# Calcium Intake Is Associated with Adiposity in Black and White Men and White Women of the HERITAGE Family Study<sup>1,2</sup>

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IN; <sup>1</sup>Department of Kinesiology, Indiana University, logy, Texas A&M University, College Station, TX; and ool of Medicine and Departments of Genetics and he, St. Louis, MO e regulation of body weight. Increased Ca<sup>2+</sup> intake has y measures in cross-sectional studies. We examined the FFQ, and overall and abdominal adiposity in Black and 3MI, the percentage of body fat (%FAT), the sum of 8 minal fat (TAF), abdominal visceral (AVF) and abdominal easured in 362 men (109 Blacks, 253 Whites) and 462 into tertiles of energy-adjusted Ca<sup>2+</sup> intake. Adiposity ulso regressed against the energy-adjusted Ca<sup>2+</sup> intake s appeared in Black men and White women. Black men e low Ca<sup>2+</sup> intake group: BMI 23.4 ± 0.9 vs. 26.7 ± 1.1 : 0.05. In White women, regression analyses showed 3MI (P = 0.02), %FAT (P = 0.001), TAF (P = 0.006), AVF of White men in the highest Ca<sup>2+</sup> intake group was 0.04). No significant associations were found in Black liposity, particularly in men and White women. J. Nutr. *ition* • *adiposity* • *abdominal fat* amination Survey (NHANES I)<sup>4</sup> found a significant inverse association between Ca<sup>2+</sup> intake and body weight (2). More precent cross-sectional studies confirmed this early finding, with increased Ca<sup>2+</sup> intake being associated with lower BMI and generation. ABSTRACT Calcium (Ca<sup>2+</sup>) intake may play a role in the regulation of body weight. Increased Ca<sup>2+</sup> intake has been associated with lower body weight, BMI, and adiposity measures in cross-sectional studies. We examined the association between Ca<sup>2+</sup> intake, derived from the Willett FFQ, and overall and abdominal adiposity in Black and White men and women of the HERITAGE Family Study. BMI, the percentage of body fat (%FAT), the sum of 8 skinfold thicknesses, computerized tomography total abdominal fat (TAF), abdominal visceral (AVF) and abdominal subcutaneous (ASF) fat, and waist circumference were measured in 362 men (109 Blacks, 253 Whites) and 462 women (201 Blacks, 261 Whites). Subjects were divided into tertiles of energy-adjusted Ca2+ intake. Adiposity measures across tertiles were compared by ANOVA and also regressed against the energy-adjusted Ca<sup>2+</sup> intake to test for a linear trend. The strongest inverse associations appeared in Black men and White women. Black men in the high Ca<sup>2+</sup> intake group were leaner than those in the low Ca<sup>2+</sup> intake group: BMI 23.4  $\pm$  0.9 vs. 26.7  $\pm$  1.1 kg/m<sup>2</sup> (P = 0.01); for all other adiposity measures, P < 0.05. In White women, regression analyses showed significant inverse associations between Ca<sup>2+</sup> intake and BMI (P = 0.02), %FAT (P = 0.001), TAF (P = 0.006), AVF (P = 0.03), and ASF (P = 0.01). The percentage of fat of White men in the highest Ca<sup>2+</sup> intake group was significantly lower than in the lowest  $Ca^{2+}$  group (P = 0.04). No significant associations were found in Black women. Low  $Ca^{2+}$  intake may be associated with higher adiposity, particularly in men and White women. 134: 1772-1778, 2004.

## KEY WORDS: • dietary calcium intake • body composition • adiposity • abdominal fat HERITAGE Family Study

Most research on the effects of diet on weight control has focused on the optimal combination of macronutrients, whereas the role of micronutrients has gained much less attention. An emerging body of evidence suggests that calcium  $(Ca^{2+})$  intake may play an important role in the regulation of body weight and adiposity (1). More than 20 years ago, a study of the relation between blood pressure and nutrient intake based on data of the 1st National Health and Nutrition Ex-

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recent cross-sectional studies confirmed this early finding, with  $\frac{1}{2}$  increased Ca<sup>2+</sup> intake being associated with lower BMI and  $\frac{1}{2}$ body weight (1,3-6), less total fat (4,6-9) and abdominal fat  $\boxed{9}$ (4,6), a lower prevalence of obesity (5), higher fat oxidation,  $\frac{1}{2}$ and a lower respiratory quotient (10). For example, in young women, a 1 mg/g increase in the Ca<sup>2+</sup>-to-protein ratio was  $\frac{6}{2}$ associated with a 0.186 kg/m<sup>2</sup> decrease in BMI, which trans-  $\frac{1}{2}$ lates into a predicted 0.82-kg body weight reduction for every  $\stackrel{N}{\sim}$  100 mg increase in Ca<sup>2+</sup> intake (3). In middle-aged women, weight gain was estimated to be 0.038 kg/y less for every 1 mg/g increase in the  $Ca^{2+}$ -to-protein ratio (3). The contribution of  $Ca^{2+}$  intake to the variance in body weight was estimated to be 3% (3). Others reported a contribution of

<sup>&</sup>lt;sup>4</sup> Abbreviations used: AI, adequate intake; ANCOVA, analysis of covariance; ASF, abdominal subcutaneous fat; AVF, abdominal visceral fat; %FAT, percentage of body fat; FFM, fat-free mass; NHANES, National Health and Nutrition Examination Survey; SF8, sum of 8 skinfold thicknesses; TAF, total abdominal fat; WC, waist circumference.

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 $Ca^{2+}$  intake to the variance in fat oxidation of as much as 10% (10). During energy restriction, increasing  $Ca^{2+}$  intake markedly reduced body weight and fatness compared with a low  $Ca^{2+}$  intake (3,6,11).

Studies in mice support the association between  $Ca^{2+}$  intake and body composition. In a study with transgenic mice overexpressing the agouti gene in adipocytes, a low- $Ca^{2+}$  diet resulted in significantly more weight gain compared with calcium-supplemented diets (7). A high- $Ca^{2+}$  diet in energy-restricted mice resulted in a significantly greater reduction in body weight and fat mass compared with a low- $Ca^{2+}$  diet (12).

Until recently, little was known about the mechanisms by which  $Ca^{2+}$  intake regulates body weight and adiposity. On the basis of the mouse studies, it was hypothesized that low  $Ca^{2+}$  intake leads to increased intracellular concentrations of  $Ca^{2+}$  ( $[Ca^{2+}]_i$ ) due to an increase in circulating calciumregulating hormones. Increased  $[Ca^{2+}]_i$  reduced lipolysis and enhanced lipogenesis in adipocytes (7). Another potential mechanism was based on findings in rats and stipulated that high  $Ca^{2+}$  intake leads to the formation of indigestible calcium soaps in the gastrointestinal tract, which in turn reduces the absorption of dietary energy and substantially increases fecal loss of fatty acids (13). Two randomized trials in humans found that  $Ca^{2+}$  supplementation increased the percentage of fecal fatty acid excretion (14,15).

To date, research on the  $Ca^{2+}$  intake-adiposity relation in humans has concentrated on BMI and overall adiposity, mainly in White women (3,9,16,17). In the present study, we examined the relation between total  $Ca^{2+}$  intake and body composition, including overall and abdominal adiposity, in Black and White men and women of the HERITAGE Family Study.

#### MATERIALS AND METHODS

**Subjects.** This study was based on the baseline data from 362 men (109 Blacks and 253 Whites) and 462 women (201 Blacks and 261 Whites) from the HERITAGE Family Study. Race classification was based on self-report, i.e., whether the subjects considered themselves as Black or White.

The study design and inclusion criteria of the HERITAGE Family Study were described previously (18). Briefly, eligible individuals were required to be between the ages of 17 and 65 y, healthy but sedentary (no regular strenuous physical activity over the previous 6 mo), with BMI < 40 kg/m<sup>2</sup> and systolic/diastolic blood pressures  $\leq$  159/99 mm Hg. A few participants with BMIs > 40 kg/m<sup>2</sup> (n = 6), who were considered by the supervising physician to be healthy and able to complete the required exercise training program, were included. Further, individuals with confirmed or possible coronary heart disease, chronic or recurrent respiratory problems, and uncontrolled endocrine and metabolic disorders (including diabetes, hypoglycemia, and the use of antihypertensive or lipid-lowering drugs) were excluded. The study protocol was approved by each of the Institutional Review Boards of the HERITAGE Family Study research consortium. Written informed consent was obtained from all participants. Although the HERITAGE Family Study involved a 20-wk aerobic exercise training program, only data from the baseline in the sedentary state are considered here.

Anthropometric and adiposity measurements. A series of anthropometric measurements were obtained. Standing height and body mass were measured to the nearest 0.1 cm and 0.1 kg using a stadiometer and a balance beam scale, respectively. BMI (kg/m<sup>2</sup>) was calculated as body weight divided by height squared. Skinfold thickness was measured at biceps, triceps, subscapular, suprailiac, abdominal, midaxillary, medial calf, and thigh skinfold sites to 0.1 mm accuracy using a Harpenden skinfold caliper (Quinton Instruments, #03496–001). The 8 skinfold thicknesses were summed (SF8) to evaluate the overall degree of subcutaneous fat (19). Waist circumference (WC) was measured to 0.1 cm accuracy using a fiberglass anthropometric tape (Grafco Fiberglass Tape, Model 17–1340-2). All measurements were taken in duplicate. A third measurement was taken if the first 2 measurements differed by more than a predetermined amount, i.e., >0.5 cm for height, >200 g for body mass, >1.0 mm for skinfolds, and >1.0 cm for circumference. When it was necessary to take a third measurement, the 2 closest measurements were averaged. When the third measurement fell equally between the first 2, all 3 were averaged. The measurements were taken in accordance with procedures recommended by Lohman et al. (20) as defined elsewhere (21).

Underwater weighing was performed to determine total body density, which was converted to percentage body fat (%FAT) using the equation of Siri (22) for White men, Lohman (23) for White women, Schutte et al. (24) for Black men, and Ortiz et al. (25) for Black women. A correction was made for residual lung volume by the oxygen-dilution method (26) at 3 clinical centers, and the helium-dilution technique (27) at the 4th clinical center.

Abdominal fat (total, visceral and subcutaneous) was measured by computed tomography scans (28). Subjects were examined in the supine position with their arms stretched above their heads. The abdominal scan was obtained at the level of the fourth and fifth lumbar vertebrae. The attenuation interval used in the quantification of the areas of adipose tissue was between -190 and -30 Hounsfield units. The abdominal visceral fat (AVF) area was defined by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal subcutaneous fat (ASF) area was calculated by subtracting the amount of visceral fat from the total abdominal fat area (TAF).

All measurement protocols were standardized and carefully monitored using an extensive quality assurance and quality control program (29). The reproducibility of adiposity measures was high, with intraclass correlations for repeated measures  $\geq 0.95$  (21).

Dietary record. Daily energy, macronutrient, and micronutrient intakes were collected using the Willett FFQ (30). The questionnaire provided data on a subject's usual eating habits, dietary supplements, food items in 5 major food groups, food preparation, seasonings, and favorite foods. The questionnaire also included quantitative data on intake of nutrients and related substances, such as caffeine and alcohol over the past year. The questionnaire was self-administered by the subjects and reviewed with the subject by an interviewer for completeness. The scoring of the questionnaires and calculation of nutrient intake were done at Channing Laboratory at Harvard University, where the questionnaire was developed and validated. A study on the reproducibility and validity of the FFQ was documented elsewhere (30). In brief, the intraclass correlations between 2 measurements at an interval of 1 y for nutrient intake estimated by the  $\overline{P}$ Willett questionnaire were similar to those computed from a 7-d diet grecord. Correlation coefficients between the mean energy-adjusted g intakes from 1-wk diet records and those from the questionnaire completed after the diet records ranged from 0.36 to 0.75. It should be noted that the study was based on women only (34-59 y), and, although micronutrient intake (vitamin A, B, and C) was included, no direct validation results on Ca<sup>2+</sup> intake in particular were reported.

**Health habits.** Subjects completed a health habit questionnaire, including questions on smoking, alcohol consumption, and educational status, the ARIC-Baecke Physical Activity Questionnaire (31) and a menstrual cycle history, including questions on the use of oral contraceptives, menopausal status, and hormone replacement therapy.

**Statistical analyses.** All analyses were performed with the SAS Statistical Software (SAS Institute, Version 8.2). Data were analyzed separately by sex and race. Ca<sup>2+</sup> intake was expressed relative to total energy consumed (mg/1000 kcal) (1 kcal = 4.186 kJ) to minimize the effect of total food intake. For analyses, subjects were divided into tertiles (low, intermediate, high) according to the energy-adjusted Ca<sup>2+</sup> intake.

Adiposity among the 3 groups was compared by one-way analyses of covariance, controlling for age, generation, and height. Other covariates (physical activity, educational status, smoking, macronutrient intake, menstrual and hormonal status) that could potentially affect adiposity were included in the analyses to test their effect on the Ca<sup>2+</sup> intake-adiposity relation. Possible interactions between

 $Ca^{2+}$  intake and covariates were tested by including main effects and interaction terms in the same model. Furthermore, measures of adiposity were regressed against the energy-adjusted  $Ca^{2+}$  intake to test for a linear trend, while controlling for age, generation, and height.

Because the study was designed as a family study, subjects were related within families. However, because data for men and women were analyzed separately within race, the effect on the analysis of this relatedness among subjects was less than it would have been if whole nuclear families were considered. Nonetheless, because 71% of families had more than 1 family member even after classification by sex and race, both the ANOVAs and the regression analyses were performed using the SAS MIXED model procedure. A mixed model is a generalization of ANOVA and regression that estimates group differences and regression coefficients while accounting for multiple levels of analysis. In this study, there were 2 levels, families and subjects within family. The method assumed that the same degree of dependency existed among all subjects within a family. SE of the differences and regression coefficients were computed using the asymptotically consistent (i.e., unbiased in large samples) sandwich estimator (32,33).

Finally, the prevalence of overweight and obesity (BMI  $\geq 25$  kg/m<sup>2</sup>) and of obesity only (BMI  $\geq 30$  kg/m<sup>2</sup>) among the 3 tertile groups was compared by a  $\chi^2$ -likelihood ratio test. The Cochran-Armitage test was performed to test for a trend across the 3 groups. The  $\alpha$  level used to identify significant differences was 0.05.

## RESULTS

White men were slightly taller and had significantly more AVF than Black men. Black women had a significantly higher BMI, and more total (%FAT, SF8) and abdominal fat (TAF, ASF, WC) than White women (Table 1).

The total and energy-adjusted  $Ca^{2+}$  intake was significantly lower in Blacks compared with Whites, and men had a significantly lower energy-adjusted  $Ca^{2+}$  intake than women. Among Whites, 46% reached the adequate intake (AI) (1000 mg/d) (34), whereas only 20–26% did so among Blacks.

The strongest inverse associations between Ca<sup>2+</sup> intake

and body composition and abdominal adiposity were found in Black men and White women (Table 2 and Table 3).

Black men in the high  $Ca^{2+}$  intake group had significantly lower values for all adiposity measures compared with those in the low  $Ca^{2+}$  intake group. The results of the regression analyses showed significant ( $P \leq 0.01$ ) inverse associations between the energy-adjusted  $Ca^{2+}$  intake and adiposity. For example, the strongest inverse association was observed for BMI (P = 0.001), i.e., for every 100 mg/1000 kcal increase in  $Ca^{2+}$  intake, BMI decreased by 1.03 kg/m<sup>2</sup>. The fat-free mass (FFM) tended (P = 0.05) to be lower in the high  $Ca^{2+}$  intake group. In White men, a significant inverse association was found only for %FAT, with men in the high  $Ca^{2+}$  intake group having on average 3% units less %FAT than men in the low  $Ca^{2+}$  intake group.

low  $Ca^{2+}$  intake group. In White women, the energy-adjusted  $Ca^{2+}$  intake was negatively correlated ( $P \le 0.03$ ) with BMI, %FAT, TAF, AVF, and ASF. In contrast, Black women in the high  $Ca^{2+}$ intake group tended to have a higher BMI (P = 0.05) and WC (P = 0.1) and had significantly more FFM (P = 0.02) compared with women in the low  $Ca^{2+}$  intake group. No associations were found between other measures of adiposity and  $Ca^{2+}$  intake.

When comparing the slope of the regression equations, we found the association between energy-adjusted Ca<sup>2+</sup> intake and body composition to be significantly different (0.002 < P < 0.05) between Blacks and Whites for all measures, except for FFM (men and women) and SF8 (women). In Blacks, the associations were significantly different (0.004 < P < 0.02) between men and women, with the exception of FFM and SF8. In Whites, significantly different associations for men and women were found for TAF (P = 0.03) and ASF (P = 0.04).

Total energy intake and the intake of other macronutrients, both in absolute weight or in energy %, did not differ across the 3  $Ca^{2+}$  intake groups, with the exception of a higher

TABLE 1

Descriptive characteristics of subjects1

		Men			Women		Carralit	£	<b>D</b>
			Race			Race	Sex dif	ference	$\begin{array}{c} Race \times \\ Sex \end{array}$
	Blacks	White	difference P	Blacks	White	difference P	Blacks <i>P</i>	Whites <i>P</i>	interaction P
п	109	253		201	261				
Age, y	$33.5 \pm 1.2$	$36.2 \pm 0.9$	0.08	$33.0 \pm 0.8$	$35.0 \pm 0.9$	0.10	0.72	0.35	0.72
Body weight, kg	$84.9 \pm 1.8$	$84.2 \pm 1.0$	0.72	$74.8 \pm 1.3$	$67.3 \pm 0.9$	< 0.001	< 0.001	< 0.001	0.005
Height, <i>cm</i>	$175.9 \pm 0.7$	$177.7 \pm 0.4$	0.01	$162.4 \pm 0.5$	$163.7 \pm 0.4$	0.85	< 0.001	< 0.001	0.57
BMI, <i>kg/m</i> 2	$27.4 \pm 0.5$	$26.6 \pm 0.3$	0.14	$28.4 \pm 0.5$	$25.0 \pm 0.3$	< 0.001	0.19	< 0.001	0.002
%FAT	$23.3 \pm 0.8$	$22.7 \pm 0.6$	0.58	$36.0 \pm 0.7$	$30.1 \pm 0.6$	< 0.001	< 0.001	< 0.001	<0.001
SF8, <i>mm</i>	$121.7 \pm 6.3$	$129.5 \pm 3.5$	0.26	179.1 ± 5.4	$164.5 \pm 3.6$	0.02	< 0.001	< 0.001	0.02
FFM, <i>kg</i>	$64.1 \pm 0.9$	$63.3 \pm 0.5$	0.41	$46.4 \pm 0.5$	$45.5 \pm 0.3$	0.12	< 0.001	< 0.001	0.91
TAF, <i>cm</i> <sup>2</sup>	314 ± 21	337 ± 12	0.35	423 ± 15	$370 \pm 12$	0.005	< 0.001	0.04	0.001
AVF, cm <sup>2</sup>	$79 \pm 5.6$	$108 \pm 4.1$	<0.001	$70 \pm 3.0$	$77 \pm 3.3$	0.12	0.17	< 0.001	0.007
ASF, <i>cm</i> <sup>2</sup>	$236 \pm 16$	$228 \pm 9$	0.69	353 ± 13	$293 \pm 9$	<0.001	<0.001	< 0.001	0.02
WC, cm	$92.6 \pm 1.6$	$94.5 \pm 0.9$	0.29	90.2 ± 1.1	$86.2 \pm 0.9$	0.005	0.22	< 0.001	0.008
Total Ca intake, <i>mg/d</i>	766 ± 49	$1098 \pm 38$	<0.001	825 ± 42	$1060 \pm 34$	<0.001	0.37	0.45	0.25
Ca/energy intake, <sup>2</sup> mg/1000									
kcal	327 ± 11	454 ± 12	<0.001	$367 \pm 10$	522 ± 14	<0.001	0.01	< 0.001	0.33
Reaching DRI <sup>3</sup> (1000 mg/d),									
%	20.2	46.3	<0.001	26.4	46.0	< 0.001	0.22	0.95	0.29
Taking Ca supplements, %	12.8	9.5	0.3	12.9	24.1	0.003	0.98	< 0.001	0.01

<sup>1</sup> Values are means  $\pm$  SEM.

 $^{2}$  1 kcal = 4.186 kJ.

<sup>3</sup> DRI, dietary reference intake.

Low Intermediate Higher Higher and the second set the second set of the set of the second set of the		Trend change per 100 mg/ per 1000 kcal increase 0.01 -1.03 0.029 -1.36 0.048 -9.5 0.18 -1.04 0.004 -38.1 0.003 -28.1 0.003 -28.1 0.003 -3.0 1.16 0.003 -3.0 1.16 0.003 tertiles of ener	ange mg/ ccal 36 0.001 36 0.008 5 0.013 5 0.013 5 0.013 5 0.002 5 0.0020 5 0.002000000000000000000000000000000000	Lc 8 275 649 649 8 275 649 3 133 133 133 133 114 2 259 2 96.9 2 96.9 2 96.9 2 96.9 2 96.9 2 96.9 2 96.9 2 2 10.0 2	Low 84 5 + 5 5 + 5 9 + 28 2 + 112 4 + 10.9 3 + 1.15 9 + 1.1 6 + 11.1 6 + 11.1 6 + 11.1 6 + 11.1 6 + 11.1 6 + 11.1 7 9 + 25 9 + 2.5 9 + 2.5 9 + 2.5 1 for age, ger	Trend change       Trend change       Low       Intermediate $per 100 \text{ mad}$ $1000 \text{ kcal}$ $D_{000} \text{ kcal}$ $D_{000} \text{ kcal}$ $B_{1000} \text{ kcal}$ $P$ $per 100 \text{ mad}$ $D_{000} \text{ kcal}$ $P$ $D_{000} \text{ kcal}$ $B_{11} \text{ sc}$ $B_{100} \text{ conse}$ $B_{100} \text{ conse}$ $B_{100} \text{ conse}$ $B_{11} \text{ sc}$ $B_{11} \text{ sc}$ $B_{110} \text{ conse}$ $D_{001} \text{ conse}$ $D_{110} \text{ conse}$ $B_{11} \text{ sc}$ $B_{11} \text{ sc}$ $E 236$ $0.90$ $-1.03$ $0.001 \text{ cons}$ $27.4 \pm 0.9$ $26.5 \pm 0.7$ $226.5 \pm 0.7$ $E 1.3$ $0.0229 \text{ cond}$ $-1.04$ $0.003$ $133 \pm 7.9$ $132 \pm 2.8$ $26.5 \pm 0.7$	High B3 $674 \pm 18$ $674 \pm 18$ $1637 \pm 62$ $22410 \pm 108$ $26.9 \pm 0.9$ $22.9 \pm 1.6$ $131 \pm 10.2$ $63.7 \pm 1.1$ $353 \pm 34$ $108 \pm 9.8$ $245 \pm 27$ $94.9 \pm 2.6$ ght.	ANOVA P 0.041 0.048 0.48 0.46 0.46	Trend change per 100 mg/ 1000 kcal increase 1.3 0.0 1.9 0.0	Р 0.78 0.69 0.69 0.61 0.61 0.61
$36$ $36$ $36$ $36$ $36$ $31$ $ccal$ $214 \pm 6$ $305 \pm 3$ $458 \pm 3$ $458 \pm 3$ $ntake, mg/d$ $517 \pm 40$ $748 \pm 69$ $1025 \pm 3$ $458 \pm 3$ $ntake, mg/d$ $517 \pm 40$ $748 \pm 69$ $1025 \pm 3$ $458 \pm 1$ $ntake, 2236 \pm 224$ $2319 \pm 236$ $2208 \pm 34 \pm 1$ $22.34 \pm 37$ $22.34 \pm 37$ $22.7 \pm 2.1$ $20.1 \pm 1.6$ $103 \pm 12.3$ $65.1 \pm 1.7$ $23.4 \pm 37$ $22.85 \pm 1.2$ $62.1 \pm 4.1.7$ $243 \pm 4.1$ $179 \pm 35.7$ $32.4 \pm 4.7$ $32.4 \pm 4.7$ $24.3 \pm 4.1$ $173 \pm 36.9$ $127 \pm 35.7$ $32.3 \pm 4.1.7$ $59.7 \pm 45.7$ $32.4 \pm 4.7$ $24.3 \pm 4.1$ $173 \pm 36.9$ $32.7 \pm 34.7$ $127 \pm 35.7$ $32.3 \pm 4.2.7$ $59.7 \pm 36.7$ $32.7 \pm 34.7$ $127 \pm 35.7$ $32.6 \pm 3.2.6$ $32.7 \pm 4.5$ $32.7 \pm 34.7$ $127 \pm 35.7$ $32.6 \pm 3.2.6$ $32.7 \pm 4.5$ $32.7 \pm 34.7$ $127 \pm 35.7$ $32.6 \pm 3.2.6$ $32.7 \pm 4.5$ $32.7 \pm 4.5$ $32.7 \pm 4.5$ $32.7 \pm 4.5$ $45.6 \pm 4.5$ <		90 -1.5 -01 -1.6 -029 -1.5 -029 -1.6 -018 -1.6 -012 -11.6 -012 -11.6 -012 -11.6 -012 -11.6 -012 -11.6 -003 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	03 0.001 36 0.001 56 0.005 56 0.005 56 0.002 56 0.002 58 11 0.002 51 51 61 61 61 61 61 61 61 61 61 61 61 61 61	275 645 645 8 25.5 3 135 3 11/ 8 255 2 366 3 11/ 8 255 2 96.5 adjusted	84 5 ± 5 5 ± 5 2 ± 112 4 ± 0.9 3 ± 1.5 4 ± 1.1 4 ± 1.1 4 ± 1.1 6 ± 8.6 9 ± 2.4 9 ± 2.4 1 for age, ger	85 413 ± 5 1008 ± 50 2362 ± 111 24.4 ± 1.4 135 ± 2.1 350 ± 29 107 ± 7.9 244 ± 22 95.3 ± 2.1 95.3 ± 2.1	$\begin{array}{c} 83\\ 674\pm18\\ 1637\pm62\\ 2410\pm108\\ 26.9\pm0.9\\ 226.9\pm1.6\\ 131\pm1.6\\ 131\pm1.6\\ 131\pm1.6\\ 131\pm1.6\\ 353\pm34\\ 108\pm9.8\\ 245\pm27\\ 94.9\pm2.6\\ 94.9\pm2.6\end{array}$	0.73 0.96 0.96 0.48 0.48 0.48 0.46		0.78 0.10 0.69 0.69 0.61 0.61
/ intake, kcal $214 \pm 6$ $305 \pm 3$ $458 \pm 401$ intake, $mg/d$ $517 \pm 40$ $748 \pm 69$ $1025 \pm 458$ intake, $mg/d$ $517 \pm 40$ $748 \pm 69$ $1025 \pm 458$ intake, $22326 \pm 224$ $2319 \pm 236$ $2208 \pm 428$ $225.7 \pm 2.1$ $20.1 \pm 1.6$ $18 \pm 103$ $22.85 \pm 1.2$ $62.1 \pm 1.7$ $23.4 \pm 1$ $32.4 \pm 13.6$ $66 \pm 10.5$ $24.3 \pm 41$ $179 \pm 45$ $32.7 \pm 237.4 \pm 38$ $175 \pm 34$ $117$ $475 \pm 45$ $33.7.4 \pm 38$ $37.5 \pm 3.0$ $82 \pm 45$ are means $\pm$ SEM. = 4.186 kJ. d %FAT were adjusted for age and generation. All other d %FAT were adjusted for age and generation. All other d %FAT were adjusted for age and generation. All other $Body composition, Ca^{2+}$ intake and total en $Body composition, Ca^{2+}$ intake and total en		.90 .01 .029 .048 .048 .018 .012 .012 .012 .012 .012 .012 .012 .012	03 0.001 36 0.001 04 0.05 5 0.015 5 0.002 5 0.002 5 0.002 0 0.002 0000000000	275 649 649 8 25.5 8 25.5 6 6 6 6 7.4 8 255 8 255 8 255 8 255 2 96.5 adjusted	5 + 5 9 + 28 2 + 112 2 + 112 4 + 0.9 3 + 1.5 3 + 7.9 4 + 1.1 4 + 1.1 4 + 1.1 6 + 86 6 + 86 7 + 9 2 + 2.4 1 for age, ger	$\begin{array}{c} 413 \pm 5 \\ 1008 \pm 50 \\ 2362 \pm 111 \\ 26.5 \pm 0.7 \\ 24.4 \pm 1.4 \\ 132 \pm 8.8 \\ 132 \pm 8.8 \\ 132 \pm 9.10 \\ 350 \pm 1.0 \\ 350 \pm 1.0 \\ 350 \pm 2.1 \\ 95.3 \pm 2.1 \\ 95.3 \pm 2.1 \\ 95.3 \pm 2.1 \\ 350 + 22 \\ 95.3 \pm 2.1 \\ 350 + 22 \\ 350 +$		0.73 0.96 0.96 0.76 0.76 0.87 0.87 0.87		0.78 0.46 0.69 0.69 0.78 0.61 0.61
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108.8 ± 13.9       103 ± 12.3       76.9 $82.85 \pm 1.2$ $62.1 \pm 1.7$ 59.7 ± $324 \pm 47$ $62.1 \pm 1.7$ 59.7 ± $324 \pm 47$ $62.1 \pm 1.7$ 59.7 ± $84 \pm 13.6$ $66 \pm 10.5$ $45 \pm 177$ $84 \pm 3.3$ $87.5 \pm 3.4$ $127 \pm 32$ $87.5 \pm 3.4$ $127 \pm 32$ $82 \pm 3.4$ $93.14 \pm 3.3$ $87.5 \pm 3.0$ $82 \pm 127 \pm 34$ $87.5 \pm 3.0$ $82 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $82 \pm 3.0$ $87.5 \pm 3.0$ $87 \pm 3.0$ $82 \pm 3.0$ $87.6 \pm 0.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $87.6 \pm 0.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $87.6 \pm 0.0$ $87.5 \pm 3.0$ $82 \pm 3.0$ $87.6 \pm 0.0$ $87.6 \pm 0.0$ $81.6 \pm 0.0$ $80.0$ $87.6 \pm 0.0$ $81.6 \pm 0.0$ $80.0$ $80.0$ <td></td> <td>048 -9.2 18 -1.0 004 -39.0 009 -28.1 0003 -3.0 0003 -3.0 7 body compo</td> <td>500013 04005 00000000000000000000000000000000</td> <td>adjusted</td> <td>3 + 7.9 4 + 1.1 4 + 1.1 6 + 8.6 2 + 25 9 + 2.4 2 + 25 9 + 2.4 1 for age, ger</td> <td>132 ± 8.8 62.9 ± 1.0 350 ± 29 107 ± 7.9 95.3 ± 2.1 95.3 ± 2.1</td> <td>131 ± 10.2 63.7 ± 1.1 353 ± 34 108 ± 9.8 245 ± 27 94.9 ± 2.6 94.9 ± 2.6</td> <td>0.96 0.48 0.76 0.87 0.87 0.87</td> <td></td> <td>0.46 0.99 0.69 0.61 0.97</td>		048 -9.2 18 -1.0 004 -39.0 009 -28.1 0003 -3.0 0003 -3.0 7 body compo	500013 04005 00000000000000000000000000000000	adjusted	3 + 7.9 4 + 1.1 4 + 1.1 6 + 8.6 2 + 25 9 + 2.4 2 + 25 9 + 2.4 1 for age, ger	132 ± 8.8 62.9 ± 1.0 350 ± 29 107 ± 7.9 95.3 ± 2.1 95.3 ± 2.1	131 ± 10.2 63.7 ± 1.1 353 ± 34 108 ± 9.8 245 ± 27 94.9 ± 2.6 94.9 ± 2.6	0.96 0.48 0.76 0.87 0.87 0.87		0.46 0.99 0.69 0.61 0.97
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93.14 ± 3.3       87.5 ± 3.0       82 ± 3.3         are means ± SEM.       = 4.186 kJ.       82 ± 4.186 kJ.         a %FAT were adjusted for age and generation. All other       Block         Body composition, Ca <sup>2+</sup> intake and total en       Black		of body compo <b>TAB</b>	0 0.00 bition were <b>3LE 3</b> of energy-a	2 96.6 adjusted <i>adjusted</i>	<u>∃</u> ± 2.4 for age, ger I Ca <sup>2+</sup> intal	95.3 ± 2.1 neration, and hei	94.9 ± 2.6 ght.	0.46		0.97
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Low Intermediate							Whites			
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67 67	66				86	87	86			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	536 ± 15 1171 ± 76			ςο	308 ± 6 642 ± 26	$479 \pm 5$ 1043 $\pm 53$	$779 \pm 20$ 1494 $\pm 54$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	+  +			20	+1 +1	+1 +1	+  +	0.19 0.30		.019
33.76 ± 2.0 35.7 ± 2.1 36.1 166 ± 9.0 164 ± 10.8 164	+  +			0.30 31	+1 +	+1 +	+1 +	0.01		003
44.84 ± 0.9 46.9 ± 1.1 47.2	+  -				+  -	+  -	+  -	0.92		
$369 \pm 35$ $373 \pm 38$ $428$ $61 \pm 4.5$ $60 \pm 5.9$ $64$	+  +				+1 +1	+1 +1	+  +	0.19		030
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$364 \pm 36$ 90.8 $\pm 2.9$	0.19 0.10	15.02 1.2 0.	0.12 3 0.09 88	$316 \pm 16$ $88.7 \pm 1.9$	$307 \pm 17$ 86.9 ± 1.7	276 ± 18 86.3 ± 1.8	0.10 0.44	-8.70	0.010 0.140

TABLE 2

CALCIUM INTAKE AND ADIPOSITY

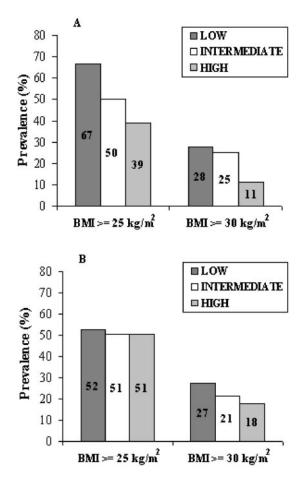
1775

<sup>3</sup> BMI and %FAT were adjusted for age and generation. All other measures of body composition were adjusted for age, generation, and height. Downloaded from https://academic.oup.com/jn/article/134/7/1772/4688598 by guest on 16 August 2022 protein intake (P = 0.003) in the high Ca<sup>2+</sup> intake group in White men and a lower fat intake (P = 0.004) in the high Ca<sup>2+</sup> intake group in White women. However, including the macronutrients as covariates in the analyses did not change the association between Ca<sup>2+</sup> intake and adiposity (results not shown). Including such covariates as physical activity, educational status, smoking, menopause, and hormonal replacement therapy to the ANCOVA or into the regression analysis did not change the results.

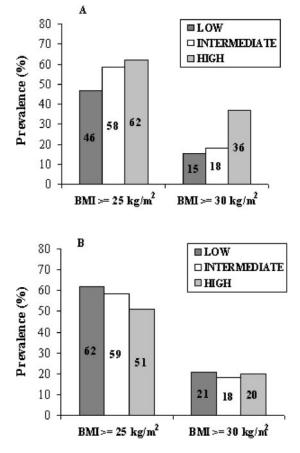
In Black men, the prevalence of overweight (BMI  $\geq 25$  kg/m<sup>2</sup>) decreased significantly (P = 0.018) with increased Ca<sup>2+</sup> intake (**Fig. 1**). The same tendency (P = 0.08) was observed for the prevalence of obesity (BMI  $\geq 30$  kg/m<sup>2</sup>), with only 11% of Black men in the high Ca<sup>2+</sup> intake group being obese compared with 28% in low Ca<sup>2+</sup> intake group. A similar tendency (P = 0.15) was observed for the prevalence of obesity in White men, but not for the prevalence of overweight (Fig. 1).

In contrast, the prevalence of obesity (P = 0.003) and overweight (P = 0.07) in Black women increased with higher Ca<sup>2+</sup> intake (**Fig. 2**). In White women, a nonsignificant trend (P = 0.17) was observed for overweight, with a lower prevalence in the high Ca<sup>2+</sup> intake group (Fig. 2).

Overall, the findings remained the same after the exclusion of subjects who were taking calcium supplements.



**FIGURE 1** Prevalence (%) of obesity (BMI  $\ge$  30 kg/m<sup>2</sup>) and overweight (BMI  $\ge$  25 kg/m<sup>2</sup>) by tertiles of energy-adjusted Ca<sup>2+</sup> intake (Low, Intermediate, High) in Black (*A*) and White (*B*) men. Cochran-Armitage test for trend: BMI  $\ge$  25 kg/m<sup>2</sup>: *P* = 0.018 for Blacks and *P* = 0.82 for Whites, BMI  $\ge$  30 kg/m<sup>2</sup>: *P* = 0.08 for Blacks and *P* = 0.015 for Whites.



**FIGURE 2** Prevalence (%) of obesity (BMI  $\ge$  30 kg/m<sup>2</sup>) and overweight (BMI  $\ge$  25 kg/m<sup>2</sup>) by tertiles of energy-adjusted Ca<sup>2+</sup> intake (Low, Intermediate, High) in Black (A) and White (B) women. Cochran-Armitage test for trend: BMI  $\ge$  25 kg/m<sup>2</sup>: P = 0.07 for Blacks and P = 0.17 for Whites, BMI  $\ge$  30 kg/m<sup>2</sup>: P = 0.003 for Blacks and P = 0.85 for Whites.

## DISCUSSION

Our data showed that total Ca<sup>2+</sup> intake was inversely associated with measures of adiposity in Black men and White women. Subjects with a high energy-adjusted Ca<sup>2+</sup> intake had lower values for BMI, %FAT, SF8, TAF, AVF, ASF, and WC. In White men, a negative association was found only for %FAT, whereas the association with FFM was positive in Black women. In addition, the prevalence of overweight and obesity in Black men was highest in subjects with the lowest energy-adjusted Ca<sup>2+</sup> intake. The same tendencies were observed in White men and women, respectively. In contrast, the prevalence of obesity and overweight in Black women was highest in the group with a high energy-adjusted Ca<sup>2+</sup> intake.

These findings are, in part consistent with the growing body of literature supporting the hypothesis that low  $Ca^{2+}$  intake may increase overall adiposity and abdominal fat mass. Inverse associations have been reported in Whites (3,4,9–11,35) and Blacks (1,7,9,35). Furthermore, most associations were found with BMI and overall fat mass, but there also were some with abdominal adiposity (4,6). However, not all studies found an inverse association between  $Ca^{2+}$  intake and adiposity. Barr (36) reviewed the results of 26 randomized studies in which dairy product intake (n = 9) or  $Ca^{2+}$  intake (n = 17) was experimentally supplemented. Only 1 study found greater weight loss in the  $Ca^{2+}$ -supplemented group, whereas no

differences in body composition were found between the control and supplemented groups in the remaining studies. However, it is noteworthy that only 3 of the 26 studies included men and only 1 study was conducted in premenopausal women; all others were performed in children and adolescents or in postmenopausal women and older men. These findings suggest that the effect of Ca<sup>2+</sup> intake on adiposity may be present only in young and middle-aged premenopausal adults. In a recent study, data of three 25-wk randomized doubleblind, placebo-controlled trials were combined (37). One hundred women received 1000 mg/d  $Ca^{2+}$  supplementation (n = 46) or placebo (n = 54) during a weight loss intervention. There was no significant difference in body weight (placebo  $-6.2 \text{ kg vs. } \text{Ca}^{2+} -7.0, P = 0.43) \text{ or fat mass (placebo } -4.5)$ kg vs.  $Ca^{2+}$  -5.5, P = 0.23) change between the placebo and the Ca<sup>2+</sup>-supplemented groups. However, that study lacked power because post-hoc analyses showed that a study requires  $\sim$ 500 subjects/group to attain 80% power to detect a 0.8-kg difference in weight change.

The sex differences that were observed in both Whites and Blacks are of interest in the present study. In Whites, the inverse association was present in women for most measures of adiposity, whereas it was observed only for %FAT in men. Similar sex differences were reported for the Québec Family Study (4), in which subjects were categorized in 3 groups of  $Ca^{2+}$  intake. Women in the low  $Ca^{2+}$  intake group (<600 mg/d) had significantly higher values for body weight, %FAT, fat mass, BMI, WC, and TAF than the other 2 groups (600– 1000 mg/d and >1000 mg/d). No associations were found in men. Sex differences were also reported in the NHANES III study in which subjects were categorized into quartiles for Ca<sup>2+</sup> intake and for body fat. Women had a strong reduction in the risk of being in the highest quartile of body fat with increasing  ${\rm Ca}^{2+}$  intake, whereas no association was found for men (7).

In contrast to Whites, the inverse association between Ca<sup>2+</sup> intake and body composition in Blacks was present only in men, whereas no association was found in women. The influence of  $Ca^{2+}$  intake on adiposity in Blacks has not been widely studied, but inverse associations were reported for both men and women. In a clinical trial on the antihypertensive effect of  $Ca^{2+}$  intake in obese African-Americans (7),  $Ca^{2+}$ intake was increased from 447 mg/d to 1029 mg/d by providing supplemental yogurt for 12 mo. In men, body fat decreased by 4.9 kg over 1 y; the results in women were not reported. A study on lactose intolerance in premenopausal African-American women reported a significantly lower Ca<sup>2+</sup> intake in lactose-intolerant women (388 mg/d) compared with lactosetolerant women (763 mg/d) (1). The lactose-intolerant women had a significantly higher BMI, and Ca<sup>2+</sup> intake was negatively associated with BMI ( $r^2 = 0.47$ ). The CARDIA study included both men and women, and Blacks and Whites (35). Dairy consumption was inversely associated with all components of the metabolic syndrome, including obesity. For each increase in dairy serving/d, the odds for obesity decreased by 20%. This association was similar for Blacks and Whites and for men and women.

In addition to the sex difference, we found that the association between Ca<sup>2+</sup> intake and adiposity was significantly different between Blacks and Whites, particularly in women. A consistent inverse association was found in White women, whereas the association in Black women, unexpectedly, tended to be positive for BMI (P = 0.05), WC (P = 0.10), and for the prevalence of overweight (P = 0.07) and obesity (P= 0.003). Race differences have also been reported in another study in which African-American and White women were

compared (9). Similar to the present findings, significant negative associations (P < 0.05) were found between energyadjusted Ca<sup>2+</sup> intake and BMI and %FAT (partial correlation: r = -0.21 for BMI and r = -0.25 for %FAT) in White women. In contrast, no associations were found with either BMI or %FAT in African-American women. The observed race difference was significant for BMI (P = 0.04) and suggestive for %FAT (P = 0.07). Differences in diet and lifestyle between Black and White women, other than those controlled for in the present study, may underlie the ethnic differences.

Ca<sup>2+</sup> intake was not only associated with overall adiposity (BMI, %FAT), but a strong inverse association was found with abdominal adiposity (TAF, AVF, ASF, and WC) in Black men and White women. Similar results were reported for women of the Québec Family Study; subjects in the lowest  $Ca^{2+}$  intake group (<600 mg/d) had significantly more TAF and a larger WC than women whose  $Ca^{2+}$  intake was higher than 600 mg (4). Along the same line, during a 6-mo clinical trial in obese patients consuming energy deficit diets, the low  $Ca^{2+}$  diet (400–500 mg/d) resulted in a 5.3% reduction in trunk fat, whereas the high  $Ca^{2+}$  diets (supplement and dairy, respectively) resulted in a 12.9 to 14% reduction (6).

respectively) resulted in a 12.9 to 14% reduction (6). It was suggested that the effect of  $Ca^{2+}$  intake is dependent on achieving a threshold concentration (11). Our results did not support this because adiposity measures were linearly re-lated to increasing  $Ca^{2+}$  intake in Black men and in Whites. It could be argued that the  $Ca^{2+}$  intake in Black women was too low to elicit an effect on body composition. However, Black men had about the same range of  $Ca^{2+}$  intake and did show significant negative associations with adiposity measures. Data in humans (6,8,11) and mice (12) suggest that dairy sources of calcium exert stronger effects than nondairy sources. Unfortunately, the questionnaire used in the present study did not allow for separation between the 2 sources of  $Ca^{2+}$  intake.

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not allow for separation between the 2 sources of Ca<sup>2+</sup> intake. Ca<sup>2+</sup> intake reached the AI (1000 mg/d) only in Whites (38) and was significantly higher in Whites than in Blacks (see Table 1). This is in agreement with the findings of others (5,9). However, the reported mean Ca<sup>2+</sup> intake in the present study was higher compared with the results of the Nationwide Food Consumption Survey (5) from 1987 to 1988 (non-Hispanic Blacks: 592 mg/d, non-Hispanic Whites: 765 mg/d) and panic Blacks: 592 mg/d, non-Hispanic Whites: 765 mg/d) and g compared with a more recent study in African-American (518 mg/d) and White women (758 mg/d) (9). These differences may be due to our relatively healthy study sample or to differences in dietary intake assessment methods.

The strengths of the present study are the large numbers of Black as well as White subjects, the quality control of the data, and the variety of available adiposity measures. However, there are some limitations that should be mentioned. First, like  $\gtrsim$  other studies that have examined the Ca<sup>2+</sup> intake-adiposity  $\gtrsim$ relation, the HERITAGE Family Study was not designed primarily to examine the effects of  $Ca^{2+}$  intake on adiposity. Randomized controlled intervention trials designed to investigate the Ca<sup>2+</sup> intake-body composition relation would provide more compelling data than the current study. Second, the limitations of self-reported dietary intake are well recognized (39). Although the FFQ used in the present study has a reasonable reproducibility and validity (30), it may not be the best method with which to assess Ca<sup>2+</sup> intake. Third, we recognize that cross-sectional analyses do not establish whether Ca<sup>2+</sup> intake exerts a direct effect on body composition and adiposity. It is possible that  $Ca^{2+}$  intake serves only as a marker for other nutrients that directly modulate total and abdominal adiposity.

In summary, the present study suggests that Ca<sup>2+</sup> intake is inversely associated with measures of adiposity, particularly in Black men and White women. We conclude that  $Ca^{2+}$  intake may play a role in the regulation of energy balance, although the mechanisms remain to be determined. However, the observation of sex and ethnic differences indicates that the results should be interpreted with caution. Large clinical trials should be undertaken to establish whether there is a causal association between  $Ca^{2+}$  intake and body weight regulation.

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