Multiple linear regression analysis was used to calculate the proportion of variation (*R*<sup>2</sup>) in percentage fat explained by BMI and leptin individually and jointly. Quadratic terms for BMI and leptin were considered for inclusion in the models and retained if they improved the *R*<sup>2</sup>. Analyses were adjusted for age, field center site,

and race (in analyses of men and women). Sex-specific models that best predicted percentage fat from BMI and leptin individually and jointly were determined. The models were tested by calculating the proportion of participants for whom they predicted the correct percentile group (as fifths, quarters, or thirds) of the measured percentage fat. The proportions correctly classified were compared between models by using McNemar's test. The effects of sex and measured percentage fat percentile on the ability of BMI and log<sub>10</sub> leptin, independently and jointly, to correctly classify participants were evaluated using logistic regression analysis. Because BMI and leptin were correlated ( $\rho = 0.56$ ), collinearity in multiple regression models was evaluated by using variance inflation factor and tolerance (14). Substantial collinearity was not found. Analyses were performed by using SAS 9.1 software (15).

## RESULTS

Total percentage fat, serum leptin concentrations, and BMI were measured in 2911 participants (889 white men, 528 black men, 807 white women, and 687 black women). Mean ( $\pm$ SD) total percentage fat was higher in the women than in the men ( $40.5 \pm 5.7\%$  compared with  $29.2 \pm 5.0\%$ ) and, within sex groups, was higher in the black women and in the white men (**Table 1**). Geometric mean leptin concentrations were higher in the women than in the men ( $16.4 \pm 2.3$  ng/mL compared with  $5.6 \pm 2.5$  ng/mL) and higher in the black women than in the white women. No significant ethnic differences in leptin concentrations were observed among the men. BMI was higher in the women than in the men and higher in the black than the white women, but it did not differ significantly between black and white men.

Percentage fat was strongly associated with BMI, leptin, and log<sub>10</sub> leptin in separate analyses in both the men and the women (**Figure 1**, **Figure 2**, **Figure 3**, and **Table 2**). A test for interaction on total percentage fat was significant for sex, race, and log<sub>10</sub> leptin (*P* = 0.002) and borderline for sex, race, and BMI (*P* = 0.090). Two-way interactions were nonsignificant for sex and BMI (*P* = 0.39) and for sex and race (*P* = 0.56) and significant for race and BMI (*P* = 0.014). Because of significant interactions, separate sex-race models are shown. In analyses

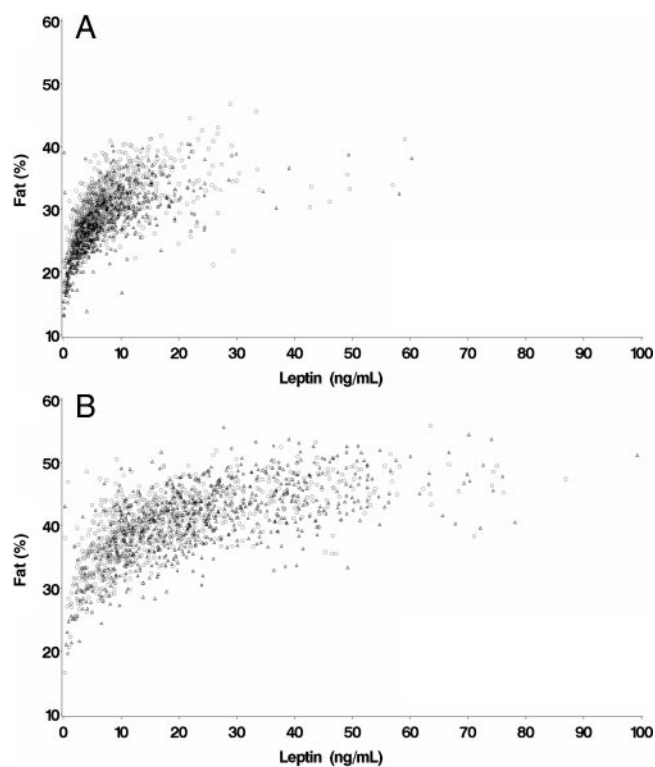


**FIGURE 1.** Distribution of percentage fat and body mass index (BMI) among well-functioning older black ( $\Delta$ ,  $n = 528$ ) and white ( $\circ$ ,  $n = 889$ ) men (A) and among well-functioning older black ( $\Delta$ ,  $n = 687$ ) and white ( $\circ$ ,  $n = 807$ ) women (B).

with BMI and  $\log_{10}$  leptin, percentage fat remained independently associated with both in both sexes. As a result, the proportion of variation in percentage fat explained by BMI and  $\log_{10}$  leptin jointly was greater among both the men ( $R^2 = 0.68$ ) and the women ( $R^2 = 0.71$ ) than was that explained by BMI and  $\log_{10}$  leptin alone (Table 2). Among the men, there was little difference between  $\log_{10}$  leptin and BMI in the ability to predict percentage fat. This was true for both blacks and whites. Among the women, BMI appeared to be a better predictor of percentage fat than was  $\log_{10}$  leptin among both whites and blacks. BMI and  $\log_{10}$  leptin combined had a similar ability to predict percentage fat in the men and women. The combined predictive ability of BMI and  $\log_{10}$  leptin was lowest in the white men and highest in the black women but did not vary greatly among sex-ethnicity subgroups ( $R^2 = 0.65$ – $0.72$ ) (Table 2).

To evaluate the linearity of the relations of percentage fat with  $\log_{10}$  leptin and BMI and to develop the best fitting predictive equations, the addition of quadratic terms to the models was tested. Inclusion of quadratic terms for BMI to predict percentage fat increased the  $R^2$  by 1% in equations for the men and 3–4% in equations for the women. However, in combination with  $\log_{10}$  leptin, BMI squared increased the  $R^2$  only in equations for women and only by 1%. Inclusion of quadratic terms for  $\log_{10}$  leptin had minimal effect on the  $R^2$  (Table 2). The models that best predicted percentage fat from BMI and  $\log_{10}$  leptin individually and jointly are shown in Table 3.

The ability of BMI and  $\log_{10}$  leptin to correctly categorize percentage fat by DXA is shown in Table 4 according to quintiles



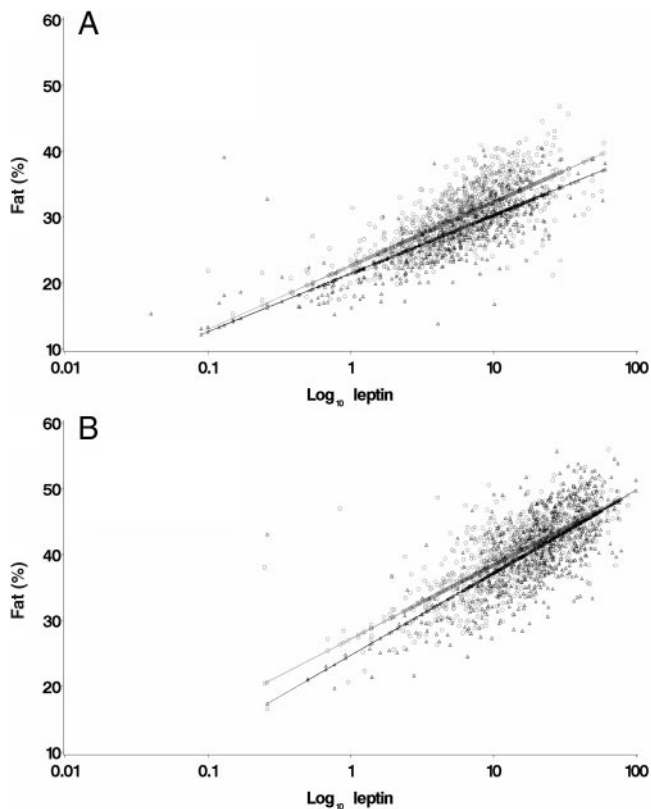
**FIGURE 2.** Distribution of percentage fat and leptin among well-functioning older black ( $\Delta$ ,  $n = 528$ ) and white ( $\circ$ ,  $n = 889$ ) men (A) and among well-functioning older black ( $\Delta$ ,  $n = 687$ ) and white ( $\circ$ ,  $n = 807$ ) women (B).

for men and for women. Inclusion of both BMI and  $\log_{10}$  leptin increased the proportion correctly classified over using just one measure.  $\log_{10}$  leptin contributed more among the men than the women ( $P < 0.001$ ), and BMI contributed more among women than the men ( $P < 0.001$ ). BMI alone classified women with the lowest and highest DXA-measured percentage fat more accurately than for women with percentage fat in the midrange ( $P = 0.044$ ), whereas there was no significant difference based on percentage fat quintile among the men ( $P = 0.37$ ;  $P$  for sex-percentage fat quintile interaction =  $0.042$ ).  $\log_{10}$  leptin alone predicted percentage fat better among the women than among the men ( $P = 0.047$ ) and better among the participants with lower DXA-measured percentage fat than among those with higher levels ( $P < 0.001$ ). BMI and  $\log_{10}$  leptin combined did not significantly differ in predictive ability by sex ( $P = 0.74$ ), but predicted percentage fat better at the lowest and highest quintiles than in the middle ( $P = 0.005$ ). The overall correct classification was 49% among the men and 50% among the women when using the equations in Table 3. As expected, if percentage fat was divided into larger categories, a higher proportion would be correctly classified. With 4 categories (quartiles), the percentage classified correctly was 54% among the men and 58% among the women. With 3 categories (tertiles), the percentage classified correctly was 67% among the men and 68% among the women.

## DISCUSSION

In the United States and many other countries, overweight and obesity are problems of epidemic proportion that increase the risk





**FIGURE 3.** Distribution of percentage fat and  $\log_{10}$  leptin among well-functioning older black ( $\Delta$ ,  $n = 528$ ) and white ( $\circ$ ,  $n = 889$ ) men (A) and among well-functioning older black ( $\Delta$ ,  $n = 687$ ) and white ( $\circ$ ,  $n = 807$ ) women (B).

of numerous medical conditions (16, 17). Consequently, accurate and easily measured indicators of body fat are needed to perform comparisons across populations, to monitor trends, and to study the increased health risks of obesity. They may have a place in clinical medicine as well. BMI is a commonly used surrogate for adiposity that is inexpensive and easily measured, but its correlation with body fat is imperfect. The greatest limitation is that BMI does not discriminate between fat and lean body mass. This can be misleading, because the relation between BMI and body fat is dependent on sex, age, race-ethnicity, and

fitness level. Women have a higher proportion of body fat than do men with the same BMI. For example, in the current study, white women had lower BMI than did white men but had considerably higher percentage body fat. Percentage body fat increases with age for a given BMI, particularly after middle age and during menopause in women (18, 19). African Americans have a lower percentage body fat than do whites at a given BMI, whereas the reverse is true of many Asian ethnicities (18, 20, 21).

In the current study of older black and white adults, total percentage fat was better estimated by using both  $\log_{10}$  serum leptin concentrations and BMI than by using either alone. Independent relations of  $\log_{10}$  leptin and BMI with total percentage fat were found across strata of sex and ethnicity. BMI was a better predictor of percentage fat in the women than was  $\log_{10}$  leptin, whereas there was no significant difference between the 2 in the men. Because BMI reflects lean mass as well as fat mass, it may have been a less accurate predictor in men who have a higher proportion of lean mass compared with women. The men exhibited greater variation in percentage fat within BMI categories than did the women (data not shown), so the addition of  $\log_{10}$  leptin improved specificity in the men and compensated for the lower predictive ability of BMI.

Although the present analysis shows an improved estimate of percentage fat with the use of both BMI and  $\log_{10}$  leptin, their performance does not suggest that they can substitute for more accurate measures. By using DXA as the reference and best fit equations that included  $\log_{10}$  leptin, BMI, ethnicity, age, and examination site, not more than one-half of the men and women were classified into the correct quintile of percentage body fat (Table 4). Although this is much better than the expected 20% correct classification by chance alone, this degree of accuracy is somewhat disappointing given the relatively narrow age-range. The lower predictive ability at the highest percentage fat quintiles may have resulted in part from flattening of the leptin-percentage fat curves at higher levels of percentage fat (Figure 2A and B). However, we attempted to address this nonlinear relation using  $\log_{10}$  transformed leptin in the regression models and by evaluating quadratic terms for  $\log_{10}$  leptin and BMI in the models. The flattening of the leptin curves reflects a greater increase in leptin per unit increase in percentage fat at higher levels of percentage fat. This is consistent with leptin resistance that occurs in most obese persons (22, 23). Substituting height and weight, or the

**TABLE 2**  
Relation ( $R^2$ ) of total percentage fat with BMI and serum leptin concentration by sex and race<sup>1</sup>

Model	Men			Women		
	Total	White ( $n = 889$ )	Black ( $n = 528$ )	Total	White ( $n = 807$ )	Black ( $n = 687$ )
BMI ( $\text{kg}/\text{m}^2$ ) and BMI <sup>2</sup>	0.56	0.53	0.56	0.65	0.64	0.67
$\log_{10}$ leptin (ng/mL) and $\log_{10}$ leptin <sup>2</sup>	0.57	0.54	0.59	0.54	0.56	0.52
$\log_{10}$ leptin (ng/mL), $\log_{10}$ leptin <sup>2</sup> , BMI ( $\text{kg}/\text{m}^2$ ), and BMI <sup>2</sup>	0.68	0.65	0.70	0.71	0.71	0.72

<sup>1</sup> From linear regression analysis adjusted for race (models for all men and all women), age, and examination site. Quadratic terms were included in all models of BMI alone; in models of leptin alone for all men, all women, black men, and black women; for  $\log_{10}$  leptin in the combined model for black men; and for BMI in combined models for all women, white women, and black women. All  $P$  for BMI and  $\log_{10}$  leptin were  $< 0.05$ . A test for interaction on total percentage fat was significant for sex, race, and  $\log_{10}$  leptin ( $P = 0.002$ ) and borderline for sex, race, and BMI ( $P = 0.090$ ). Two-way interactions were nonsignificant for sex and BMI ( $P = 0.39$ ) and for sex and race ( $P = 0.56$ ) and significant for race and BMI ( $P = 0.014$ ).

**TABLE 3**

Coefficients for best-fit linear regression models for percentage fat using BMI, log<sub>10</sub> leptin, or both and after control for race, age, and examination site<sup>1</sup>

	Men (n = 1417)			Women (n = 1494)		
	BMI alone	Leptin alone	BMI and leptin	BMI alone	Leptin alone	BMI and leptin
Intercept	-15.1	20.0	3.5	-5.8	26.5	3.6
Age (y)	0.13	0.046	0.11	0.040	-0.0044	0.053
Race <sup>2</sup>	-2.0	-1.8	-1.9	-2.2	-1.1	-2.2
Site <sup>3</sup>	0.16	0.98	0.62	0.28	2.0	0.92
BMI (kg/m <sup>2</sup> )	1.8	—	0.55	2.4	—	1.4
BMI <sup>2</sup>	-0.016	—	—	-0.026	—	-0.013
Log <sub>10</sub> leptin (ng/mL)	—	7.9	5.9	—	8.3	5.7
Log <sub>10</sub> leptin <sup>2</sup>	—	1.3	—	—	1.8	—

<sup>1</sup> All variables were significant (*P* < 0.05) except age in all models for women and in the model for leptin alone in men and except site in the models for BMI alone in men and in women.

<sup>2</sup> 1 for white and 2 for black.

<sup>3</sup> 1 for Memphis and 2 for Pittsburgh.

reciprocal of BMI, for BMI did not improve the predictive ability (data not shown). Furthermore, the best fitted equations for estimating percentage fat included ethnicity, age, and study site, which suggests that they could not be generalized to other populations. Whether leptin and BMI independently predict percentage fat in younger adults and among other ethnic groups requires further study.

**TABLE 4**

Correct quintile categorization of percentage fat among men and women by BMI, log<sub>10</sub> leptin, and BMI and log<sub>10</sub> leptin regression models<sup>1</sup>

Percentage fat	BMI	Log <sub>10</sub> leptin	BMI and log <sub>10</sub> leptin
<b>Men (n = 1417)</b>			
<25.1 (%)	42	50	57
25.1 to <28.0 (%)	35	43	46
28.0 to <30.4 (%)	38	46	47
30.4 to <33.3 (%)	36	47	42
≥33.3 (%)	46	36	52
Total [n (%)]	558 (39)	630 (44)	693 (49)
<b>Women (n = 1494)</b>			
<35.8 (%)	60	47	64
35.8 to <39.4 (%)	44	40	47
39.4 to <42.3 (%)	39	43	41
42.3 to <45.3 (%)	33	37	37
≥45.3 (%)	56	36	58
Total [n (%)]	693 (46)	610 (41)	740 (50)

<sup>1</sup> Models were adjusted for race, age, and examination site. The effects of sex and dual-energy X-ray absorptiometry (DXA)-measured percentage fat quintile on the ability of the models to correctly categorize the participants were evaluated by using logistic regression analysis with “correctly categorized (yes or no)” as the dependent variable and sex, DXA-measured percentage fat quintile, and the interaction between sex and percentage fat quintile as independent variables. The interaction between sex and percentage fat quintile was significant for “correctly categorized by BMI” (*P* = 0.042), but not for “correctly categorized by log<sub>10</sub> leptin” (*P* = 0.99) or for “correctly categorized by BMI and log<sub>10</sub> leptin” (*P* = 0.56). Correct categorization by BMI was associated with DXA-measured percentage fat quintile in the women (*P* = 0.044), but not in the men (*P* = 0.37). Correct categorization by log<sub>10</sub> leptin was associated with both sex (*P* = 0.047) and DXA-measured percentage fat quintile (*P* < 0.001). Correct categorization by BMI and log<sub>10</sub> leptin was associated with DXA-measured percentage fat quintile (*P* = 0.005), but not sex (*P* = 0.74).

A better estimate of body fat can be obtained with DXA than with BMI or leptin, but DXA is more complex, time consuming, and expensive than is measuring BMI or leptin. DXA has its own limitations as a measure of fat. The estimation of fat depends on the model of the machine used and even varies from machine to machine, although differences between machines tend to be systematic across the range of body weights. Further, very obese persons cannot undergo DXA measurements because of weight limitations for the equipment. The correlation with other criterion measures of body fat is excellent, although the model used in the current study may underestimate total fat (24).

Because obesity is defined as an excess of body fat and is increasingly common in nearly all age groups and in all populations, it is critical that more accurate measures of body fat be developed that can be applied to large populations. With the ever-increasing public health significance of obesity, it is perhaps surprising that few studies have examined measures other than height and weight and a limited number of other anthropometric measures for this purpose. Bioelectrical impedance is a simple, fast, inexpensive, and reproducible method to use in epidemiologic studies; however, its use is limited by the inability to generalize the prediction equations (25). Leptin may yet prove to be one element in such a search for body fat measures for use in population studies, but the results of the current analysis indicate that it performs better when combined with BMI. Longitudinal studies of body composition changes and health outcomes will demonstrate whether leptin has additional clinical utility.

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CER designed and conducted the data analysis and wrote the manuscript. TBH designed and collected data for the Health ABC study, designed the data analysis, edited the manuscript, and gave advice and consultation. JD designed the data analysis and edited the manuscript. BHG designed and collected data for the Health ABC study and gave advice and consultation for the study. AMK edited the manuscript and gave advice and consultation for the study. SBK designed and collected data for the Health ABC study and gave advice and consultation for the study. EMS designed and collected data for the Health ABC study, edited the manuscript, and gave advice and consultation for the study. FAT designed and collected data for the Health ABC study, edited the manuscript, and provided advice and consultation for the study. JEE designed and collected data for the Health ABC study, analyzed



the data, edited the manuscript, and provided advice and consultation for the study. None of the authors have a conflict of interest.

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