

Independent effects of age-related changes in waist circumference and BMI z scores in predicting cardiovascular disease risk factors in a prospective cohort of adolescent females^{1–4}

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ABSTRACT

Background: Cross-sectional data indicate that central adiposity is associated with cardiovascular disease risk, independent of total adiposity. The use of longitudinal data to investigate the relation between changes in fat distribution and the emergence of risk factors is limited.

Objective: We tested the hypothesis that age-related change in waist circumference (to reflect central adiposity) during adolescence is a significant predictor of longitudinal change in cardiovascular disease risk, after adjustment for change in body mass index (BMI) z score (to reflect total adiposity) in a cohort of postmenarcheal adolescent females. We also tested whether race modified this relation.

Design: We analyzed publicly available data from the National Heart, Lung, and Blood Institute Growth and Health Study. Longitudinal regression models were fitted to investigate the independent effects of changes in waist circumference on cardiovascular disease risk factors.

Results: Steeper age-related increases in waist circumference over time were associated with a greater increase in LDL-cholesterol concentrations, systolic blood pressure, diastolic blood pressure, and homeostasis model assessment of insulin resistance, after adjustment for BMI z score, in white but not in black females. Change in waist circumference was not a statistically significant predictor of age-related changes in HDL-cholesterol, triglyceride, insulin, and glucose concentrations, after adjustment for changes in BMI z score, in either white or black females.

Conclusions: Our research suggests that monitoring waist circumference in addition to BMI z score has the potential to identify adolescents at risk of the emergence of cardiovascular disease risk factors, at least in white females. The data also suggest that race may modify the relation between fat distribution pattern and cardiovascular disease risk factors. *Am J Clin Nutr* 2011;93:392–401.

INTRODUCTION

Obesity, a leading contributor to cardiovascular disease morbidity and mortality in the United States, places a heavy burden on society (1). Obesity's effect on cardiovascular disease risk often emerges in childhood and adolescence; those with excess adiposity during these critical periods have an increased risk of later cardiovascular disease and obesity (2–5). Because these risk factors track from childhood into adulthood, it is

important to study them early, even if frank heart disease rarely presents before adulthood (6–15).

In adults, the intraindividual distribution of fat has long been recognized as important, with central adiposity conferring greater disease risk, perhaps because of the visceral fat depot (16–24). Although visceral fat stores in children are small before puberty, they increase and show considerable variability after puberty (25–29). The importance of fat distribution is evident in children and adolescents, with visceral fat (measured by magnetic resonance imaging) positively related to blood pressure and total cholesterol (TC), LDL-cholesterol, triglyceride, and basal insulin concentrations and inversely associated with HDL-cholesterol concentrations and insulin sensitivity (30–38). Not all studies, however, have yielded significant results (39).

Significant relations with cardiovascular disease risk factors are also seen when central adiposity is measured indirectly with an anthropometric measure such as waist circumference (WC). Such measures are commonly used in epidemiologic studies that investigate the role of central adiposity in disease risk of adults and have been used as a proxy for visceral fat in children (40). Cross-sectionally, in simple regression models, WC is a significant predictor of blood pressure and TC, LDL-cholesterol, HDL-cholesterol, and triglyceride concentrations (41–45). Because WC is correlated with total body fat, both variables must be included in regression models to investigate their independent effects (40). Some evidence indicates that cross-sectional relations between WC (or associated ratios such as waist-to-hip ratio

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or waist-to-height ratio) and cardiovascular disease risk (blood pressure and TC, LDL-cholesterol, HDL-cholesterol, and triglyceride concentrations) are independent of total adiposity, as measured by body mass index (BMI) (46–54). Other research, however, has suggested that BMI and WC do not have strong independent effects on risk factors (55). WC and related ratios predict cardiovascular disease risk, motivating the publication of percentiles from many pediatric populations (56–64). Racial differences in patterns of fat distribution emerge as early as age 7–10 y, and some, but not all, studies (35, 65) have found that race modifies the effect of central adiposity on cardiovascular disease risk (52, 66). We identified racial differences in the deposition of central adiposity during adolescence in previous analyses of this cohort (67).

The use of longitudinal data to investigate the relation between central adiposity and cardiovascular disease risk has been limited. We aimed to determine whether changes in central adiposity during adolescence, independent of changes in total adiposity, are significant predictors of cardiovascular disease risk in a large, biracial cohort. We tested the hypothesis that age-related change in WC (reflecting central adiposity) during adolescence was a significant predictor of longitudinal change in cardiovascular disease risk factors after adjusting for change in BMI *z* score (reflecting total adiposity). We also tested whether race modified this relation.

SUBJECTS AND METHODS

Data

We analyzed publicly available data from the subjects in the National Heart, Lung, and Blood Institute Growth and Health Study (NGHS)—a prospective cohort that was established to investigate how dietary patterns, physical activity levels, and psychosocial factors are related to the development of obesity in girls. This study was described previously in detail (68). Briefly, this multicenter, annual, longitudinal study consisted of 2379 girls enrolled in 1987–1988 at the age of 9–10 y in racially concordant households (race self-declared as black or white; Hispanic children were excluded) from public and parochial schools (recruited from the Richmond School district near Berkeley, CA, and from Cincinnati, OH) and a large Health Maintenance Organization in the Washington, DC area. Of the eligible girls, 78% were enrolled. At each study center, the respective Institutional Review Board approved the NGHS protocol, and all participants and their parents gave informed consent. Our investigation was approved by the Institutional Review Board of Tufts Medical Center.

Measurements

All NGHS measurements were made according to study protocol by certified, trained staff who were annually retrained and were monitored for consistency (68). At each annual visit, height and weight were measured in duplicate. Height was measured to the nearest 0.1 cm in subjects wearing socks, using custom-made stadiometers, and weight was measured by using Health-O-Meter electronic scales, to the nearest 0.1 kg, with subjects in gowns. The minimum above-waist circumference (the smallest circumference of the torso, at the “natural waist,” against

the skin) was measured annually, in duplicate, beginning with NGHS visit 2. BMI was calculated as weight (in kg) divided by the square of height (in m). Study participants were asked annually whether they had started menstruation; the data set included self-reported age at which menstruation started, measured in years to one decimal place.

Fasting TC, HDL-cholesterol, and triglyceride concentrations were measured in the morning of annual visits 3, 5, 7, and 10. TC, HDL-cholesterol, and triglyceride concentrations were analyzed enzymatically with a commercially available method, and LDL cholesterol was calculated by using a modified Friedewald formula. Fasting insulin and glucose concentrations were measured at NGHS visits 7 and 10. Blood pressure was measured in triplicate at each annual visit with a standard mercury sphygmomanometer while subjects were seated with feet resting flat and the right arm resting at heart level. Cuff sizes appropriate to upper arm circumferences were used.

Statistical analyses

Subjects who had data from ≥ 2 valid postmenarcheal visits were included in this analysis. We calculated age-specific BMI *z* score, using the Centers for Disease Control and Prevention growth reference, to serve as a measure of total adiposity (69, 70). The homeostasis model assessment (HOMA) was calculated as an index of insulin resistance, and used to investigate the longitudinal change thereof (71, 72). Blood pressure *z* scores were calculated as recommended by the National High Blood Pressure Education Program (73).

For each subject, individual change trajectories for each outcome were constructed. We examined each trajectory for outliers and investigated whether a linear model was appropriate for age-related changes in risk. Separately for each risk factor, linear longitudinal growth was modeled in SAS by using PROC MIXED, with the risk factor level as the continuous time-varying outcome variable. Age (in mo) relative to menarche was the continuous “time” variable, which was calculated by subtracting the subject’s age at menarche from their age at the study visit. WC and BMI *z* score were modeled as time-varying covariates. Data were stratified a priori on race, given the racial differences in age-related growth in central adiposity in this cohort; formal statistical tests of the interaction by race are still provided (67). All analyses were conducted in SAS (version 9.1; SAS Institute, Cary, NC).

We generated hypothetical trajectories for the risk factors of interest to represent the experiences of prototypical “average” NGHS subjects. First, the average BMI *z* score was calculated, by race and age (in y). Then, the WC values representing the 25th, 50th, and 75th percentiles were extracted. Using these values and the parameter estimates from the regression models, we created theoretical risk factor trajectories for girls with an average BMI *z* score, who differed only with respect to WC.

RESULTS

Subjects who had data from ≥ 2 valid postmenarcheal visits were included in this analysis. For analyses on HDL-cholesterol, LDL-cholesterol, and triglyceride concentrations, the sample size was 678 white females and 797 black females, with data from 1753 and 2200 subject visits, respectively, from visit 3, 5,

TABLE 1
Subject characteristics by visit: postmenarcheal data only[†]

	Visit									
	2	3	4	5	6	7	8	9	10	
White										
Age (y)	11.39 ± 0.52	12.29 ± 0.55	13.10 ± 0.54	14.02 ± 0.56	15.00 ± 0.56	15.99 ± 0.57	17.01 ± 0.59	17.94 ± 0.58	19.03 ± 0.64	
WC (cm)	68.98 ± 7.72 (93)	69.10 ± 8.47 (305)	70.05 ± 8.64 (587)	70.14 ± 8.97 (794)	70.73 ± 8.99 (783)	71.27 ± 9.52 (854)	72.41 ± 9.88 (900)	73.35 ± 10.23 (926)	74.71 ± 11.19 (977)	
BMI z score	0.93 ± 0.77 (94)	0.69 ± 0.85 (304)	0.66 ± 0.84 (590)	0.51 ± 0.88 (802)	0.46 ± 0.87 (791)	0.37 ± 0.92 (871)	0.32 ± 0.95 (904)	0.31 ± 1.00 (944)	0.29 ± 1.01 (920)	
LDL-C (mg/dL)	—	90.51 ± 23.95 (221)	—	91.51 ± 24.28 (581)	—	93.17 ± 26.43 (645)	—	—	98.62 ± 30.58 (625)	
HDL-C (mg/dL)	—	50.96 ± 10.35 (222)	—	53.86 ± 10.50 (582)	—	52.09 ± 10.10 (646)	—	—	52.44 ± 11.27 (627)	
TG (mg/dL)	—	83.18 ± 40.85 (221)	—	84.71 ± 43.95 (580)	—	85.11 ± 41.80 (644)	—	—	92.85 ± 43.54 (627)	
SBP z score	-0.20 ± 0.80 (93)	-0.03 ± 0.81 (305)	-0.10 ± 0.79 (589)	-0.17 ± 0.82 (802)	-0.41 ± 0.79 (793)	-0.32 ± 0.86 (876)	-0.38 ± 0.88 (917)	-0.33 ± 0.86 (951)	-0.36 ± 0.85 (940)	
DBP z score	-0.33 ± 1.09 (91)	-0.10 ± 0.83 (301)	-0.26 ± 0.79 (583)	-0.09 ± 0.81 (800)	-0.29 ± 0.89 (792)	-0.01 ± 0.88 (875)	-0.20 ± 0.85 (917)	-0.20 ± 0.84 (951)	-0.02 ± 0.84 (940)	
log Insulin (μU/mL)	—	—	—	—	—	2.33 ± 0.51 (624)	—	—	1.94 ± 0.75 (706)	
Glucose (mg/dL)	—	—	—	—	—	75.22 ± 13.21 (609)	—	—	91.99 ± 69.21 (735)	
HOMA	—	—	—	—	—	2.20 ± 1.50 (606)	—	—	2.07 ± 3.64 (706)	
Black										
Age (y)	11.37 ± 0.52	12.28 ± 0.54	13.13 ± 0.56	14.09 ± 0.59	15.07 ± 0.58	16.09 ± 0.58	17.07 ± 0.58	18.04 ± 0.58	19.16 ± 0.65	
WC (cm)	69.87 ± 9.47 (271)	71.31 ± 10.21 (602)	71.69 ± 10.43 (877)	72.93 ± 11.20 (1004)	73.49 ± 11.97 (937)	75.10 ± 12.58 (952)	76.17 ± 13.30 (971)	77.50 ± 13.95 (969)	79.19 ± 14.41 (1041)	
BMI z score	0.97 ± 0.90 (272)	0.88 ± 0.96 (599)	0.83 ± 0.94 (879)	0.79 ± 0.98 (1006)	0.75 ± 1.00 (957)	0.75 ± 1.00 (962)	0.73 ± 1.07 (957)	0.71 ± 1.11 (969)	0.70 ± 1.12 (932)	
LDL-C (mg/dL)	—	97.17 ± 24.38 (421)	—	91.65 ± 25.17 (691)	—	94.60 ± 29.31 (687)	—	—	97.94 ± 28.55 (718)	
HDL-C (mg/dL)	—	54.41 ± 12.03 (422)	—	57.38 ± 11.41 (691)	—	55.66 ± 11.61 (687)	—	—	54.68 ± 12.33 (718)	
TG (mg/dL)	—	70.65 ± 30.30 (423)	—	66.73 ± 26.68 (691)	—	68.85 ± 30.63 (689)	—	—	70.49 ± 32.35 (718)	
SBP z score	-0.17 ± 0.79 (272)	0.05 ± 0.79 (602)	-0.054 ± 0.80 (878)	-0.08 ± 0.84 (1006)	-0.21 ± 0.91 (958)	-0.12 ± 0.83 (968)	-0.16 ± 0.86 (971)	-0.10 ± 0.86 (988)	-0.05 ± 0.92 (963)	
DBP z score	-0.19 ± 0.88 (266)	-0.07 ± 0.86 (588)	-0.20 ± 0.85 (873)	-0.06 ± 0.83 (1005)	-0.09 ± 0.88 (953)	0.08 ± 0.87 (966)	0.01 ± 0.93 (969)	0.00 ± 0.89 (984)	0.18 ± 0.85 (962)	
log Insulin (μU/mL)	—	—	—	—	—	2.60 ± 0.61 (662)	—	—	2.25 ± 0.81 (777)	
Glucose (mg/dL)	—	—	—	—	—	77.36 ± 21.23 (658)	—	—	89.95 ± 39.09 (798)	
HOMA	—	—	—	—	—	3.55 ± 5.96 (647)	—	—	2.98 ± 4.19 (767)	

[†] All values are means ± SDs; *n* in parentheses. HOMA, homeostasis model assessment; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, LDL cholesterol; TG, triglycerides; WC, waist circumference.

TABLE 2Race-specific longitudinal regression models predicting changes in lipid concentrations from age-related changes in waist circumference: postmenarcheal data only for visits 3, 5, 7, and 10¹

	LDL cholesterol (mg/dL)		HDL cholesterol (mg/dL)		Triglycerides (mg/dL)	
	White females	Black females	White females	Black females	White females	Black females
<i>n</i>	678 (1753 obs)	797 (2200 obs)	679 (1758 obs)	797 (2201 obs)	678 (1753 obs)	798 (2204 obs)
Intercept	86.94**	73.03**	71.21**	72.00**	-19.34	21.54
Age (y postmenarche)	-7.05*	-1.55	0.34	-0.06	-3.56	-4.67*
Waist (cm)	0.04	0.26	-0.26**	-0.19*	1.51**	0.69**
Age × waist	0.11**	0.02	-4.9 × 10 ⁻³	-1.1 × 10 ⁻³	0.05	0.05
BMI <i>z</i> score	2.65	2.25	-0.90	-2.37*	0.25	-0.47
Age × BMI <i>z</i> score	-0.40	0.06	0.32*	0.18	-0.86	-0.52

¹ For SEs, see the supplemental tables under "Supplemental data" in the online issue. obs, observations. **P* < 0.05, ***P* < 0.001.

7, and 10 (**Table 1**). For analyses on longitudinal changes in blood pressure, the sample size was 1071 white females and 1153 black females, with 6070 and 7372 subject visits, respectively. For analyses on insulin, glucose, and HOMA, the sample size was 424 white females and 439 black females, with data from visits 7 and 10, respectively. Biologically implausible values for 14 measurements were excluded from the analyses.

WC increased during adolescence, as expected, with steeper increases seen in black females. On average, BMI *z* scores decreased during adolescence, and the decrease was relatively larger in white females than in black females. Both LDL-cholesterol and triglyceride concentrations increased in white females, but not in black females. The HDL-cholesterol concentration did not change significantly in either group. Glucose concentrations increased in both groups. Insulin concentrations and HOMA decreased, which reflected the end of pubertal development and its associated insulin resistance.

Multilevel regression models were fitted to test whether the change in central adiposity was a significant predictor of change in each risk factor, after adjustment for change in total adiposity. Steeper age-related increases in WC over time were associated with an increase in LDL-cholesterol concentrations, after adjustment for BMI *z* score, but only in white females (**Table 2**; *P* < 0.001). This significant relation with LDL-cholesterol concentration was not seen in black females (the formal test for the interaction by race was statistically significant, *P* = 0.008). Prototypical trajectories representing the characteristics of subjects with an average BMI *z* score at 3 contrasting levels of WC indicate steeper age-related increase in white females (**Figure 1**).

For age-related changes in HDL-cholesterol and triglyceride concentrations, change in WC was not a statistically significant predictor after adjustment for changes in BMI *z* score, in either white or black females (Table 2; HDL: *P* = 0.74 for white females and *P* = 0.90 for black females; triglyceride: *P* = 0.45 for white females and *P* = 0.06 for black females). The estimates for black and white females were similar in magnitude, and the formal test of the interaction was not statistically significant for HDL-cholesterol or triglyceride concentrations (*P* = 0.50 and 0.29, respectively; Figure 1). Postmenarcheal age-related increases in blood pressure (both systolic blood pressure and diastolic blood pressure *z* score) were significantly predicted by increases in WC after adjustment for changes in BMI *z* score; however, again, only in white females (systolic blood pressure:

P = 0.002 in white females and *P* = 0.21 in black females; diastolic blood pressure: *P* = 0.018 in white females and *P* = 0.07 in black females, **Table 3, Figure 2**).

For postmenarcheal changes in insulin and glucose concentrations and in HOMA, models were fitted to data from NGHs visits 7 and 10. Changes in WC did not predict changes in insulin or glucose concentrations, after adjustment for changes in BMI *z* score (insulin: *P* = 0.14 for white females and 0.23 for black females; glucose: *P* = 0.22 for white females and 0.81 for black females; **Table 4, Figure 3**); formal tests for the interaction by race were not statistically significant. Steeper increases in WC predicted significantly higher HOMA after adjustment for BMI *z* score, but only in white females (*P* = 0.003; Table 4, Figure 3; the test for the interaction by race was significant, *P* = 0.014). The same relations remained statistically significant after a Bonferroni correction for the parameter estimates of interest.

DISCUSSION

We tested the hypothesis that change in the WC of females during adolescence, as a measure of central adiposity, was a significant predictor of longitudinal change in cardiovascular disease risk, after adjusting for change in BMI *z* score (a proxy for total adiposity). We found that increases in WC significantly predicted increases in LDL-cholesterol concentrations, systolic and diastolic blood pressure, and HOMA, independent of changes in total adiposity, but only in white females. HDL-cholesterol, triglyceride, glucose, and insulin concentrations were not related to changes in WC after adjustment for BMI *z* score in either white or black females.

In cross-sectional data on children and adolescents, LDL-cholesterol concentrations, blood pressure, and insulin resistance have been linked to central adiposity, independent of total adiposity. For example, children aged 5–17 y in the Bogalusa Study who had high WC had significantly higher LDL-cholesterol concentrations than did those of comparable height and weight with a low WC (74). Results similar to ours have also been seen for blood pressure; in prepubertal Italian children, WC was associated with higher blood pressure readings after adjustment for BMI (46). Other evidence also supports this BMI-independent link between WC and blood pressure (52). Finally, insulin resistance, which we approximated on the basis of HOMA, has been shown to be related to WC, after adjustment for BMI *z* score (47).

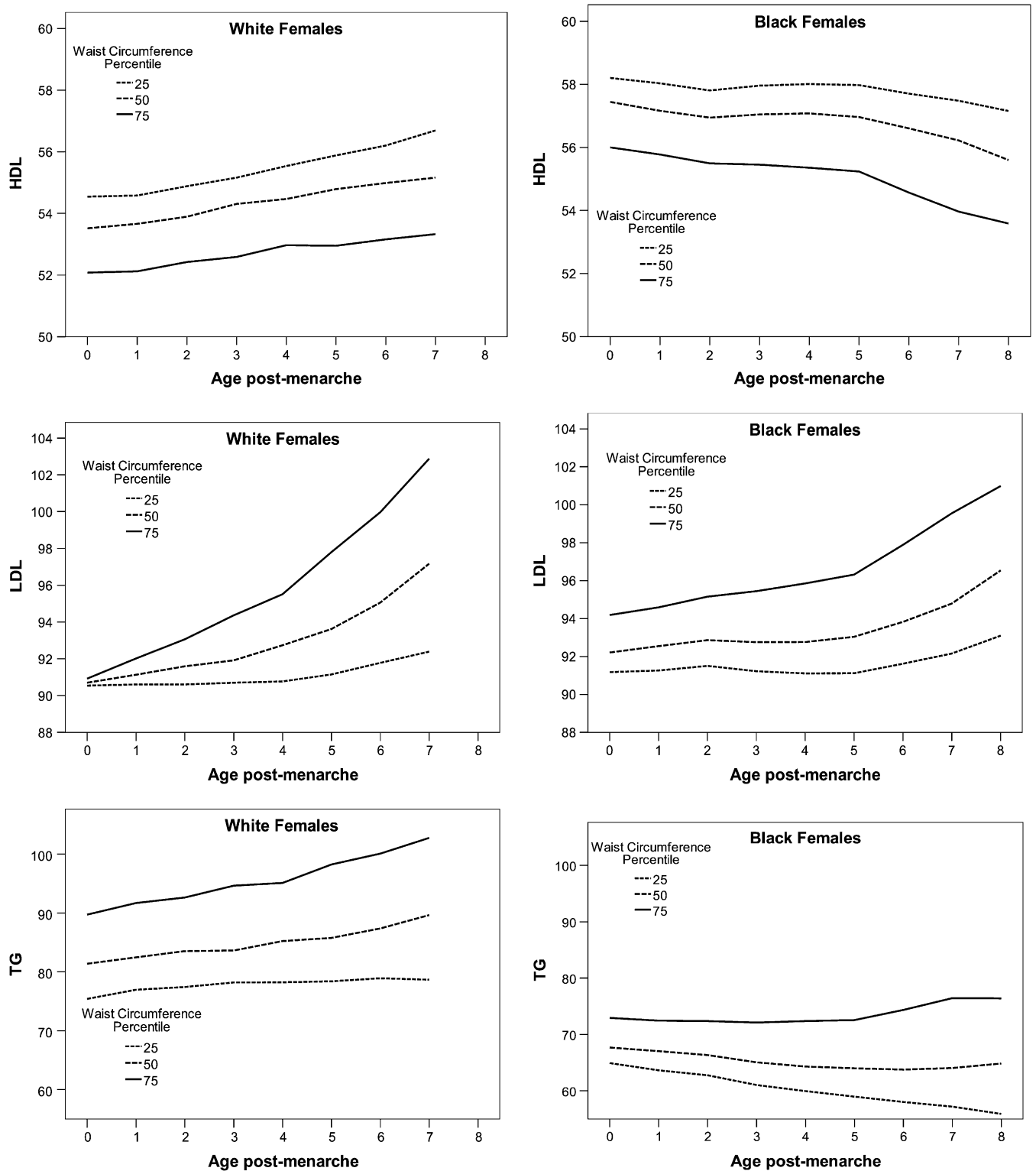


FIGURE 1. Prototypical LDL-cholesterol, HDL-cholesterol, and triglyceride (TG) (mg/dL) trajectories for girls with an average BMI z score and select waist circumferences.

We found no evidence that changes in WC were predictive of changes in HDL-cholesterol, triglyceride, insulin, or glucose concentrations. Some cross-sectional studies have yielded results similar to ours. In Spanish females aged 13–18 y, WC was not related to HDL-cholesterol concentration after control for BMI

(48). Other researchers, however, have found that central adiposity is a significant predictor of these risk factors, such as the aforementioned study on prepubertal Italian children (46). In Portuguese children of ≈13 y of age, high central adiposity (measured by skinfold thickness) was a significant predictor of

TABLE 3

Race-specific longitudinal regression models predicting changes in blood pressure (z scores) from age-related changes in waist circumference: postmenarcheal data only for visits 2–10¹

	Systolic blood pressure		Diastolic blood pressure	
	White females	Black females	White females	Black females
<i>n</i>	1071 (6086 obs)	1153 (7412 obs)	1071 (6070 obs)	1153 (7372 obs)
Intercept	-0.64*	-0.71**	-0.43	-0.16
Age (y postmenarche)	-0.18**	-0.04	-0.12*	-0.04
Waist (cm)	4.3×10^{-3}	5.6×10^{-3}	3.0×10^{-3}	-9.9×10^{-4}
Age \times waist	2.3×10^{-3} *	6.0×10^{-4}	1.9×10^{-3} *	1.1×10^{-3}
BMI z score	0.28**	0.26**	0.02	0.07
Age \times BMI z score	-0.02*	-0.01*	-0.01	-0.01

¹ For SEs, see the supplemental tables under “Supplemental data” in the online issue. obs, observations. * $P < 0.05$, ** $P < 0.001$.

low HDL-cholesterol concentration, after control for total body fat as measured by dual-energy X-ray absorptiometry (49). In prepubertal children in the nationally representative National Health and Nutrition Examination Survey (NHANES), central adiposity (based on waist-to-hip ratio) was associated with increased triglyceride concentrations, after adjustment for BMI (50). In addition, in the aforementioned Bogalusa Study, WC predicted insulin after adjustment for height and weight (74).

In some cross-sectional studies, race modified the effect of WC on cardiovascular disease risk, after adjustment for BMI. In girls aged 7–10 y, increased subcutaneous abdominal adipose tissue (measured by magnetic resonance imaging; $n = 40$) was significantly related to insulin concentrations in black, but not in white, females (66). This racial difference, however, was not evident with respect to the subjects’ lipid profiles. Similarly, in prepubertal girls who had visceral fat measured by computed

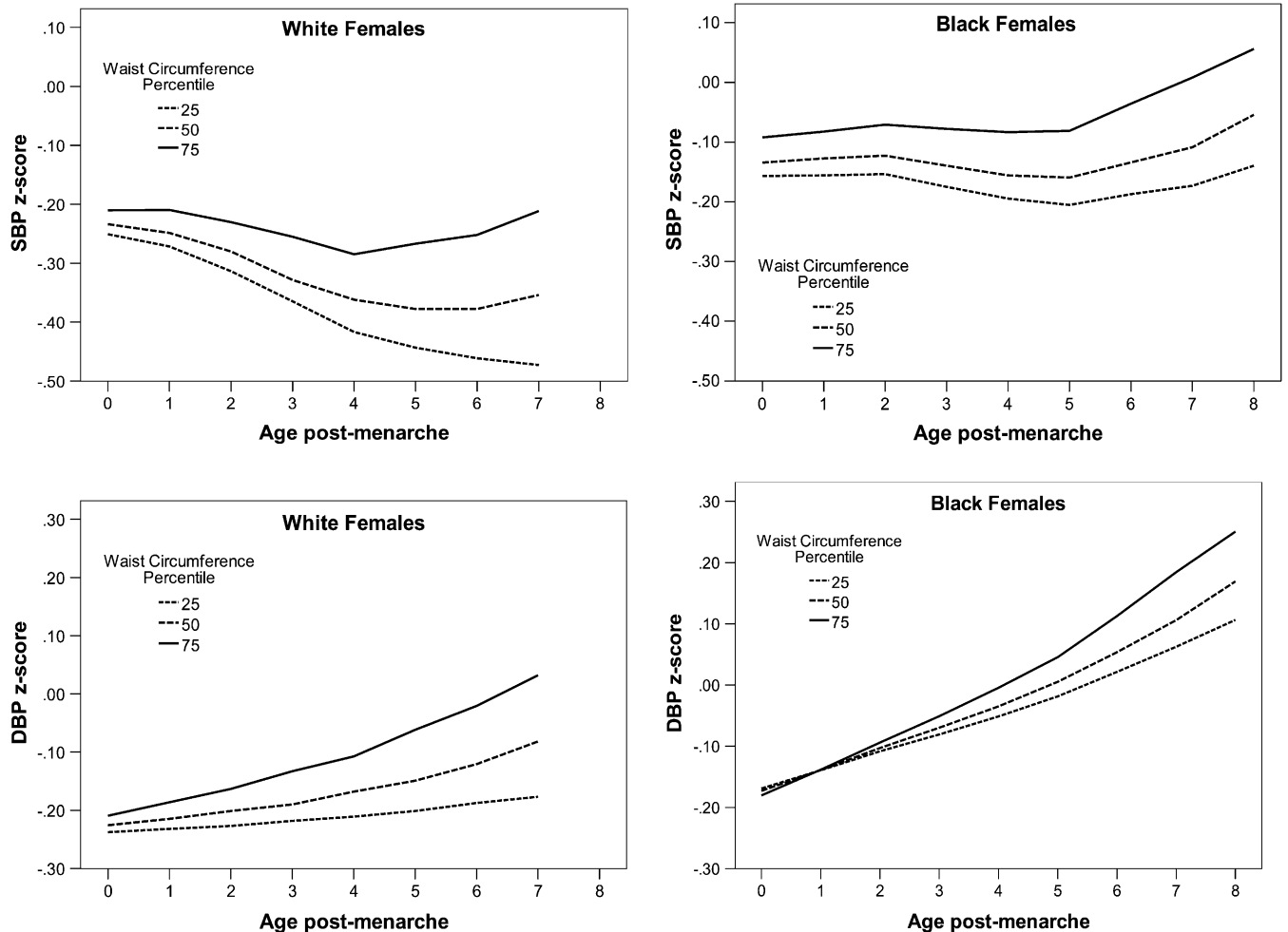


FIGURE 2. Prototypical systolic blood pressure (SBP) and diastolic blood pressure (DBP) z score trajectories for girls with an average BMI z score and select waist circumferences.

TABLE 4

Race-specific longitudinal regression models predicting change in insulin (ln), glucose, and homeostasis model assessment (HOMA) from age-related change in waist circumference: postmenarcheal data only for visits 7 and 10¹

	Insulin ($\mu\text{U/mL}$)		Glucose (mg/dL)		HOMA	
	White females	Black females	White females	Black females	White females	Black females
<i>n</i>	428	453	436	453	424	439
Intercept	2.4742**	2.42**	61.14*	24.82	2.27	-7.97
Age (y postmenarche)	-0.2917*	-0.25*	-3.55	2.97	-1.10*	0.75
Waist (cm)	4.9×10^{-4}	5.5×10^{-3}	8.1×10^{-2}	0.65*	2.1×10^{-4}	0.16*
Age \times waist	2.7×10^{-3}	1.9×10^{-3}	0.11	-1.1×10^{-2}	0.01*	-0.01
BMI <i>z</i> score	0.1865*	0.09	-0.56	-5.76	0.46*	-0.32
Age \times BMI <i>z</i> score	-0.01	0.01	-1.02	0.43	-0.09	0.09

¹ For SEs, see the supplemental tables under "Supplemental data" in the online issue. * $P < 0.05$, ** $P < 0.001$.

tomography ($n = 61$), no evidence that the relation between central adiposity and cardiovascular disease risk (insulin sensitivity, triglycerides, and HDL cholesterol) differed by race was observed, after adjustment for total fat (35). In adults, central adiposity confers greater disease risk in white woman than in black women, independent of total adiposity (75, 76), which suggests that differences arise during adolescence.

One explanation for the racial differences in our analysis is that central adiposity comprises both visceral and subcutaneous fat depots. In adults, black women have less visceral fat than whites after total adiposity is accounted for (77, 78). Similarly, white children have more total and intraabdominal fat than do black children of similar BMI (26, 29, 79, 80). If the visceral adipose depot is important in the relation between fat distribution and cardiovascular disease risk factors, differential deposition of fat by black and white female adolescents could explain our findings.

A major strength of our analysis was the collection of longitudinal data during adolescence to investigate changes in cardiovascular disease risk over this critical period. This permits investigations about changes in body composition and their effects on risk factors—hypotheses not testable with cross-sectional data. The NGHS provides data for the longitudinal analysis of a large sample of girls with an exceptionally high follow-up rate (89% at the final visit), which allows statistical control for variables of interest.

We elected to use commonly used clinical measures: WC as a proxy for central adiposity and BMI *z* score to reflect total adiposity. A limitation of our analyses was the absence of dual-energy X-ray absorptiometry and computed tomography data—direct measures of visceral fat. If these tools were used, some common critiques of BMI would be avoided, such as the inability of BMI to distinguish between differences in body composition (eg, higher bone density of black females relative to whites) (81). These measures, however, are not feasible in a large epidemiologic study such as the NGHS (82). The use of BMI and WC allows for large sample sizes and provides ample statistical power to detect significant differences. Although BMI and WC could contribute to measurement error, it is likely to be random and thus does not introduce bias to the observed relations. Also, although the NGHS measurement protocol for WC does not accord to current recommendations by the National Institutes of Health or the World Health Organization, the use of a consistent protocol over the course of the cohort likely outweighs the small differences that arise from different measure-

ment protocols (83, 84). Of note, visceral fat stores, which are small during adolescence, might not be the only factor linking central adiposity and cardiovascular disease risk (27). Thus, it is possible that WC is more appropriate in this situation, given that the measure also encompasses subcutaneous fat, which has been suggested to have a role in insulin resistance for children with small amounts of visceral fat (85).

Another potential limitation of our analysis was the generalizability of the NGHS data. This study was not designed to be representative of any specific population; thus, the descriptive statistics for this large cohort of black and white females—enrolled over 20 y ago from 3 parts of the country—do not necessarily reflect the contemporary US population, in which the prevalence of obesity is high. The NGHS sample did, however, have a baseline prevalence of obesity comparable with the contemporaneous NHANES III and a final-year prevalence similar to NHANES 1999–2000 (86, 87). For example, in NHANES 1999–2000, the prevalence of overweight (>85th percentile BMI *z* score) at age 12–19 y was 25.4% in white females and 45.4% in black females; in our NGHS analysis, the respective values were 22.9% in white females and 43.7% in black females. Also, the prevalences of obesity in NHANES 1999–2000 and the final year of NGHS were similar: 12.4% of white females and 26.6% of black females in NHANES compared with 10.9% of white females and 24.7% of black females in the NGHS. Furthermore, there is no reason to believe that our major finding—that changes in WC during adolescence can lead to changes in select risk factors—would not be replicated in other cohorts of postmenarcheal adolescent females.

In conclusion, we found that changes in central adiposity during adolescence were significant predictors of changes in LDL-cholesterol concentrations, blood pressure, and insulin resistance for white, but not black, females. These relations were independent of changes in total adiposity. This suggests that monitoring WC in addition to BMI *z* score has the potential to identify adolescents at risk of the emergence of cardiovascular disease risk factors, at least in white females. The data also suggest that race is a potential effect modifier in the relation between fat distribution patterns and cardiovascular disease risk—an observation that should be taken into consideration for future research.

The authors' responsibilities were as follows—DJT: responsible for the study design, data analysis, and writing of the manuscript under the

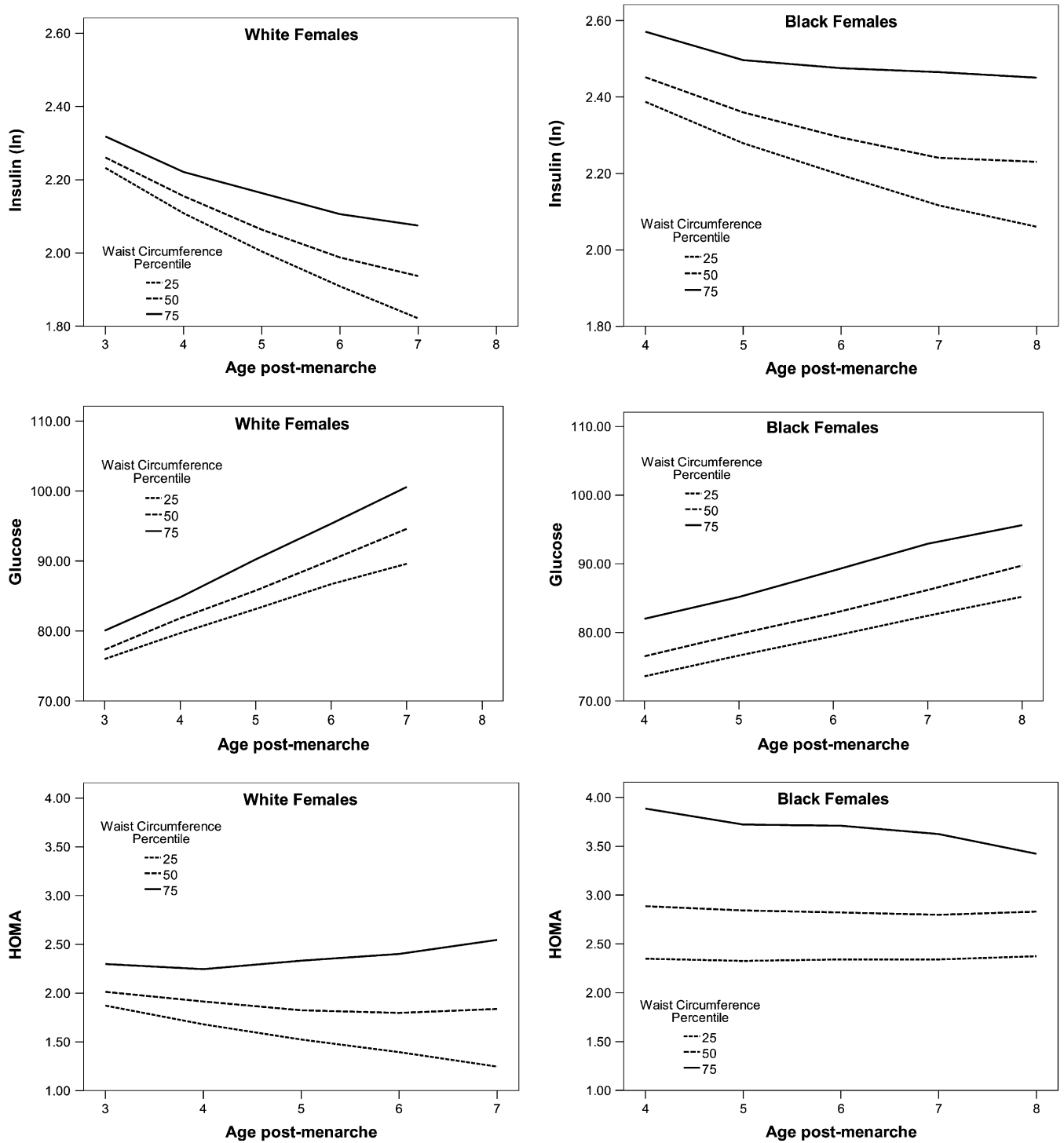


FIGURE 3. Prototypical glucose (mg/dL), insulin (μ U/mL), and homeostasis model assessment (HOMA) trajectories for girls with an average BMI z score and select waist circumferences.

supervision of AM; GED: provided statistical consultation; and AHL and SRD: provided critical input and advice. All authors contributed manuscript revisions and approved the final version. None of the authors had any conflicts of interest to report.

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