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ORIGINAL RESEARCH

Association of Adiposity With Incident Diabetes Among Black Adults in the Jackson Heart Study

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BACKGROUND: The prognostic value of anthropometric, adipokine, and computed tomography measures of adiposity to predict diabetes in Black, specifically by normoglycemia versus prediabetes, remains incompletely understood.

METHODS AND RESULTS: Among Black participants without diabetes in the JHS (Jackson Heart Study), waist circumference [WC], body mass index, adiponectin, leptin, and leptin:adiponectin ratio were standardized in sample 1 (2422 participants at baseline [2000–2004]) and WC, body mass index, visceral adipose tissue (VAT), subcutaneous adipose tissue, and liver attenuation in 1537 participants at examination 2 (2005–2008) (sample 2). Hazard ratios (HRs) for diabetes were estimated using interval-censored Cox modeling adjusting for traditional risk factors and validated with the C index. Over 5 years, 300 and 122 incident diabetes cases occurred in sample 1 and sample 2, respectively. In sample 1 and sample 2, a 1-SD higher log-leptin:adiponectin ratio and VAT had the strongest associations (HR, 1.95 [95% CI, 1.67–2.27] and 1.76 [95% CI, 1.52–2.04]) and discriminatory power (C index 0.68 [95% CI, 0.64–0.71] and C index 0.67 [95% CI, 0.61–0.74]) with diabetes. The normoglycemic compared with the prediabetes group had a 1.3 to 1.9 times greater magnitude of associations with diabetes for WC, liver attenuation, and VAT (*P* interaction <0.10). In sample 2, C indices for WC (HR, 0.84; 95% CI, 0.73–0.95), VAT (HR, 0.91; 95% CI, 0.85–0.98), and liver attenuation (HR, 0.90; 95% CI, 0.77–1.00) were greater than HbA_{1c} (HR, 0.74; 95% CI, 0.57–0.90) in normoglycemia, whereas HbA_{1c} was best in prediabetes (HR, 0.72; 95% CI, 0.66–0.78).

CONCLUSIONS: Overall, among Black adults, multiple measures of adiposity were associated with incident diabetes with modest predictive ability. In Black patients with normoglycemia, WC, liver attenuation, and VAT may appropriately identify those at high risk for diabetes, whereas HbA_{1c} was the best predictor in individuals with prediabetes.

Key Words: adiposity ■ Black adults ■ diabetes ■ health equity ■ visceral adipose tissue ■ waist circumference

Type 2 diabetes and obesity are more prevalent among Black compared with non-Hispanic White individuals.[1,2] Elevated adiposity, as assessed by body mass index (BMI), increases the lifetime risk of developing type 2 diabetes.[3] Evidence from numerous studies suggests that central obesity is associated with global low-grade inflammation, which disrupts proper insulin signaling.[4] Moreover, the state of obesity is characterized by dysregulated adipokine production with high leptin and low adiponectin, which may consequently further increase systemic inflammation and insulin resistance.[5] These mechanistic hypotheses are consistent with cross-sectional studies among Black participants in JHS (Jackson Heart Study), wherein visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were positively associated with fasting

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CLINICAL PERSPECTIVE

What is New?

- In Black, multiple measures of adiposity were associated with incident diabetes with leptin-adiponectin ratio and visceral adipose tissue having the strongest associations and risk prediction with type 2 diabetes.
- In Black with normoglycemia, waist circumference, liver attenuation and visceral adipose tissue may identify those at high risk for diabetes, whereas hemoglobin A_{1c} was the best predictor in those with prediabetes.

What Are the Clinical Implications?

- Providers should check waist circumference as part of routine care of Black with normoglycemia to identify individuals at higher risk for type 2 diabetes and address modifiable lifestyle behaviors to prevent type 2 diabetes.
- Future technology innovations allowing cost-effective visceral adipose tissue and liver attenuation measurement may improve diabetes risk prediction in patients with normoglycemia.

Nonstandard Abbreviations and Acronyms

AHA	American Heart Association
ARIC	Atherosclerosis Risk in Communities
HOMA-IR	homeostatic model assessment of insulin resistance
JHS	Jackson Heart Study
LA	liver attenuation
SAT	subcutaneous adipose tissue
VAT	visceral adipose tissue
WC	waist circumference

plasma glucose and prevalent diabetes, with a larger effect size for VAT and liver fat versus SAT.[6,7]

Prospective studies have assessed the associations and predictive abilities of anthropometric measures with incident diabetes in diverse cohorts, which included Black.[8–13] However, these studies did not distinguish the discriminative ability of these metrics between those who had normoglycemia and those who had prediabetes. Further, none were able to assess the predictive ability of more refined measures of adiposity such as adipokine levels (adiponectin and leptin) and depot-specific adipose tissue volumes (VAT, SAT, and liver attenuation [LA]) for incident diabetes. One small, cross-sectional study in China that included participants with normoglycemia, prediabetes, and diabetes found that magnetic resonance imaging measures of total VAT volume and hepatic proton-density fat fraction were strong predictors of prevalent diabetes (C indices of 0.80 and 0.79 [both $P<0.01$], respectively).[14] However, there is a general lack of prospective data assessing the predictive ability of adipokine levels and depot-specific measures of adiposity and incident diabetes among Black. Furthermore, to our knowledge, the effect modification of baseline glycemic status in the association and predictive accuracy of anthropometric measures with risk of incident diabetes has not been assessed in a large Black cohort. Thus, we examined the associations and discriminatory power of anthropometric (BMI and WC), adipokines (adiponectin, leptin, and leptin:adiponectin ratio), and computed tomographic (CT) measures (VAT, SAT, LA) of adiposity with incident diabetes among Black participants in JHS, along with the modifying effect of baseline glycemia (normoglycemia versus prediabetes).

METHODS

Study Sample

The JHS is a prospective cohort study of cardiovascular disease among 5306 Black adults, aged 21 to 96 years, from the tri-county area of metropolitan Jackson, Mississippi. Enrollment and baseline examinations were performed from 2000 to 2004 with 2 subsequent in-person follow-up examinations from 2005 to 2008 and 2009 to 2013. Details about the study design, recruitment, and methods have been described elsewhere.[15] The study was approved by the institutional review boards of University of Mississippi Medical Center, Jackson State University, and Tougaloo College, and the participants gave written informed consent. Two samples of participants in JHS were examined. The first sample (sample 1) consisted of participants without diabetes with data on anthropometric measures and biomarker measures (adiponectin, leptin, leptin:adiponectin ratio) at examination 1 with follow-up at examination 2 (n=2422 after exclusions). The second sample (sample 2) consisted of participants without diabetes with data on anthropometric measures and body composition (VAT, SAT, and LA) at examination 2 with follow-up at examination 3 (n=1537 after exclusions).

Baseline Assessments

Baseline information was obtained using standardized questionnaires including demographics, occupation (management/professional versus not), educational attainment (bachelor's degree or higher versus less than a bachelor's degree), alcohol use, and current prescription medication usage. Smoking status was

classified as optimal (never smoking or quit ≥12 months ago), average (quit <12 months ago), or poor (current smoking) health.[16] Resting seated blood pressure was measured twice at 5-minute intervals using an appropriately sized cuff with standard Hawksley random-zero instruments, and measurements were averaged. Fasting blood samples were processed and stored using a standardized protocol.[15,17] Fasting glucose and insulin concentrations were measured on a Vitros 950 or 250, Ortho-Clinical Diagnostics analyzer using standard procedures that met the College of American Pathologists accreditation requirement.[17] Insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR; fasting plasma glucose [mg/dL]×fasting plasma insulin [mU/mL])÷405).[18] A high-performance liquid chromatography system (Tosoh Corporation) was used to measure hemoglobin A_{1c} (HbA_{1c}) concentrations. Physical activity was assessed using the validated JHS Physical Activity Cohort survey[19] and defined according to the American Heart Association (AHA) categorization.[20] Dietary intake was assessed using a culturally appropriate, validated 158-item food frequency questionnaire administered in person by trained Black interviewers.[21] Diet quality was operationalized using AHA categorization with slight modifications, as previously described.[20,22]

Assessment of Adiposity

Adiponectin, Leptin, and Leptin:Adiponectin Ratio

Leptin was analyzed with a Human Leptin RIA kit (LINCO Research) and the acceptable coefficient of variation was 10%.[23] Serum concentrations of total adiponectin were measured by an ELISA system (R&D Systems) with an interassay coefficient of variation of 8.8%.[24] Leptin:adiponectin ratio was calculated by dividing leptin by adiponectin.

BMI and WC

Calibrated devices were used by certified technicians and nurses to measure participants' weight and height. BMI was calculated as weight (kilograms)/height^2 (meters). WC in centimeters was the average of 2 measurements at the level of the umbilicus.

CT Measures of Adiposity (VAT, SAT, and LA)

VAT, SAT, and LA were measured via multidetector CT. The protocol for CT assessment in the JHS has been described elsewhere.[7] Briefly, a 16-channel multidetector CT system equipped with cardiac gating (Lightspeed 16 Pro; GE Healthcare) was used to scan the heart and lower abdomen.

Glycemic Status Ascertainment

Normoglycemia was defined as fasting glucose <100 mg/dL and HbA_{1c} <5.7%. Prediabetes was defined as fasting glucose 100 to 125 mg/dL or HbA_{1c} 5.7% to 6.4%. Diabetes was defined as HbA_{1c} ≥6.5%, fasting blood glucose ≥126 mg/dL, taking diabetes medications, or a self-reported physician diagnosis.[25] Participants without diabetes at baseline, who met criteria for diabetes at a subsequent examination, were considered to have incident diabetes.

Statistical Analysis

Because of the non-normal distribution of adiponectin and leptin, these variables were log-transformed before analyses were performed. The baseline characteristics of participants were compared by incident diabetes status using 2-sample *t* test or Wilcoxon rank sum test for continuous variables and chi-square test for categorical variables. To allow comparison among adiposity measures with different units, we created *z* scores, using the equation z_i equals $(x_i - \overline{x})/s$), where $\overline{x}$ is the sample mean and *s* is the sample SD and x_i is the measurement for the i^{th} participant. We estimated a correlation matrix of adiposity measures between examination 1 and 2. Given that diabetes could develop anytime between examination visits (sample 1: examination 1 to 2 or sample 2: examination 2 to 3), interval-censored Cox modeling was used to estimate hazard ratios (HRs, 95% CI) for incident diabetes by *z* scores of adiposity measures. Participants were censored at the last attended follow-up examination. Sequential multivariable adjustment modeling was performed: model 1: age, sex, education, occupation, smoking, drinking, physical activity, nutrition, and systolic blood pressure; model 2: model 1+BMI; and model 3: model 1+WC. For analyses using sample 1: models 1 to 3 were the same as in cross-sectional analyses, model 4: model 1+*z*-waist, *z*-BMI, *z*-log-leptin:adiponectin ratio; and model 5: model 1+*z*-waist, *z*-BMI, *z*-log-adiponectin, and *z*-log-leptin at examination 1. For sample 2: models 1 to 3 were the same as in cross-sectional analyses, model 4: model 1+*z*-LA, *z*-SAT, and *z*-VAT at examination 2. The C index examined the discriminatory power of the models including the adiposity measures and other covariates. The bootstrap percentile method estimated 95% CIs for differences in C index values between models, including the selected measures, based on the 2.5th and 97.5th percentiles from 1000 bootstrap samples. Statistical significance of these analyses was defined as $P<0.05$.

The association of adiposity measures with diabetes may differ by age, sex, and baseline glycemic status (normoglycemia [fasting glucose <100 mg/dL and HbA_{1c} <5.7%] versus prediabetes [fasting glucose 100–125 mg/dL or HbA_{1c} 5.7%–6.4%]); thus, we tested for interaction

of these factors with glycemic status by inserting an interaction term in the model using the likelihood ratio test in unadjusted models with statistical significance defined as $P<0.10$. Analyses were performed using SAS 9.4 (SAS Institute Inc.) and R version 4.0.0.

Role of the Funding Source

The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the article; and decision to submit the article for publication.

RESULTS

Baseline Characteristics

The baseline characteristics of samples 1 and 2, stratified by the development of diabetes are presented in Table 1. In sample 1, participants who did not develop diabetes were younger, had lower BMIs, WCs, systolic blood pressures, glucose, HbA_{1c}, leptin, leptin:adiponectin ratios, and HOMA-IRs, with higher levels of adiponectin ($P<0.0001$), education ($P<0.0119$), professional employment ($P<0.0188$), physical activity ($P=0.0023$), and current alcohol intake ($P=0.0162$). Similar patterns were observed among sample 2 participants who did not develop diabetes. However, in this sample, they also had lower levels of SAT and VAT and higher LA (lower liver fat) ($P<0.0001$), while sociodemographic characteristics and blood pressure were nonsignificantly different. The correlation matrix between adiposity measures at examination 1 and examination 2 is presented in Table S1. Interclass (Pearson) correlation coefficients between WC and BMI were high (Table S1). After testing for effect modification of the associations by age, sex, and glycemic status, we found no interaction by age or sex. However, glycemic status significantly interacted with these relationships and thus we performed stratified analyses.

Sample 1: Association of Adiposity Measures With Incident Diabetes

In sample 1, 300 participants developed diabetes (incidence rate, 24.6 per 1000 person-years) between examination 1 and 2, with a median follow-up of 5 years between examinations (Table 1). The adjusted HRs for incident diabetes associated with adiposity measures are presented in Table 2. In sample 1, after adjustment for traditional risk factors (model 1), 1-unit SD increase in BMI, WC, log-leptin, and log-leptin:adiponectin were associated with a 44%, 56%, 76%, and 95% higher risk of diabetes, respectively, and a 1-SD increase in adiponectin was associated with a 39% lower risk of diabetes (all $P<0.0001$). The findings remained significant for WC, log-adiponectin, and log-leptin:adiponectin ratio after adjustment for other measures of adiposity.

Sample 2: Association of Adiposity Measures With Incident Diabetes

In sample 2, 122 participants developed diabetes (incidence rate, 28.0 per 1000 person-years) between examination 1 and 2, with a median follow-up of 5 years (Table 1). After adjustment for traditional risk factors (model 1), 1-unit SD increases in BMI, WC, SAT, and VAT were associated with a 66%, 59%, 54%, and 76% higher risk for diabetes, respectively, whereas a 1-unit SD increase in LA was associated with a 39% lower risk of diabetes (all $P<0.0001$). After adjustment for all other measures of adiposity, the findings remained significant for VAT and LA (Table 2).

Sample 1: Association of Adiposity Measures With Incident Diabetes Stratified by Baseline Glycemic Status

In sample 1, glycemic status modified the association between WC and risk of incident diabetes, with the effect size being greater in individuals with normoglycemia (Table 3). In Table 4, after simultaneous adjustment for other measures of adiposity, a 1-SD increase in WC (HR, 2.41; 95% CI, 1.32–4.37) and log-adiponectin (HR, 0.66; 95% CI, 0.47–0.93) remained significant among participants with normoglycemia. Among participants with prediabetes, a 1-SD increase in log-adiponectin (HR, 0.74; 95% CI, 0.65–0.85) and log-leptin:adiponectin ratio (HR, 1.42; 95% CI, 1.18–1.72) remained significant.

Sample 2: Association of Adiposity Measures With Incident Diabetes Stratified by Baseline Glycemic Status

In sample 2, there were significant differences for individuals with normoglycemia and those with prediabetes in the association of WC, BMI, LA, and VAT with incident diabetes (Table 3). A 1-SD increase in BMI (HR, 15.0; 95% CI, 2.37–94.4) and LA (HR, 0.41; 95% CI, 0.20–0.81) remained significant among participants with normoglycemia. Among participants with prediabetes, a 1-SD increase in LA (HR, 0.74; 95% CI, 0.64–0.86) and VAT (HR, 1.31; 95% CI, 1.04–1.64) remained significant (Table 5).

Sample 1: C Indices for Adiposity Measures

The top panel of Table 6 shows the results of prediction modeling using the C index for sample 1 overall and Figure 1A shows these results stratified by glycemic

Table 1. Baseline Characteristics of the Study Populations

	Sample 1 (examination 1 to examination 2)				Sample 2 (examination 2 to examination 3)			
	Overall (n=2422)	Incident diabetes at examination 2 (n=300)*	No diabetes at exam 2 (n=2122)		Overall (n=1537)	Incident diabetes at examination 3 (n=122)*	No diabetes at examination 3 (n=1415)	
	n (%)	n (%)	n (%)	*P* value†	n (%)	n (%)	n (%)	*P* value†
Sex				0.9865				0.2114
Men	887 (36.6)	110 (36.7)	777 (36.6)		559 (36.4)	38 (31.2)	521 (36.8)	
Women	1535 (63.4)	190 (63.3)	1345 (63.4)		978 (63.6)	84 (68.8)	894 (63.2)	
Education				0.0119				0.4737
Bachelor's degree or higher	927 (38.3)	95 (31.7)	832 (39.2)		652 (42.4)	48 (39.3)	604 (42.7)	
Other	1495 (61.7)	205 (68.3)	1290 (60.8)		885 (57.6)	74 (60.7)	811 (57.3)	
Occupation				0.0188				0.7641
Management/professional	966 (39.9)	101 (33.7)	865 (40.8)		675 (43.9)	52 (42.6)	623 (44.0)	
Other	1456 (60.1)	199 (66.3)	1257 (59.2)		862 (56.1)	70 (57.4)	792 (56.0)	
Current smoking				0.7568				0.5139
Yes	254 (10.5)	33 (11.0)	221 (10.4)		152 (9.9)	10 (8.2)	142 (10.0)	
No	2168 (89.5)	267 (89.0)	1901 (89.6)		1385 (90.1)	112 (91.8)	1273 (90.0)	
Current alcohol intake				0.0162				0.7587
Yes	1223 (50.5)	132 (44.0)	1091 (51.4)		789 (51.3)	61 (50.0)	728 (51.4)	
No	1199 (49.5)	168 (56.0)	1031 (48.6)		748 (48.7)	61 (50.0)	687 (48.6)	
AHA physical activity‡				0.0023				0.1131
Ideal health	539 (22.3)	50 (16.6)	489 (23.0)		369 (24.0)	30 (24.6)	339 (23.9)	
Intermediate health	800 (33.0)	89 (29.7)	711 (33.5)		526 (34.2)	51 (41.8)	475 (33.6)	
Poor health	1083 (44.7)	161 (53.7)	922 (43.5)		642 (41.8)	41 (33.6)	601 (42.5)	
AHA dietary intake§				0.8701				0.9673
Ideal health	19 (0.8)	2 (0.7)	17 (0.8)		16 (1.0)	1 (0.8)	15 (1.1)	
Intermediate health	914 (37.7)	117 (39.0)	797 (37.6)		587 (38.2)	47 (38.5)	540 (38.2)	
Poor health	1489 (61.5)	181 (60.3)	1308 (61.6)		934 (60.8)	74 (60.7)	860 (60.8)	
	Mean (SD)	Mean (SD)	Mean (SD)	*P* value†	Mean (SD)	Mean (SD)	Mean (SD)	*P* value†
Age, y	52.6 (12.3)	55.7 (10.7)	52.1 (12.4)	<0.0001	58.0 (10.7)	58.1 (10.5)	58.0 (10.8)	0.8743
BMI	31.2 (7.0)	33.9 (7.1)	30.8 (6.8)	<0.0001	30.9 (6.0)	34.1 (6.0)	30.6 (5.9)	<0.0001
WC, cm	98.4 (15.5)	106.0 (14.4)	97.4 (15.4)	<0.0001	98.8 (14.1)	105.9 (13.6)	98.2 (14.0)	<0.0001
SBP, mm Hg	124.5 (17.1)	127.7 (18.4)	124.1 (16.9)	0.0016	125.2 (17.0)	127.8 (17.5)	125.0 (16.9)	0.0817
DBP, mm Hg	79.8 (10.2)	80.9 (10.2)	79.6 (10.2)	0.0452	78.2 (9.8)	79.0 (10.9)	78.2 (9.7)	0.3575

(*Continued*)

Table 1. Continued

	Mean (SD)	Mean (SD)	Mean (SD)	*P* value†	Mean (SD)	Mean (SD)	Mean (SD)	*P* value†
Glucose, mg/dL	89.8 (8.8)	98.3 (11.0)	88.6 (7.7)	<0.0001	95.2 (9.1)	102.9 (10.5)	94.5 (8.6)	<0.0001
HbA_{1c} %	5.5 (0.5)	5.9 (0.4)	5.4 (0.4)	<0.0001	5.6 (0.4)	6.0 (0.4)	5.6 (0.4)	<0.0001
Log-adiponectin, ng/mL	8.4 (0.7)	8.1 (0.6)	8.4 (0.7)	<0.0001	NA	NA	NA	
Log-leptin (ng/mL)	2.9 (1.0)	3.2 (0.9)	2.9 (1.0)	<0.0001	NA	NA	NA	
Log-leptin-adiponectin ratio	−5.4 (1.1)	−5.0 (1.0)	−5.5 (1.1)	<0.0001	NA	NA	NA	
Subcutaneous adipose tissue cm^3	NA	NA	NA		2242.7 (986.9)	2637.6 (908.6)	2208.7 (986.3)	<0.0001
Visceral adipose tissue cm^3	NA	NA	NA		750.9 (342.7)	963.5 (342.0)	732.6 (336.7)	<0.0001
Liver attenuation (Hounsfeld Units)	NA	NA	NA		60.0 (8.3)	54.8 (11.3)	60.4 (7.8)	<0.0001
	Median (quartile 1, quartile 3)	**Median (quartile 1, quartile 3)**	**Median (quartile 1, quartile 3)**	*P* value†				
Adiponectin, ng/mL	4261.8 (2736.2–6656.2)	3290.6 (2240.5–4929.8)	4440.0 (2841.1–6852.5)	<0.0001	NA	NA	NA	
Leptin, ng/mL	22.3 (9.8–38.8)	27.9 (14.4–44.3)	21.6 (9.4–38.2)	<0.0001	NA	NA	NA	
Leptin-adiponectin ratio	0.005 (0.002–0.010)	0.008 (0.004–0.014)	0.005 (0.002–0.009)	<0.0001	NA	NA	NA	
HOMA-IR	3.00 (2.19–4.33)	4.56 (3.22–6.38)	2.86 (2.11–4.02)	<0.0001	NA	NA	NA	
Follow-up time, y	Median: 4.8 (quartile 1: 4.4, quartile 3: 5.5), range: 3.4–8.0		Median: 3.0 (quartile 1: 2.4, quartile 3: 3.2), range: 0.2–5.7					

BMI indicates body mass index; DBP, diastolic blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance; NA, not available; SBP, systolic blood pressure; and WC, waist circumference.

*Incident diabetes was defined based on hemoglobin A_{1c} (HbA_{1c}) ≥6.5%, fasting blood glucose ≥126 mg/dL, or taking diabetes medications or a self-reported physician diagnosis based on 2010 American Diabetes Association guidelines among participants without diabetes at sample baseline (examination 1 for sample 1 and examination 2 for sample 2).

†Mean (SD) or percentages are listed. *P* values were calculated using chi-square (categorical variables), 2-sample *t* test (normally distributed continuous variables), and Wilcoxon 2-sample nonparametric test (not normally distributed data continuous variables)

‡American Heart Association (AHA) ideal physical activity and dietary intake recommendations were defined by AHA 2020 guidelines. Physical activity was considered ideal if the participant achieved ≥150 min/wk of moderate-intensity or ≥75 min/wk of vigorous-intensity physical activity.

§AHA dietary intake was considered ideal if the participant met 4 or 5 of 5 of the following recommendations: fruits and vegetables ≥4.5 cups/d; fish ≥two 3.5-oz servings/wk (preferably oily fish); fiber-rich whole grains ≥three 1 oz.-equivalent servings/d; sodium <1500 mg/d; and sugar-sweetened beverages ≤450 kcal (36 oz)/wk.

Table 2. Association of Adiposity Measures With Incident Diabetes*

Sample 1, examination 1 to examination 2†, n=2422	Unadjusted	Model 1	Model 2	Model 3	Model 4	Model 5
	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* alue	HR (CI), *P* value
z-BMI	1.39	1.44	1.08	NA	0.98	1.06
	(1.27–1.51)	(1.31–1.59)	(0.89–1.30)		(0.79–1.21)	(0.86–1.30)
	P<0.0001	*P*<0.0001	*P*=0.4533		*P*=0.8502	*P*=0.6118
z-WC	1.56	1.56	NA	1.47	1.26	1.31
	(1.42–1.72)	(1.41–1.72)		(1.22–1.76)	(1.03–1.55)	(1.07–1.61)
	P<0.0001	*P*<0.0001		*P*<0.0001	*P*=0.026	*P*=0.0080
z-Log-adiponectin	0.69	0.61	0.66	0.64	NA	0.65
	(0.61–0.77)	(0.55–0.69)	(0.58–0.74)	(0.56–0.72)		(0.58–0.74)
	P<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001		*P*<0.0001
z-Log-leptin	1.32	1.76	1.20	1.36	NA	1.19
	(1.17–1.50)	(1.49–2.08)	(0.96–1.50)	(1.11–1.68)		(0.94–1.50)
	P<0.0001	*P*<0.0001	*P*=0.1139	*P*=0.0038		*P*=0.1593
z-Log-leptin:adiponectin Ratio	1.68	1.95	1.68	1.77	1.69	NA
	(1.48–1.91)	(1.70–2.24)	(1.42–1.99)	(1.51–2.08)	(1.42, 1.99)	
	P<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001	
Sample 2, examination 2 to examination 3,‡ n=1537	**Unadjusted**	**Model 1**	**Model 2**	**Model 3**	**Model 4**	
z-BMI	1.60	1.66	1.43	NA	1.24	NA
	(1.37–1.86)	(1.41–1.96)	(1.01–2.02)		(0.81–1.89)	
	P<0.0001	*P*<0.0001	*P*=0.0420		*P*=0.3157	
z-WC	1.54	1.59	NA	1.18	1.01	NA
	(1.33–1.79)	(1.36–1.85)		(0.85–1.64)	(0.70–1.46)	
	P<0.0001	*P*<0.0001		*P*=0.3209	*P*=0.9538	
z-LA	0.62	0.61	0.66	0.66	0.70	NA
	(0.55–0.71)	(0.54–0.70)	(0.57–0.75)	(0.58–0.75)	(0.61–0.81)	
	P<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001	
z-SAT	1.45	1.54	1.01	0.85	0.99	NA
	(1.23–1.71)	(1.28–1.85)	(0.74–1.37)	(0.60–1.21)	(0.67–1.46)	
	P<0.0001	*P*<0.0001	*P*=0.9470	*P*=0.3593	*P*=0.9592	
z-VAT	1.67	1.76	1.58	1.54	1.37	NA
	(1.45–1.91)	(1.52–2.04)	(1.30–1.92)	(1.28–1.87)	(1.11–1.69)	
	P<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001	*P*=0.0040	

HR indicates hazard ratio; and NA, not available.

Model 2: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, and waist circumference (WC).

Model 3: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, and body mass index (BMI).

Model 4: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, *z*-waist, *z*-BMI, *z*-log-leptin:adiponectin ratio.

Model 5: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, *z*-WC, *z*-BMI, *z*-log-adiponectin, *z*-log-leptin.

Model 2: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, and WC.

Model 3: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, and BMI.

Model 4: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, SBP, *z*-WC, *z*-BMI, *z*-liver attenuation (LA), *z*-subcutaneous adipose tissue (SAT), and *z*-visceral adipose tissue (VAT).

*Incident diabetes was defined based on hemoglobin A_{1c} (HbA_{1c}) ≥6.5%, fasting blood glucose ≥126 mg/dL, taking diabetes medications or with a self-reported physician diagnosis based on 2010 American Diabetes Association guidelines among participants without diabetes at sample baseline (examination 1 for sample 1, examination 2 for sample 2).

†Model 1: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, and systolic blood pressure (SBP).

‡Model 1: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, and SBP.

status. C indices are reported for each adiposity measure in unadjusted models and for overall models, including covariates and individual adiposity measures. The discriminatory power for individual adiposity measures including age, sex, and education (model 1) in sample 1 are modest, ranging from 0.64 to 0.68.

Table 3. Association of Adiposity With Incident Diabetes Stratified by Normoglycemia Versus Prediabetes*

	Sample 1 (examination 1 to 2)				Sample 2 (examination 2 to 3)			
	Normoglycemia† (n=1392)	Prediabetes (n=1030)	*P* for Interaction		Normoglycemia† (n=602)	Prediabetes (n=935)	*P* for Interaction
	HR (CI), *P* value	HR (CI), *P* value			HR (CI), *P* value	HR (CI), *P* value	
z-BMI	1.52 (1.14–2.03), *P*=0.0045	1.23 (1.11–1.37), *P*=0.0002	*P*=0.4563	z-BMI	2.86 (1.56–5.22), *P*=0.0007	1.41 (1.18–1.68), *P*=0.0001	*P*=0.0747
z-WC	1.76 (1.34–2.30), *P*<0.0001	1.28 (1.14–1.44), *P*<0.0001	*P*=0.0442	z-WC	2.38 (1.30–4.35), *P*=0.0050	1.38 (1.17–1.62), *P*=0.0001	*P*=0.0651
z-Log-adiponectin	0.62 (0.45–0.86), *P*=0.0038	0.72 (0.63–0.82), *P*<0.0001	*P*=0.1722	z-LA	0.37 (0.24–0.56), *P*<0.0001	0.70 (0.61–0.80), *P*<0.0001	*P*=0.0008
z-log-leptin	1.53 (0.98–2.37), *P*=0.0594	1.37 (1.13–1.67), *P*=0.0016	*P*=0.3458	z-Subcutaneous adipose tissue	1.82 (0.94–3.49), *P*=0.0738	1.37 (1.12–1.68), *P*=0.0023	*P*=0.9333
z-log- leptin:adiponectin ratio	1.78 (1.22, 2.60), *P*=0.0027	1.53 (1.31, 1.79), *P*<0.0001	*P*=0.9626	z-visceral adipose tissue	2.52 (1.55, 4.08), *P*=0.0002	1.51 (1.28, 1.78), *P*<0.0001	*P*=0.0008

BMI indicates body mass index; HR, hazard ratio; LA, liver attenuation; and WC, waist circumference.

*Incident diabetes was defined based on hemoglobin A_{1c} (HbA_{1c}) ≥6.5%, fasting blood glucose ≥126 mg/dL, taking diabetes medications or with a self-reported physician diagnosis based on 2010 American Diabetes Association guidelines among participants without diabetes at sample baseline (examination 1 for sample 1, examination 2 for sample 2). Analyses adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, dietary intake, and systolic blood pressure.

†Normoglycemia was defined as fasting glucose <100 mg/dL and HbA_{1c} <5.7%.

‡Prediabetes was defined as fasting glucose 100 to 125 mg/dL or HbA_{1c} 5.7% to 6.4%.

In prediabetes, addition of HbA_{1c} to the basic demographic risk model (age, sex, and education) performs best as a predictor of incident diabetes compared with the addition of individual adiposity measures. However, in the normoglycemic state, WC improves prediction of incident diabetes compared with HbA_{1c} when added to the demographic risk model in sample 1 (C index, 0.76 [95% CI, 0.67–0.84] versus 0.68 [95% CI, 0.58–0.78], respectively [model 1]). Figure 2 (visit 1) presents bootstrapping estimates analyzing differences in C indices for selected measures before adjustment for covariates for sample 1. Addition of WC to age, sex, and education improved discrimination of diabetes compared with HbA_{1c} in individuals with normoglycemia. However, addition of HbA_{1c} was more predictive than WC in individuals with prediabetes.

Sample 2: C Indices for Adiposity Measures

The bottom panel of Table 6 shows the results of prediction modeling using the C index for sample 2 overall and Figure 1B shows these results stratified by glycemic status. Similar to sample 1, the C indices for adiposity measures are modest, ranging from 0.62 to 0.67 (model 1). WC remains a strong predictor among individuals with normoglycemia (C index, 0.84; 95% CI, 0.73–0.95), along with VAT and LA (C indices, 0.91 [95% CI, 0.85–0.98] and 0.90 [95% CI, 0.77–1.00]) compared with HbA_{1c} (C index, 0.74; 95% CI, 0.57–0.90) when added to the basic demographic risk model (age, sex, and education). However, in the state of prediabetes, addition of HbA_{1c} once again produces the best predictive model of diabetes (Figure 1B). Figure 2 (sample 2) shows that VAT and LA were better discriminators of diabetes compared with HbA_{1c} among those with normoglycemia when added to age, sex, and education. VAT, but not LA, outperformed WC in terms of discrimination of incident diabetes.

DISCUSSION

In this large, prospective community-based cohort study of Black adults, risk of incident diabetes was higher among those with higher BMI, WC, leptin:adiponectin ratio, SAT, and VAT, and lower among those with higher adiponectin and LA. The risk of incident diabetes associated with increasing WC and VAT and lower LA was higher for participants with normoglycemia compared with participants with prediabetes. WC, VAT, and LA were better predictors of incident diabetes compared with HbA_{1c} among individuals with normoglycemia when added to age, sex, and education, whereas HbA_{1c} was more predictive in this model among individuals with prediabetes.

Table 4. Association of Adiposity With Incident Diabetes Stratified by Normoglycemia Versus Prediabetes from Sample 1

	Unadjusted	Model 1	Model 2	Model 3	Model 4	Model 5
	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value
Normoglycemia (n=1392)						
z-BMI	1.38 (1.06–1.82), *P*=0.0188	1.52 (1.14–2.03), *P*=0.0045	0.74 (0.38–1.41), *P*=0.3580	NA	0.67 (0.34–1.33), *P*=0.2509	0.76 (0.38–1.50), *P*=0.4211
z-WC	1.73 (1.34–2.24), *P*<0.0001	1.76 (1.34–2.30), *P*<0.0001	NA	2.22 (1.27–3.86), *P*=0.0049	2.09 (1.17–3.73), *P*=0.0128	2.41 (1.32–4.37), *P*=0.0040
z-Log adiponectin	0.62 (0.46–0.84), *P*=0.0019	0.62 (0.45–0.86), *P*=0.0038	0.66 (0.47–0.93), *P*=0.0183	0.65 (0.46–0.91), *P*=0.0113	NA	0.66 (0.47–0.93), *P*=0.0163
z-Log leptin	1.06 (0.77–1.44), *P*=0.7283	1.53 (0.98–2.37), *P*=0.0594	0.73 (0.40–1.32), *P*=0.2974	1.10 (0.65–1.87), *P*=0.7253	NA	0.76 (0.41–1.43), *P*=0.3969
z-Log leptin:adiponectin ratio	1.45 (1.03–2.03), *P*=0.0342	1.78 (1.22, 2.60), *P*=0.0027	1.29 (0.82, 2.05), *P*=0.2733	1.56 (1.00, 2.41), *P*=0.0483	1.37 (0.86, 2.18), *P*=0.1905	NA
Prediabetes (n=1030)						
z-BMI	1.24 (1.12–1.37), *P*<0.0001	1.23 (1.11–1.37), *P*=0.0002	1.05 (0.86–1.29), *P*=0.6358	NA	1.00 (0.80–1.24), *P*=0.9704	1.05 (0.85–1.31), *P*=0.6358
z-WC	1.30 (1.16–1.45), *P*<0.0001	1.28 (1.14–1.44), *P*<0.0001	NA	1.23 (1.00–1.51), *P*=0.0435	1.12 (0.89–1.39), *P*=0.3349	1.15 (0.92–1.42), *P*=0.2214
z-Log adiponectin	0.78 (0.69–0.88), *P*<0.0001	0.72 (0.63–0.82), *P*<0.0001	0.74 (0.65–0.86), *P*<0.0001	0.73 (0.64–0.84), *P*<0.0001	NA	0.74 (0.65–0.85), *P*<0.0001
z-Log-leptin	1.25 (1.08–1.43), *P*=0.0021	1.37 (1.13–1.67), *P*=0.0016	1.10 (0.85–1.41), *P*=0.4819	1.16 (0.91–1.49), *P*=0.2319	NA	1.09 (0.83–1.42) *P*=0.5367
z-Log-leptin: adiponectin ratio	1.46 (1.27–1.68), *P*<0.0001	1.53 (1.31–1.79), *P*<0.0001	1.42 (1.18–1.72), *P*=0.0002	1.46 (1.22–1.75), *P*<0.0001	1.42 (1.18–1.72), *P*=0.0002	NA

HR indicates hazard ratio; and NA, not available.
Model 1: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, systolic blood pressure (SBP).
Model 2: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, and waist circumference (WC).
Model 3: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, and body mass index (BMI).
Model 4: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition. SBP, *z*-WC, *z*-BMI, *z*-log-leptin:adiponectin ratio.
Model 5: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, *z*-WC, *z*-BMI, *z*-log-adiponectin, *z*-log-leptin.

Table 5. Association of Adiposity With Incident Diabetes Stratified by Normoglycemia Versus Prediabetes from Sample 2

(B)	Unadjusted	Model 1	Model 2	Model 3	Model 4
	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value	HR (CI), *P* value
Normoglycemia (n=602)					
z-BMI	2.28 (1.41–3.68), *P*=–0.0008	2.86 (1.56–5.22), *P*=0.0007	3.18 (1.01–10.0), *P*=0.0477	NA	15.0 (2.37–94.4), *P*=0.0040
z-WC	2.25 (1.36–3.72), *P*=0.0017	2.38 (1.30–4.35), *P*=0.0050	NA	0.87 (0.25–3.04), *P*=0.8287	0.45 (0.05–4.0), *P*=0.4752
z-LA	0.39 (0.28–0.54), *P*<0.0001	0.37 (0.24–0.56), *P*<0.0001	0.42 (0.26–0.67), *P*=0.0003	0.44 (0.28–0.69), *P*=0.0003	0.41 (0.20–0.81), *P*=0.0108
z-SAT	1.37 (0.78–2.40), *P*=0.2804	1.82 (0.94–3.49), *P*=0.0738	0.54 (0.13–2.23), *P*=0.3932	0.18 (0.03–0.97), *P*=0.0460	0.21 (0.03–1.71), *P*=0.1459
z-VAT	2.82 (1.92–4.14), *P*<0.0001	2.52 (1.55–4.08), *P*=0.0002	2.26 (1.08–4.74), *P*=0.0305	1.83 (1.08–3.09), *P*=0.0238	1.08 (0.43–2.75), *P*=0.8705
Prediabetes (n=935)					
z-BMI	1.44 (1.22–1.69), *P*<0.0001	1.41 (1.18–1.68), *P*=0.0001	1.23 (0.85–1.78), *P*=0.2717	NA	1.00 (0.63–1.59), *P*=0.9949
z-waist circumference	1.37 (1.17, 1.60), *P*=0.0001	1.38 (1.17, 1.62), *P*=0.0001	NA	1.16 (0.82, 1.64), *P*=0.3993	1.05 (0.72, 1.54), *P*=0.8004
z-liver attenuation	0.71 (0.62, 0.82), *P*<0.0001	0.70 (0.61, 0.80), *P*<0.0001	0.72 (0.62, 0.83), *P*<0.0001	0.72 (0.63, 0.84), *P*<0.0001	0.74 (0.64, 0.86), *P*=0.0001
z-subcutaneous adipose tissue	1.40 (1.18, 1.65), *P*=0.0001	1.37 (1.12, 1.68), *P*=0.0023	1.04 (0.74, 1.44), *P*=0.8402	0.94 (0.64, 1.39), *P*=0.7544	1.11 (0.73, 1.70), *P*=0.6236
z-visceral adipose tissue	1.40 (1.20, 1.64), *P*<0.0001	1.51 (1.28, 1.78) *P*<0.0001	1.39 (1.13, 1.72), *P*=0.0021	1.39 (1.13, 1.71), *P*=0.0022	1.31 (1.04, 1.64), *P*=0.0214

HR indicates hazard ratio; and NA, not available.

Model 1: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, and systolic blood pressure (SBP).

Model 2: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, and waist circumference (WC).

Model 3: adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, and body mass index (BMI).

Model 4: fully adjusted for age, sex, education, occupation, smoking, alcohol intake, physical activity, nutrition, SBP, *z*-WC, *z*-BMI, *z*-liver attenuation (LA), *z*-subcutaneous adipose tissue (SAT), *z*-visceral adipose tissue (VAT).

Table 6. C Indices and CIs for *z* scores of Adiposity Measures in Samples 1 and 2

Sample 1,* n=2422	Unadjusted	Model 1	Model 2	Model 3	Model 4	Model 5
BMI	0.64 (0.60–0.68)	0.66 (0.62–0.70)	0.67 (0.64–0.71)	NA	NA	NA
WC	0.67 (0.63–0.71)	0.67 (0.64–0.71)	NA	0.67 (0.64–0.71)	NA	NA
Log-adiponectin	0.62 (0.58–0.66)	0.65 (0.61–0.68)	0.69 (0.65–0.73)	0.68 (0.65–0.72)	NA	NA
Log-leptin	0.57 (0.53–0.61)	0.64 (0.60–0.68)	0.68 (0.64–0.71)	0.66 (0.62–0.70)	NA	NA
Log-leptin:adiponectin ratio	0.64 (0.60–0.68)	0.68 (0.64–0.71)	0.69 (0.65–0.73)	0.68 (0.64–0.72)	0.69 (0.65–0.73)	0.70 (0.66–0.73)
Sample 2,† n=1537		**Unadjusted**	**Model 1**	**Model 2**	**Model 3**	**Model 4**
BMI		0.62 (0.55–0.68)	0.64 (0.57–0.70)	0.64 (0.57–0.70)	NA	NA
WC		0.60 (0.54–0.66)	0.63 (0.57–0.69)	NA	0.64 (0.57–0.70)	NA
LA		0.65 (0.59–0.72)	0.65 (0.59–0.71)	0.67 (0.61–0.73)	0.67 (0.61–0.73)	NA
SAT		0.60 (0.54–0.66)	0.62 (0.55–0.68)	0.63 (0.56–0.69)	0.64 (0.57–0.70)	NA
VAT		0.67 (0.61–0.73)	0.67 (0.61–0.74)	0.67 (0.61–0.73)	0.67 (0.61–0.74)	0.69 (0.63–0.75)

NA indicates not available. C indexes for models including covariates in addition to the adiposity measures (eg, models 1–5) correspond to the overall predictive ability of the model.

Model 1: includes age, sex, and education.

Model 2: includes age, sex, education, and *z*-waist circumference (WC).

Model 3: includes age, sex, education, and *z*-body mass index (BMI).

Model 4: includes age, sex, education, z-WC, z-BMI, z-log-leptin:adiponectin ratio.

Model 5: fully includes age, sex, education, *z*-WC, *z*-BMI, *z*-log-adiponectin, *z*-log-leptin.

Model 1: includes age, sex, and education.

Model 2: includes age, sex, education and *z*-WC.

Model 3: includes age, sex, education, and *z*-BMI.

Model 4: includes age, sex, education, *z*-WC, *z*-BMI, *z*-liver attenuation (LA), *z*-subcutaneous adipose tissue (SAT), and *z*-visceral adipose tissue (VAT).

*Sample 1: examination 1 to 2.

†Sample 2: examination 2 to 3.

Comparison With Previous Studies

In the ARIC (Atherosclerosis Risk in Communities) study,[8] several anthropometric measures of adiposity (standardized [*z* scores]) including BMI and WC were associated with higher risk of incident diabetes among 12 121 participants over an 11-year period. HRs for BMI and WC among Black men (n=1020) and women (n=1610) were comparable with those in both samples in the current study. However, it is important to note that investigators in the ARIC study only adjusted for age. In addition, similar values for BMI and WC with respect to the C statistic were identified between the current study (Table 6, model 1) and the ARIC study. Notably, the study also stratified by sex.[8] We tested for effect modification by sex, but the interaction term was nonsignificant. Additionally, it is important to note that 481 participants in sample 1 and 290 in sample 2 of the current investigation were also part of the ARIC study. Thus, part of the concordance may be explained by the overlap of participants.

There are important racial and ethnic differences in body composition between Black and non-Hispanic White individuals, with Black having less VAT and higher amounts of SAT.[26] Hardy et al[8] found that race modified the association of BMI, WC, waist to hip ratio, and waist to height ratio with risk of incident diabetes in the ARIC study. However, BMI, WC, waist to hip ratio, and waist to height ratio were comparable in their discriminative ability of incident diabetes among sex and racial groups.[8] Greater differences in predictive power for central and overall measures of adiposity with incident diabetes between Black and other racial and ethnic groups were observed in IRAS (Insulin Resistance Atherosclerosis Study).[10] Among non-Hispanic White and Hispanic Americans, BMI had the most predictive power for incident diabetes. However, in Black participants, subscapular:tricep fat ratio and the waist to hip ratio (central measure of adiposity) were more predictive than overall measures of adiposity. A meta-analysis of cross-sectional and longitudinal studies in racially and ethnically diverse samples, but not specifically among Black, found that measures of central adiposity generally had greater discriminative ability for incident diabetes.[13] The waist to height ratio had the highest pooled C statistic, but the difference in discriminative ability compared with BMI was significant only among men.[13] Overall, while anthropometric measures of central adiposity had greater predictive ability for incident diabetes, differences between BMI and these measures were relatively small.[13]

Public Health and Health Equity

The age-adjusted prevalence of prediabetes among Black is 32%, which increases monotonically with BMI.[27] Interventions such as the Diabetes Prevention Program are effective in preventing the transition from prediabetes

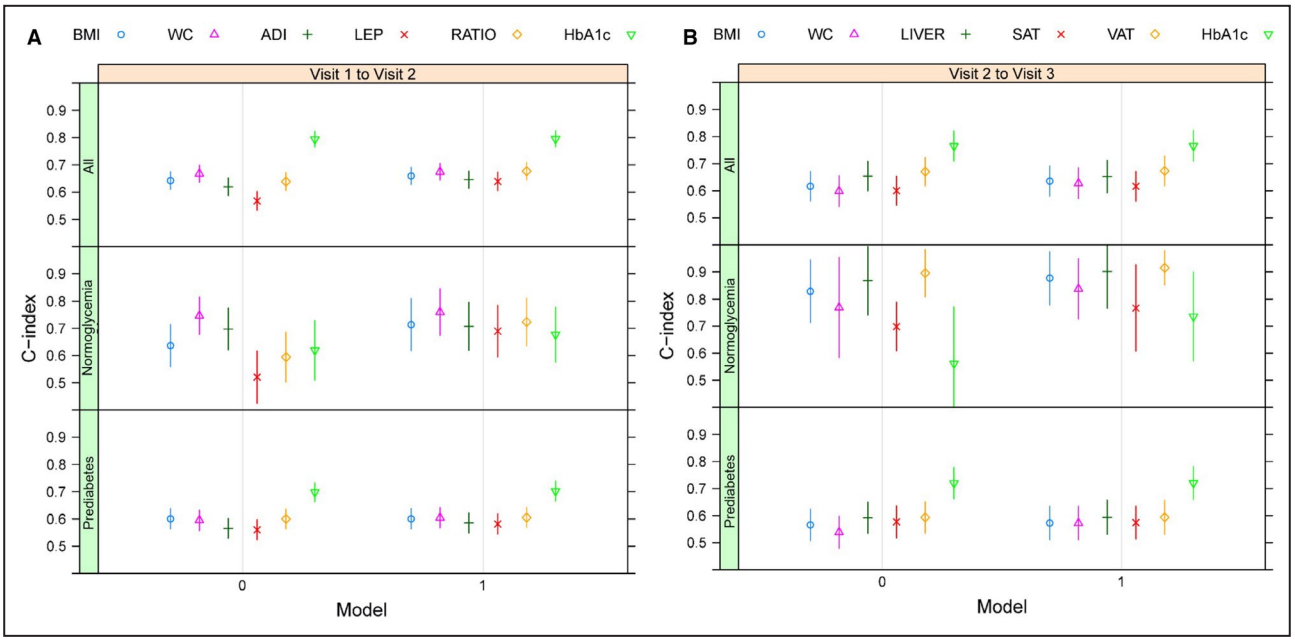

Figure 1. C indices and CIs for *z* scores of adiposity measures.
A, C indices and CIs for *z* scores of adiposity measures in sample 1. C indices from Cox models for time to diabetes between examination 1 and examination 2 (sample 1). The following variables were evaluated as predictors: BMI=*z* score for body mass index, WC=*z* score for waist circumference, ADI=*z* score for log-adiponectin, LEP=*z* score for log-leptin, ratio=*z* score for log-leptin:log-adiponectin ratio, and HbA_{1c}=hemoglobin A_{1c}. Variables were included in sequential models in stepwise fashion: model 0=unadjusted; model 1=includes age, sex, and education; plotted points give estimated C index values, while vertical bars indicate 95% CIs. **B**, CI indices and CIs for *z* scores of adiposity measures in sample 2. C indices from Cox models for time to diabetes between examination 2 and examination 3 (sample 2). The following variables were evaluated as predictors: BMI=*z* score for body mass index, WC=*z* score for waist circumference, ADI=*z*-score for log-adiponectin, LEP=*z* score for log-leptin, ratio=*z* score for log-leptin:log-adiponectin ratio, and HbA_{1c}=hemoglobin A_{1c}. Variables were included in sequential models in stepwise fashion: model 0=unadjusted; model 1=includes age, sex, and education; plotted points give estimated C index values, while vertical bars indicate 95% CIs.

to diabetes.[28] The current strategy using glycemia as the indicator of risk status has the potential to delay the initiation of high-intensity lifestyle interventions for those considered low risk by glycemic standards. In this study, we elucidate the potential utility of assessing WC, VAT, and LA to determine diabetes risk among Black with normoglycemia currently considered low risk by glycemic standards. The development of improved screening among low-risk individuals may be vital towards reducing current racial disparities in diabetes incidence. The excellent discriminative ability of WC, VAT, and LA when added to a basic demographic risk model (age, sex, and education) shows the potential value of testing these screening measures among Black adults. Given that the incidence of type 2 diabetes is decreasing among non-Hispanic White individuals but still rising among Black, strategies for earlier detection are paramount to decrease disparities in diabetes incidence and prevalence and advance cardiometabolic health equity.[1]

Mechanisms

Weight gain occurs when caloric intake exceeds energy expenditure with triacylglycerol being stored in abdominal VAT and SAT as the body's primary long-term energy reservoir, with secondary storage sites being ectopic deposition in skeletal muscle, heart, pancreas, and liver. Adipose tissue expansion occurs to accommodate increased energy storage demands. Adiposity impairs glucose metabolism by 3 main mechanisms: 1) adipokines; 2) systemic inflammation; and 3) free fatty acids. Several mechanisms by which obesity increases the risk for diabetes may be mediated via adipokines. Adiponectin, an adipokine that is decreased in obesity,[29] increases insulin sensitivity through activating AMP-activated protein kinase and peroxisome proliferator activated receptor-α.[29] In addition to adipokines, obesity-associated tissue inflammation influences insulin sensitivity, and IL-6 is a key inflammatory mediator in the pathogenesis of type 2 diabetes released from SAT.[30] Last, release of free fatty acid from adipose tissue into plasma and increased tissue free fatty acid delivery can impair the ability of insulin to suppress hepatic glucose production and stimulate muscle glucose uptake.[31]

Strengths and Limitations

Although not a strength nor a limitation, it should be noted that sample 1 and sample 2 are not designed

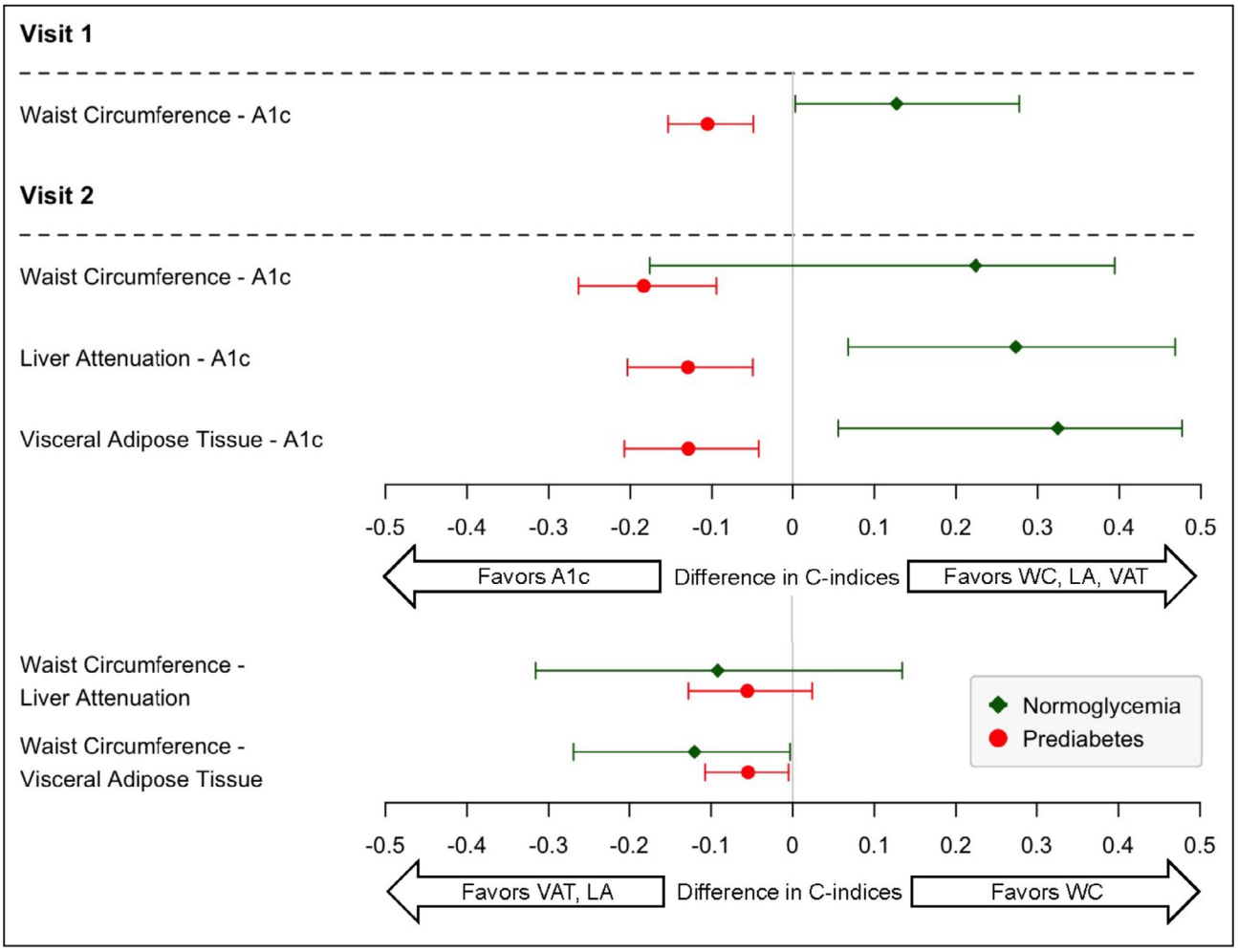

Figure 2. Difference in C index values between selected measures.
95% CIs for the difference in C index values were constructed using the bootstrap percentile method. C index values of the presented measures correspond to model 0 (Table 5). CIs are based on the 2.5th and 97.5th percentiles from 1000 bootstrap samples. HBA_{1c} indicates hemoglobin A_{1c}; LA, liver attenuation; VAT, visceral adipose tissue; WC and waist circumference.

to create a comparison. Instead, they are primarily created because of an artifact of the data collection and what variables were collected at which visit. Thus, sample 2 is a different subset of the study population because some participants from sample 1 developed diabetes before the data collection for sample 2 and were excluded. Because of this, sample 2 is by construction older and composed of those who have lived longer without developing diabetes. Thus, these analyses should be viewed as separate substudies exploring measures that capture different aspects of adiposity. The strengths of the study include a large, socioeconomically diverse, Black cohort along with validated questionnaires and a comprehensive ascertainment of diabetes, including fasting glucose, HbA_{1c}, medication use, and self-reported physician diagnosis. Furthermore, we assessed a vast array of adiposity measures and the strength of associations by including adiposity measures simultaneously in models. Such an approach has seldom been adopted in prior studies. Despite these strengths, our study has limitations. First, JHS participants are from one geographic area in the southeastern United States and may not be representative of all Black. Second, although validated, self-reported measures of physical activity and dietary intake were used, thus there was a potential for misclassification and residual confounding by these variables caused by lack of precision compared with objective measures. Third, we did not have CT measures and biomarkers at the same examination to allow for direct comparison at the same points in time, although, given that BMI and WC were similar over the 4 years, it is unlikely that CT measures significantly changed. Finally, the relationship of adiposity with incident diabetes may have been underestimated, as individuals with diabetes defined by the 2-hour post-load blood glucose criteria, may have remained undetected.

CONCLUSIONS

Among participants without diabetes, higher WC, leptin:adiponectin ratio, LA, and VAT are all associated with higher and adiponectin with lower risk of incident diabetes after full adjustment for correlated measures of adiposity. Among participants with normoglycemia, only adiponectin and LA were associated with risk of incident diabetes, and WC, VAT, and LA were much better predictors of incident diabetes among individuals with normoglycemia compared with HbA_{1c} when added to the basic demographic risk model (age, sex, and education). However, in Black adults with prediabetes, addition of HbA_{1c} to a basic demographic risk model is most predictive for incident diabetes. These findings support promotion of broader implementation of guidelines recommending checking WC, consistent with calls by Gerald Reaven and others in the late 1980s, among those with normal glycemia. Additionally, the results suggest that as technological innovation advances towards radiation-free imaging such as transient elastography, measurement of LA and VAT may improve prediction of diabetes versus HbA_{1c} and allow the identification of individuals with normoglycemia who would benefit from high-intensity interventions. These efforts, combined with intensive public health efforts targeting multiple domains (eg, health care practice [multidisciplinary care with individuals trained in weight loss], health policy [eg, sugar-sweetened beverage tax], education, and city planning [increased safe spaces for physical activity]), would advance diabetes prevention and health equity.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Table S1

REFERENCES

1. Benoit SR, Hora I, Albright AL, Gregg EW. New directions in incidence and prevalence of diagnosed diabetes in the USA. *BMJ Open Diab Res Care*. 2019;7:e000657. DOI: 10.1136/bmjdrc-2019-000657.
2. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. *NCHS Data Brief*. 2020;1–8.
3. Narayan KM, Boyle JP, Thompson TJ, Gregg EW, Williamson DF. Effect of BMI on lifetime risk for diabetes in the U.S. *Diabetes Care*. 2007;30:1562–1566. DOI: 10.2337/dc06-2544.
4. Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. *Diabetes Res Clin Pract*. 2014;105:141–150. DOI: 10.1016/j.diabres.2014.04.006.
5. Jung UJ, Choi MS. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. *Int J Mol Sci*. 2014;15:6184–6223. DOI: 10.3390/ijms15046184.
6. Liu J, Fox CS, Hickson DA, May WD, Hairston KG, Carr JJ, Taylor HA. Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: the Jackson Heart Study. *J Clin Endocrinol Metab*. 2010;95:5419–5426. DOI: 10.1210/jc.2010-1378.
7. Liu J, Fox CS, Hickson D, Bidulescu A, Carr JJ, Taylor HA. Fatty liver, abdominal visceral fat, and cardiometabolic risk factors: the Jackson heart study. *Arterioscler Thromb Vasc Biol*. 2011;31:2715–2722. DOI: 10.1161/ATVBAHA.111.234062.
8. Hardy DS, Stallings DT, Garvin JT, Xu H, Racette SB. Best anthropometric discriminators of incident type 2 diabetes among white and black adults: a longitudinal ARIC study. *PLoS One*. 2017;12:e0168282. DOI: 10.1371/journal.pone.0168282.
9. Schulze MB, Heidemann C, Schienkiewitz A, Bergmann MM, Hoffmann K, Boeing H. Comparison of anthropometric characteristics in predicting the incidence of type 2 diabetes in the EPIC-potsdam study. *Diabetes Care*. 2006;29:1921–1923. DOI: 10.2337/dc06-0895.
10. MacKay MF, Haffner SM, Wagenknecht LE, D'Agostino RB, Hanley AJ. Prediction of type 2 diabetes using alternate anthropometric measures in a multi-ethnic cohort. *Diabetes Care*. 2009;32:956–958. DOI: 10.2337/dc08-1663.
11. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev*. 2012;13:275–286. DOI: 10.1111/j.1467-789X.2011.00952.x.
12. He S, Chen X. Could the new body shape index predict the new onset of diabetes mellitus in the Chinese population? *PLoS One*. 2013;8:e50573. DOI: 10.1371/journal.pone.0050573.
13. Lee CM, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol*. 2008;61:646–653. DOI: 10.1016/j.jclinepi.2007.08.012.
14. Wang M, Luo Y, Cai H, Xu L, Huang M, Li C, Dong Z, Li ZP, Feng ST. Prediction of type 2 diabetes mellitus using noninvasive MRI quantitation of visceral abdominal adiposity tissue volume. *Quant Imaging Med Surg*. 2019;9:1076–1086. DOI: 10.21037/qims.2019.06.01.
15. Taylor HA, Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, Nelson C, Wyatt SB. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis*. 2005;15:S6–4–17.
16. Joseph JJ, Echouffo Tcheugui JB, Carnethon MR, Bertoni AG, Shay CM, Ahmed HM, Blumenthal RS, Cushman M, Golden SH. The Association of ideal cardiovascular health with incident type 2 diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis. *Diabetologia*. 2016;59:1893–1903. DOI: 10.1007/s00125-016-4003-7.
17. Carpenter MA, Crow R, Steffes M, Rock W, Skelton T, Heilbraun J, Evans G, Jensen R, Sarpong D. Laboratory, reading center, and coordinating center data management methods in the Jackson Heart Study.

Am J Med Sci. 2004;328:131–144. DOI: 10.1097/00000441-200409000-00001.
18. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28:412–419. DOI: 10.1007/BF00280883.
19. Smitherman TA, Dubbert PM, Grothe KB, Sung JH, Kendzor DE, Reis JP, Ainsworth BE, Newton RL, Lesniak KT, Taylor HA. Validation of the Jackson Heart Study physical activity survey in African Americans. *J Phys Act Health*. 2009;6(Suppl 1):S124–S132. DOI: 10.1123/jpah.6.s1.s124.
20. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, et al; on behalf of the American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction. *Circulation*. 2010;121:586–613. DOI: 10.1161/CIRCULATIONAHA.109.192703.
21. Carithers TC, Talegawkar SA, Rowser ML, Henry OR, Dubbert PM, Bogle ML, Taylor HA, Tucker KL. Validity and calibration of food frequency questionnaires used with African-American adults in the Jackson Heart Study. *J Am Diet Assoc*. 2009;109:1184–1193. DOI: 10.1016/j.jada.2009.04.005.
22. Joseph JJ, Echouffo-Tcheugui JB, Talegawkar SA, Effoe VS, Okhomina V, Carnethon MR, Hsueh WA, Golden SH. Modifiable lifestyle risk factors and incident diabetes in African Americans. *Am J Prev Med*. 2017;53:e165–e174. DOI: 10.1016/j.amepre.2017.06.018.
23. Liu J, Butler KR, Buxbaum SG, Sung JH, Campbell BW, Taylor HA. Leptinemia and its association with stroke and coronary heart disease in the Jackson Heart Study. *Clin Endocrinol*. 2010;72:32–37. DOI: 10.1111/j.1365-2265.2009.03627.x.
24. Bidulescu A, Liu J, Musani SK, Fox ER, Samdarshi TE, Sarpong DF, Vaccarino V, Wilson PW, Arnett DK, Din-Dzietham R, et al. Association of adiponectin with left ventricular mass in African Americans: the Jackson Heart Study. *Circ Heart Fail*. 2011;4:747–753. DOI: 10.1161/CIRCHEARTFAILURE.110.959742.
25. American Diabetes Association. Standards of medical care in diabetes–2010. *Diabetes Care*. 2009;33:S11–S61. DOI: 10.2337/dc10-S011.
26. Katzmarzyk PT, Bray GA, Greenway FL, Johnson WD, Newton RL, Ravussin E, Ryan DH, Smith SR, Bouchard C. Racial differences in abdominal depot–specific adiposity in white and African American adults. *Am J Clin Nutr*. 2010;91:7–15. DOI: 10.3945/ajcn.2009.28136.
27. Zhu Y, Sidell MA, Arterburn D, Daley MF, Desai J, Fitzpatrick SL, Horberg MA, Koebnick C, McCormick E, Oshiro C, et al. Racial/ethnic disparities in the prevalence of diabetes and prediabetes by BMI: Patient Outcomes Research To Advance Learning (PORTAL) multisite cohort of adults in the U.S. *Diabetes Care*. 2019;42:2211–2219. DOI: 10.2337/dc19-0532.
28. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393–403. DOI: 10.1056/NEJMoa012512.
29. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature*. 2006;444:840–846. DOI: 10.1038/nature05482.
30. Bertoni AG, Burke GL, Owusu JA, Carnethon MR, Vaidya D, Barr RG, Jenny NS, Ouyang P, Rotter JI. Inflammation and the incidence of type 2 diabetes. *Diabetes Care*. 2010;33:804–810. DOI: 10.2337/dc09-1679.
31. Bergman RN, Ader M. Free fatty acids and pathogenesis of type 2 diabetes mellitus. *Trends Endocrinol Metab*. 2000;11:351–356. DOI: 10.1016/S1043-2760(00)00323-4.

SUPPLEMENTAL MATERIAL

Table S1. Adiposity Measures Correlation Matrix for measures at Exam 1 (Sample 1) and Exam 2 (Sample 2).

	Body Mass Index (Sample 1)	Body Mass Index (Sample 2)	Waist Circumference (Sample 1)	Waist Circumference (Sample 2)	SAT (Sample 2)	VAT (Sample 2)	Liver Attenuation (Sample 2)	Adiponectin (Sample 1)	Leptin (Sample 1)	Leptin:Adiponectin Ratio (Sample 1)
Body Mass Index (Sample 1)	1	0.9	0.8	0.77	0.77	0.42	-0.16	-0.14	0.61	0.5
Body Mass Index (Sample 2)	0.9	1	0.76	0.84	0.84	0.49	-0.19	-0.14	0.56	0.47
Waist circumference (Sample 1)	0.8	0.76	1	0.84	0.64	0.56	-0.22	-0.21	0.45	0.43
Waist circumference (Sample 2)	0.77	0.84	0.84	1	0.68	0.63	-0.23	-0.22	0.4	0.4
SAT (Sample 2)	0.77	0.84	0.64	0.68	1	0.32	-0.11	-0.01	0.66	0.45
VAT (Sample 2)	0.42	0.49	0.56	0.63	0.32	1	-0.3	-0.21	0.17	0.22
Liver Attenuation (Sample 2)	-0.16	-0.19	-0.22	-0.23	-0.11	-0.3	1	0.18	-0.03	-0.17
Adiponectin (Sample 1)	-0.14	-0.14	-0.21	-0.22	-0.01	-0.21	0.18	1	0.05	-0.37
Leptin (Sample 1)	0.61	0.56	0.45	0.4	0.66	0.17	-0.03	0.05	1	0.62
Leptin:Adiponectin ratio (Sample 1)	0.5	0.48	0.43	0.4	0.45	0.22	-0.17	-0.37	0.62	1

Pearson Intra-class correlations for measures between Sample 1 and Sample 2. SAT = Subcutaneous Adipose Tissue, VAT = Visceral Adipose Tissue.