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# Associations of BMI and its fat-free and fat components with blood lipids in children: Project HeartBeat!

**Shifan Dai**[†,1], **Mona A Eissa**[2], **Lyn M Steffen**[3], **Janet E Fulton**[1], **Ronald B Harrist**[4], and **Darwin R Labarthe**[1]

[1]Centers for Disease Control & Prevention, Atlanta, GA, USA

[2]University of Texas Medical School, Houston, TX, USA

[3]University of Minnesota School of Public Health, Minneapolis, MN, USA

[4]University of Texas School of Public Health, Houston, TX, USA

## Abstract

**Aim—**This study aimed to distinguish between the roles of the two components of BMI, the fat mass (FM) index and the fat-free mass (FFM) index, in BMI's association with blood lipids in children and adolescents.

**Methods—**A total of 678 children (49.1% female, 79.9% non-black), initially aged 8, 11 and 14 years, were followed at 4-month intervals for up to 4 years (1991–1995). Total cholesterol (TC), LDL-C, HDL-C and triglycerides were determined in fasting blood samples. FFM index and FM index were calculated as FFM (kg)/height $(m)^2$ and FM (kg)/height $(m)^2$, respectively. Using a multilevel linear model, repeated measurements of blood lipids were regressed on concurrent measures of BMI or its components, adjusting for age, sex and race and, in a subsample, also for physical activity, energy intake and sexual maturity.

**Results—**Estimated regression coefficients for the relations of TC with BMI, FFM index and FM index were 1.539, −0.606 ($p > 0.05$) and 3.649, respectively. When FFM index and FM index were entered into the TC model simultaneously, regression coefficients were −0.855 and 3.743, respectively. An increase in BMI was related to an increase in TC; however, an equivalent increase in FM index was related to a greater increase in TC and, when FFM index was tested alone or with FM index, an increase in FFM index was related to a decrease in TC. Similar results were observed for LDL-C. FFM index and FM index were both inversely related to HDL-C and directly to triglycerides. Compared with FFM index, the equivalent increase in FM index showed a greater decrease in HDL-C.

[†]Author for correspondence: Division for Heart Disease & Stroke Prevention, NCCDPHP, Centers for Disease Control & Prevention, 4770 Buford Highway, NE, MS K-47, Atlanta, GA 30341-3717, USA Tel.: +1 770 488 8123 Fax: +1 770 488 8151 sdai@cdc.gov.

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**Ethical conduct of research**

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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**Conclusion—**Greater BMI was related to adverse levels of blood lipids in children and adolescents, which was mainly attributable to BMI's fat component. It is important to identify weight management strategies to halt the childhood obesity epidemic and subsequently prevent heart disease in adulthood.

### Keywords

lood lipids; BMI; body composition; children; obesity

The association of cardiovascular disease (CVD) risk factors, such as adverse blood lipid and lipoprotein cholesterol levels or hypertension, with obesity in children is well known [1–3]. In children and adults, BMI continues to be the recommended index of adiposity for epidemiological studies and for clinical practice [4]. As body mass is composed of both fat mass (FM) and fat-free mass (FFM), the associations of CVD risk factors with BMI may not be interpreted correctly as associations with adiposity only. When associations of some CVD risk factors, such as blood pressure, with the two body mass components were examined in children, the effects of FFM and FM on blood pressure were both significant and equally important [5–7]. However, to our knowledge, the effect of FFM on the relationship between BMI and blood lipids has not been accounted for. The roles that FFM index, the fat-free component of BMI, play in BMI–lipid associations should be distinguished from those of the FM index. The distinction is vital for understanding the BMI–lipid relationship; it is also important for developing interventions to prevent adverse blood lipid levels through body fat control or reduction and for monitoring the effects of such interventions.

Body composition and blood lipid concentrations change dramatically during puberty; height velocity, weight gain, FFM and bone mass increase significantly [8,9], whereas the blood cholesterol level decreases [10]. The change in body mass and lipid levels also differs between the sexes; for example, boys increase in FFM, whereas girls gain in FM [11,12], and blood cholesterol decreases more rapidly in boys than in girls [13]. These dynamic changes complicate the interpretation of findings on the relationship between BMI and blood lipids. Close observation of the constant changes in body composition and blood lipids, as well as other related factors, is required to understand their relationship. A report from the Bogalusa Heart Study, in which children aged 8 years were followed for 6 years, indicated that adiposity is associated with adverse levels of blood lipids and lipoproteins [14]. However, most studies exploring the association of adiposity with blood lipids and lipoproteins have been cross-sectional and thus unable to examine the associations of concurrent changes in body composition and blood lipids. Furthermore, these studies have not accounted for important factors that may influence these changes, such as stage of maturation, energy intake or physical activity behaviors [15–18].

The aim of this study was to examine the associations of concurrent changes in blood lipids and BMI and to compare the roles of the fat-free and fat components of BMI on these relationships in children and adolescents while adjusting for the effects of age, sex, race, energy intake, sedentary and physical activity habits and sexual maturation.

## Methods

Project HeartBeat! is a longitudinal study of CVD risk factors and related measures in childhood and adolescence. The complete design and methods were reported previously [10]. Overall, 678 children in three cohorts, aged 8, 11 and 14 years, were enrolled between October 1991 and July 1993 from The Woodlands and Conroe (TX, USA). The study participants were 49.1% female, 74.6% white, 20.1% black and 5.3% other race/ethnicity.

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They were examined three times per year until August 1995 (mean of 8.3 examinations per participant). The study protocol was approved by the institutional review committees of the University of Texas Health Science Center at Houston (TX, USA) and Baylor College of Medicine (TX, USA). For each participant, informed consent or assent and parental consent were obtained.

Plasma lipid concentrations were determined in the Lipid Research Laboratory of the Baylor College of Medicine. At each examination, the participant's blood was drawn (after an overnight fast) into powdered ethylene-diaminetetra-acetic acid-containing tubes by a trained phlebotomist at the participant's home. The blood was kept at 4°C and was separated within 1 h of collection. Aliquots were held at −70°C until laboratory testing. Total cholesterol (TC), HDL-C and triglycerides (TGs) were determined using a standard enzymatic method [19,20] and the Cobas Fara II analyzer. LDL-C was calculated using the Friedewald equation (TC − [TG/5 + HDL-C]) [21]. It was not calculated when TG was 400 mg/dl or over.

Anthropometric measurements were obtained by two trained and certified technicians working together [22]. Participants were barefoot and wore surgical scrub suits over underwear while measurements were taken. Their weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm. BMI was calculated as weight (kg)/height $(m)^2$. Skinfolds at six sites (triceps, subscapular, mid-axillary, abdominal, distal thigh and lateral calf) were measured in triplicate to the nearest 0.1 mm. FFM and FM were calculated by the sex-specific formula of Guo and colleagues based on a combination of bioelectrical impedance and body measurements [23]. FFM index and FM index were calculated as FFM (kg)/height $(m)^2$ and FM (kg)/height $(m)^2$, respectively.

Physical assessment of secondary sex characteristics involved a visual assessment of pubic hair and breast or genitalia by the method of Tanner; the ratings ranged from 1 (prepubescent) to 5 (adult) for each characteristic [24,25]. The assessment was carried out with the participant standing, either immediately before or after the anthropometry assessment. Pubic hair stage was used in the current analysis.

Dietary energy intake (kilocalories/day) was estimated from a food frequency questionnaire [26]. Trained interviewers questioned participants about the frequency and quantity of their consumption of each of the 137 foods during the previous week. Nutrient amounts were calculated and expressed in terms of average daily intake during the past week. Dietary interviews were conducted annually in the home of the participant or at the field center. Parents who were involved with the food preparation were asked to be available to help participants under the age of 11 years.

Physical activity was assessed annually using a 24-h, interviewer-administered recall questionnaire adapted from a 7-day recall instrument modified for use with preadolescent children. This questionnaire had been validated previously [27]. Using a segmented-day approach, trained interviewers asked participants to recall the physical activities and sedentary behaviors in which they had participated in the previous 24 h. Times spent actively participating in moderate-to-vigorous physical activities (MVPAs) were summed to estimate the amount of MVPA (min/day) during the previous 24 h. Times spent in sedentary behaviors, including television viewing, reading and computer use, were summed to indicate the extent of sedentary physical activity (SePA; min/day).

Ethnicity was grouped into the following two categories – non-black and black. The exact age was calculated for the day of data collection.

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Statistical analysis was performed with the SPSS statistical package [101] and the multilevel modeling software MLwiN [102]. Descriptive statistics of baseline characteristics were provided, and partial correlation coefficients were used to examine the correlations among BMI and its two components and between them and blood lipid concentrations at baseline, adjusting for age by sex. Multilevel statistical analysis was used to estimate the impact of changes in BMI and its components on blood lipids [28]. Tests of statistical hypotheses were carried out by use of the Wald test (ratio of the estimated parameter to its standard error) or deviance tests (changes in −2ln[likelihood]). The p-value of 0.05 was used as the criterion for all statistical testing. No correction was made for repeated testing.

For each of the four lipid components, multilevel linear models were fitted on concurrent measures of either BMI, FFM index or FM index, or on both FFM index and FM index. Sex and race interactions of BMI and its two components were tested. The models were adjusted for age (linear, quadratic and cubic terms of age), sex (male = 0 and female = 1) and race (non-black = 0 and black = 1), including their two-way interaction terms. These models were fitted based on 5029 valid measurements of lipids, BMI, BMI components and covariates determined at all examinations of all 678 study participants. The estimated models were further adjusted for dietary energy intake, sedentary behavior, physical activity and sexual maturation by including dietary energy intake, SePA, MVPA and pubic hair stage into the models. This part of the statistical analysis was based on 1142 observations. The smaller number of observations resulted from the availability of only baseline and annual assessments of dietary intake and physical activity, restriction of physical activity assessment to participants aged 10 years old and over (based on reliability considerations) and missing values for pubic hair stage. TC, as the sum of separate lipid components, was analyzed as one of the dependent variables, because it was recommended as the initial test for selective screening in children by the National Cholesterol Education Program Expert Panel on Blood Cholesterol Levels in Children and Adolescents (1991) and was widely used in assessment of risk in children [29].

Analysis of the Project HeartBeat! data has been an ongoing effort. Although the data were collected only until 15 years ago, we believe that the biological relationships among the collected variables would not change with time. Thus, the outcomes reported should still be valid and meaningful.

## Results

Baseline characteristics of the study participants are presented according to age group in Table 1. Mean TC and LDL-C decreased with increasing age from 8 to 14 years. These values were lower in boys than in girls among the 14-year-olds. HDL-C also decreased across age groups, especially in boys. TG levels were lower in boys than in girls among the 8-year-olds; however, TG levels increased across successive age groups more steeply in boys than in girls. Mean BMI increased between the 8- and 14-year-old age groups and was slightly higher in girls than in boys among 14-year-olds. The FFM index increased between the 8- and 14-year-old age groups and was consistently, although only slightly, higher in boys than in girls. The FM index was higher in girls than in boys, except at age 11 years. The FM index increased with age in girls for the three age groups but peaked at age 11 years in boys.

Partial correlation coefficients of BMI, FFM index and FM index with lipid components by sex and adjusted for age are shown in Table 2. BMI, FFM index and FM index were positively correlated with one another in both boys and girls, most strongly between BMI and FM index ($\gamma = 0.87$ in boys and $\gamma = 0.93$ in girls) and least strongly between FFM index and FM index ($\gamma = 0.27$ in boys and $\gamma = 0.51$ in girls). BMI and FM index were directly

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correlated with LDL-C and TGs and inversely with HDL-C in both boys and girls after adjustment for age. They were also directly correlated with TC in boys. FFM index was inversely correlated with HDL-C in both boys and girls.

Regression coefficients and standard errors of BMI, FFM index and FM index from lipid models adjusted for age, sex and race are presented in Table 3. The regression coefficients and standard errors from models further adjusted for energy intake, sedentary behavior, physical activity and Tanner stage are presented in Table 4.

An increase in BMI was significantly associated with increases in TC, LDL-C, and TGs and a decrease in HDL-C, after adjustment for sex, race and age (Table 3). The regression coefficients for the main effects of BMI on these lipid components were 1.539, 1.472, 4.308 and −0.777, respectively. The estimated effect of BMI on TGs was 2.9 mg/dl lower in black subjects than in non-black subjects.

The FFM index was not significantly associated with TC and LDL-C. However, it was negatively associated with HDL-C (regression coefficient: −0.628) and positively associated with TGs (regression coefficient: 2.575).

Similar to BMI, the FM index was positively related to TC, LDL-C and TGs, and negatively related to HDL-C. The regression coefficients for the main effects of FM index were 3.649, 3.343, 5.885 and −0.936, respectively. Sex–FM index interactions indicated that the effects were lower in girls than in boys by 1.606 mg/dl for TC and 1.387 mg/dl for LDL-C with each 1 $kg/m^2$ change in FM index. The effect of FM index on TGs was lower in black subjects than in non-black subjects (regression coefficient for interaction: −3.420).

When both FM index and FFM index were entered simultaneously into the lipid models, the estimated effects on the four lipid components related to each unit difference in FM index remained practically unchanged. However, FFM index became negatively associated with TC (regression coefficient: −0.855) and LDL-C (regression coefficient: −0.574). This finding indicates that an increase of 1 $kg/m^2$ in FFM index was related to a 0.855-mg/dl decrease in TC and a 0.574-mg/dl decrease in LDL-C. The estimated effects of FFM index on HDL-C and TG remained similar to those estimated when FM index was not included in the models.

No major changes were found in the observed relationships of lipid components with BMI and its fat-free and fat components after further adjustment for energy intake, sedentary behavior, physical activity and sexual maturation (Table 4). Differences in the results after further adjustment mainly related to changes in statistical significance of interaction terms (e.g., significant interaction terms of sex–BMI and sex–FM index in the TGs models and insignificant interaction terms of sex–FM index in the TC and the LDL-C models) and to slight changes in magnitude of regression coefficients. These minor differences could be expected because of smaller sample sizes with fewer measurements of all variables included in the lipid models adjusted for dietary energy intake, sedentary behavior, physical activity and sexual maturation. In general, the results were in agreement with those observed without these adjustments.

## Discussion

This report described the concomitant association of BMI and its fat and fat-free components with blood lipids and lipoproteins during adolescence. In general, both BMI components were significantly associated with blood lipids and lipoproteins, and the strongest associations were for FM index. Greater values for BMI and FM index were associated with adverse levels of all measured blood lipids and lipoproteins, and the

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estimated change in TGs related to each unit change in either index was greater in non-black children than in black children. Finally, higher FFM index was related to adverse levels of HDL-C and TGs but favorable levels of TC and LDL-C.

Similar associations between BMI and blood lipids in children have been reported in other studies [14–18,30]. In longitudinal analyses, results from the Bogalusa Heart Study also showed positive associations of BMI with TGs and negative associations with HDL-C, and the relationship between BMI and TGs was also weaker in black children than in white children [30]. Another report of that study indicated that the rate of increase in adiposity (based on BMI and the sum of subscapular and tricep skinfold measurements) was related to adverse changes in blood lipids [14]. The changes were greater for TGs in males, and for LDL-C and HDL-C in white participants.

Similar results have also been reported from cross-sectional studies. HDL-C levels in Cherokee Indian children aged 5–19 years were shown to decrease across increasing BMI z-quartiles in all age groups [15]. In another study, overweight males and females aged 9–17 years had lower HDL-C and higher LDL-C and TG levels than non-overweight children (overweight defined as BMI ≥85th percentile for specific age and sex groups using BMI distributions from the combined National Health and Nutrition Examination Survey [NHANES] I and II dataset) [17,18]. Furthermore, based on BMI and the sum of subscapular and tricep skinfold measurements, body fat distribution was a stronger predictor for blood lipids and lipoproteins than was body fat percentage in children [16].

BMI is a widely used indicator of adiposity. The relationships between BMI and blood lipids and lipoproteins are well established in children and adults, even though BMI is a measure of excess weight relative to height rather than a measure of excess body fat. It is well known that bone, muscle and organs are reflected in BMI measurement in addition to body fat. Reports on trajectories of adiposity measures showed distinct age-related patterns of BMI compared with body fat percentage, FM index and skinfold measures [12,31,32]. A recent study of children aged 8–18 years demonstrated that annual increases in BMI were mainly accounted for by FFM index in both sexes until late adolescence, and that increases in FM index contributed to a larger proportion of the BMI increases in girls than in boys [32]. The insight on the relative contribution of the fat and fat-free components to variance of BMI at different growth and maturation stages is important in understanding the role that each component plays in the relationship of BMI with CVD risk factors. As BMI does not allow differentiation between its fat and nonfat body components, changes in these components should be considered when the effect of body fatness on blood lipids in children and adolescents is measured.

None of the previous studies examining the effect of BMI on lipids and lipoproteins in children reported the effect of each BMI component (i.e., FM index and FFM index) separately. In the present study, FM index was significantly related to higher levels of LDL-C, TC and TG and lower levels of HDL-C. Associations of lipids with FM index, the adipose component of BMI, appeared generally stronger than those with BMI and more similar to the associations with body fat percentage and skinfold measures than to the associations with BMI [33]. Moreover, a 1-unit increase in FM index was associated with greater increases in TC, LDL-C and TG and a greater decrease in HDL-C than the equivalent increase in BMI, even among girls (difference not tested), where the effects of changes in FM index on TC and LDL-C were smaller than those in boys. The strong effect of FM index may be explained by the adipose tissue role. Adipose tissue is now recognized as an endocrine organ that controls levels of plasma free fatty acid and contributes to systemic metabolic homeostasis by producing various proteins (adipocyto-kines). In obesity, the infiltration of immune cells, such as T cells and macrophages, into adipose tissue causes

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inflammation, which is thought to contribute to loss of insulin sensitivity. Insulin resistance in adipose tissue can lead to increased release of fatty acids, secretion of inflammatory cytokines, and alterations in the balance of adipocytokines, which ultimately impact lipoprotein metabolism, especially TGs and HDL-C [34,35].

On the other hand, FFM index was negatively associated with HDL-C and positively associated with TGs, and was not significantly associated with TC and LDL-C when analyzed alone. When analyzed simultaneously with FM index, FFM index was inversely associated with TC and LDL-C. Compared with FM index, FFM index had a smaller effect on TGs and HDL-C. All of the associations were significant after adjustment for age, sex, race, energy intake, physical activity and sexual maturation.

Similarly, a recent report from a longitudinal study conducted in adults demonstrated that FM index was negatively associated with HDL-C and positively associated with TC, LDL-C and TGs, whereas FFM index had a positive association with TGs, a negative association with HDL-C and no significant association with TC or LDL-C [36]. These associations were found for both men and women and were stronger for FM index than for FFM index. The association of FFM index with adverse levels of HDL-C and TG concentrations may be explained by skeletal muscle insulin resistance. Insulin resistance in skeletal muscle diverts ingested carbohydrate away from muscle glycogen synthesis and storage into hepatic lipogenesis resulting in adverse levels of serum TGs and HDL-C [37].

Partitioning BMI into FFM index and FM index clearly shows that the relationships between BMI and blood lipids and lipoproteins, especially for TC and LDL-C, in children and adolescents are mainly attributable to its fat component, the FM index. The findings reported here, especially the inverse association between FFM index and TC and LDL-C, should be confirmed by further studies using dual energy x-ray absorptiometry (DXA) or MRI body composition methods. One of the limitations of this study includes the bioelectrical impedance method to assess FM and FFM compared with DXA, for example. Although DXA measures of body composition may be more precise than bioelectric impedance, bioelectrical impedance is practical in large-scale epidemiological studies, given the cost and time. Another limitation was the self-reported dietary intake and physical activity, an approach that may result in imprecise estimates, especially in young children. Moreover, the time period of the impact of behaviors on body composition and lipids was not accounted for in the current analysis. Nonetheless, the food frequency questionnaire was reported as a good group measure for ranking youth intakes, and the physical activity questionnaire was validated in a previous study. Both measures were intended as indicators of patterns of behavior. To further limit the potential error of measurements, children under 10 years of age were excluded when diet and physical activity measures were included in the analysis. The major strength of the present study for the purpose of this analysis was the frequency of examinations throughout adolescence, which allowed for repeated measurements of lipids along with concurrent measures of body composition as well as potential confounding factors (physical activity, sedentary behavior, energy intake and sexual maturity). Although lipid measures were related to body composition and covariates were collected at the same time in the current analysis, within each individual, the repeated measures varied over time, resulting in longitudinal changes in lipids, body composition and covariates from baseline to follow-up assessments. Variance of dependent variables (e.g., LDL-C) was separated into two levels: within individuals and between individuals. Within individuals, changes from earlier measures in dependent variables were explained by the changes in predictors/independent variables. This feature is not possible with cross-sectional data and the associations found in this kind of data analysis are much stronger indicators for real biological relationships than those in traditional cross-sectional studies. The time period for this study occurred at an age when BMI increases and cholesterol decreases; however, the

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design is critical for determining the relationships of FM and FFM with lipids when these variables are undergoing dynamic changes. Future studies are needed to examine similar questions in younger children aged 2–7 years.

## Conclusion

Using BMI as a measure of adiposity underestimates the strength of the associations between adiposity and blood lipids and lipoproteins. High FM index is related to adverse levels of all four blood lipid components, whereas high FFM index is related to adverse levels of HDL-C and TGs but favorable levels of TC and LDL-C. Adiposity is known to contribute to adverse changes in blood lipid and lipoprotein levels, and most intervention measures for preventing and controlling adverse levels of lipids are primarily based on control of adiposity. Understanding the impact of adiposity and lean body mass on blood lipids and other cardiovascular risk factors is important in designing and monitoring intervention strategies to lower cardiovascular risk for young people.

Executive summary

- An increase in BMI was signifcantly associated with increases in total cholesterol (TC), LDL-C and triglycerides (TGs) and a decrease in HDL-C, after adjustment for sex, race and age.
- Changes in TGs concurrent with changes in BMI were found to be smaller in black patients than in non-black patients.
- When tested alone, the fat-free mass (FFM) index was not signifcantly associated with TC and LDL-C; it was inversely associated with HDL-C and positively associated with TGs.
- Comparing multilevel models on BMI, FFM index or fat mass (FM) index, a unit increase in the FM index was associated with greater increases in TC, LDL-C and TGs and a greater decrease in HDL-C than that of BMI or the FFM index (difference not tested).
- When analyzed simultaneously, the FM index was positively, while the FFM index was inversely, associated with TC and LDL-C; a unit increase in FM index was associated with greater increases in TGs and a greater decrease in HDL-C than that of FFM index (difference not tested).
- Overall, an increase in BMI among children and adolescents is associated with adverse changes in all four blood lipid components.
- While an increase in the fat component of BMI is related to adverse changes in all four lipid components, an increase in the fat-free component of BMI is related to beneficial changes in TC and LDL-C.
- Distinctions need to be made when evaluating changes in BMI in children and adolescents; an increase in FM index is consistently related to adverse changes in lipid measures, whereas the effect of an increase in FFM index is inconsistent across lipid measures.

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## Bibliography

Papers of special note have been highlighted as:

▪ of interest

▪▪ of considerable interest

1. Falkner B, Gidding SS, Ramirez-Garnica G, Wiltrout SA, West D, Rappaport EB. The relationship of body mass index and blood pressure in primary care pediatric patients. J. Pediatr. 2006; 148(2): 195–200. [PubMed: 16492428]
2. Reinehr T, Andler W, Denzer C, Siegried W, Mayer H, Wabitsch M. Cardiovascular risk factors in overweight German children and adolescents: relation to gender, age and degree of overweight. Nutr. Metab. Cardiovasc. Dis. 2005; 15(3):181–187. [PubMed: 15955466]
3. Janssen I, Katzmarzyk PT, Srinivasan SR, et al. Combined influence of body mass index and waist circumference on coronary artery disease risk factors among children and adolescents. Pediatrics. 2005; 115(6):1623–1630. [PubMed: 15930225] . ▪ Provides evidence that a combination of increased BMI and waist circumference measures may increase health risks among children and adolescents.
4. Dietz WH, Bellizzi MC. Introduction: the use of body mass index to assess obesity in children. Am. J. Clin. Nutr. 1999; 70(1):123S–125S. [PubMed: 10419414]
5. Mueller WH, Chan W, Meininger JC. Utility of different body composition indicators: demographic influences and associations with blood pressure and heart rates in adolescents (Heartfelt Study). Ann. Hum. Biol. 2003; 30(6):714–727. [PubMed: 14675911]
6. Wilks RJ, Farlane-Anderson N, Bennett FI, Reid M, Forrester TE. Blood pressure in Jamaican children: relationship to body size and composition. West Indian Med. J. 1999; 48(2):61–68. [PubMed: 10492604]
7. Julius S, Majahalme S, Nesbitt S, et al. A ‘gender blind’ relationship of lean body mass and blood pressure in the Tecumseh study. Am. J. Hypertens. 2002; 5(3):258–263. [PubMed: 11939617]
8. Rodriguez G, Moreno LA, Blay MG, et al. Body composition in adolescents: measurements and metabolic aspects. Int. J. Obes. Relat. Metab. Disord. 2004; 28 Suppl. 3:S54–S58. [PubMed: 15543220]
9. Dekkers JC, Podolsky RH, Treiber FA, Barbeau P, Gutin B, Snieder H. Development of general and central obesity from childhood into early adulthood in African American and European American males and females with a family history of cardiovascular disease. Am. J. Clin. Nutr. 2004; 79(4): 661–668. [PubMed: 15051612]
10. Labarthe DR, Nichaman MZ, Harrist RB, Grunbaum JA, Dai S. Development of cardiovascular risk factors from ages 8 to 18 in Project HeartBeat! Study design and patterns of change in plasma total cholesterol concentration. Circulation. 1997; 95(12):2636–2642. [PubMed: 9193432]
11. Guo SS, Chumlea WC, Roche AF, Siervogel RM. Age- and maturity-related changes in body composition during adolescence into adulthood: the Fels Longitudinal Study. Int. J. Obes. Relat. Metab. Disord. 1997; 21(12):1167–1175. [PubMed: 9426385]
12. Eissa MA, Dai S, Mihalopoulos NL, Day RS, Harrist RB, Labarthe DR. Trajectories of body mass index, its components, and waist circumference by age in children. Project HeartBeat. Am. J. Prev. Med. 2009; 37 Suppl. 1:S34–S39. [PubMed: 19524154]
13. Labarthe DR, Dai S, Fulton JE. Cholesterol screening in children: insights from Project HeartBeat! and NHANES III. Prog. Pediatr. Cardiol. 2003; 17:169–178.
14. Srinivasan SR, Myers L, Berenson GS. Rate of change in adiposity and its relationship to concomitant changes in cardiovascular risk variables among biracial (black–white) children and young adults: the Bogalusa Heart Study. Metabolism. 2001; 50(3):299–305. [PubMed: 11230782]

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15. Blackett PR, Blevins KS, Stoddart M, et al. Body mass index and high-density lipoproteins in Cherokee Indian children and adolescents. Pediatr. Res. 2005; 58(3):472–477. [PubMed: 16148059]

16. Daniels SR, Morrison JA, Sprecher DL, Khoury P, Kimball TR. Association of body fat distribution and cardiovascular risk factors in children and adolescents. Circulation. 1999; 99(4): 541–545. [PubMed: 9927401] . ▪ Provides evidence that body fat distribution is an important indicator of adverse cardiovascular risk factors in children.

17. Morrison JA, Sprecher DL, Barton BA, Waclawiw MA, Daniels SR. Overweight, fat patterning, and cardiovascular disease risk factors in black and white girls: the National Heart, Lung, and Blood Institute Growth and Health Study. J. Pediatr. 1999; 135(4):458–464. [PubMed: 10518079]

18. Morrison JA, Barton BA, Biro FM, Daniels SR, Sprecher DL. Overweight, fat patterning, and cardiovascular disease risk factors in black and white boys. J. Pediatr. 1999; 135(4):451–457. [PubMed: 10518096]

19. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-$Mg^{2+}$ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. Clin. Chem. 1982; 28(6):1379–1388. [PubMed: 7074948]

20. Siedel J, Hagele EO, Ziegenhorn J, Wahlefeld AW. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. Clin. Chem. 1983; 29(6):1075–1085. [PubMed: 6851096]

21. Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem. 1972; 18(6):499–502. [PubMed: 4337382]

22. Lohman, TG.; Roche, AF.; Martorell, R., editors. Anthropometric Standardization Reference Manual. IL, USA: Human Kinetics; 1988.

23. Guo SM, Roche AF, Houtkooper L. Fat-free mass in children and young adults predicted from bioelectric impedance and anthropometric variables. Am. J. Clin. Nutr. 1989; 50(3):435–443. [PubMed: 2773822]

24. Marshall WA, Tanner JM. Variation in the pattern of pubertal changes in girls. Arch. Dis. Child. 1969; 44:291–303. [PubMed: 5785179] . ▪ Classic article about the pattern of pubertal changes in girls.

25. Marshall WA, Tanner JM. Variation in the pattern of pubertal changes in boys. Arch. Dis. Child. 1970; 45(239):13–23. [PubMed: 5440182] . ▪ Classic article about the pattern of pubertal changes in boys.

26. Burk BS. The dietary history as a tool in research. J. Am. Diet. Assoc. 1947; 23:1041–1048.

27. Simons-Morton BG, Taylor WC, Huang IW. Validity of the physical activity interview and Caltrac with preadolescent children. Res. Q. Exerc. Sport. 1994; 65(1):84–88. [PubMed: 8184216]

28. Goldstein, H. Multilevel Statistical Models (2nd Edition). UK: Edward Arnold; 1995.

29. National Cholesterol Education Program. Report of the expert panel on blood cholesterol levels in children and adolescents. US Department of Health and Human Services; 1991. NIH Publication. No. 91-2732

30. Freedman DS, Bowman BA, Otvos JD, Srinivasan SR, Berenson GS. Differences in the relation of obesity to serum triacylglycerol and VLDL subclass concentrations between black and white children: the Bogalusa Heart. Study. Am. J. Clin. Nutr. 2002; 75(5):827–833.

31. Dai S, Labarthe DR, Grunbaum JA, Harrist RB, Mueller WH. Longitudinal analysis of changes in indices of obesity from age 8 years to age 18 years. Project HeartBeat. Am. J. Epidemiol. 2002; 156(8):720–729. [PubMed: 12370160]

32. Maynard LM, Wisemandle W, Roche AF, Chumlea WC, Guo SS, Siervogel RM. Childhood body composition in relation to body mass index. Pediatrics. 2001; 107(2):344–350. [PubMed: 11158468] . ▪▪ Discussion of the relationships between body composition measures and BMI in childhood in order to provide clinicians with an insight into the limitations of using BMI as an index of adiposity during childhood.

33. Dai S, Fulton JE, Harrist RB, Grunbaum JA, Steffen LM, Labarthe DR. Blood lipids in children: age-related patterns and association with body fat indices, Project Heartbeat! Am. J. Prev. Med. 2009; 37 Suppl. 1:S56–S64. [PubMed: 19524157] . ▪▪ A general discussion on the age-related

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patterns of change in four blood lipid components and their association with five body fat indices among children and adolescents aged 8–18 years.

34. Kolovou GD, Anagnostopoulou KK, Cokkinos DV. Pathophysiology of dyslipidaemia in the metabolic syndrome. Postgrad. Med. J. 2005; 81:358–366. [PubMed: 15937200]
35. Gutierrez DA, Puglisi MJ, Hasty AH. Impact of increased adipose tissue mass on inflammation, insulin resistance, and dyslipidemia. Curr. Diabetes Rep. 2009; 9(1):26–32.
36. Schubert CM, Rogers NL, Remsberg KE, et al. Lipids, lipoproteins, lifestyle, adiposity and fat-free mass during middle age: the Fels Longitudinal Study. Int. J. Obes. (Lond.). 2006; 30(2):251–260. [PubMed: 16247511]
37. Petersen KF, Dufour S, Savage DB, et al. The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome. Proc. Natl Acad. Sci. USA. 2007; 104(31):12587–12594. [PubMed: 17640906] . ▪ Describes the potential mechanism for the relationship between fat-free mass and lipid levels.

## Websites

101. SPSS base system syntax reference guide. Release 6.0. IL, USA: SPSS Inc; 1993. www.spss.com
102. Rasbash, J.; Steele, F.; Browne, W.; Prosser, B. A User's Guide to MLwiN, Version 2.0. UK: University of Bristol; 2005. www.bristol.ac.uk/cmm

## Websites

101. SPSS base system syntax reference guide. Release 6.0. IL, USA: SPSS Inc; 1993. www.spss.com
102. Rasbash, J.; Steele, F.; Browne, W.; Prosser, B. A User's Guide to MLwiN, Version 2.0. UK: University of Bristol; 2005. www.bristol.ac.uk/cmm

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**Table 1**

Baseline characteristics of study participants by age and sex, Project HeartBeat!, 1991–1995 (n = 678).

| | 8-year-olds | | 11-year-olds | | 14-year-olds | |
|---|---|---|---|---|---|---|
| | ***Boys*** | ***Girls*** | ***Boys*** | ***Girls*** | ***Boys*** | ***Girls*** |
| | 159 (50.6) | 155 (49.4) | 104 (52.8) | 93 (47.2) | 82 (49.1) | 85 (50.9) |
| ***Race, n (%)*** | | | | | | |
| Blacks | 38 (23.9) | 41 (26.5) | 21 (20.2) | 17 (18.3) | 7 (8.5) | 12 (14.1) |
| Non-blacks | 121 (76.1) | 114 (73.5) | 83 (79.8) | 76 (81.7) | 75 (91.5) | 73 (85.9) |
| ***Mean age (SD)*** | | | | | | |
| Mean age in years | 8.50 (0.31) | 8.53 (0.35) | 11.49 (0.34) | 11.52 (0.40) | 14.41 (0.21) | 14.45 (0.20) |
| ***Mean plasma lipids (SD)*** | | | | | | |
| Total cholesterol (mg/dl) | 164.05 (24.57) | 164.06 (27.76) | 163.18 (29.01) | 160.11 (24.91) | 149.49 (22.53) | 159.57 (27.94) |
| LDL-C (mg/dl) | 96.06 (22.51) | 97.96 (25.47) | 94.83 (26.32) | 91.80 (23.92) | 85.75 (20.38) | 92.97 (26.95) |
| HDL-C (mg/dl) | 53.94 (11.26) | 51.00 (10.35) | 51.18 (12.54) | 51.15 (12.51) | 45.12 (9.79) | 48.71 (10.30) |
| Triglycerides (mg/dl) | 70.26 (29.62) | 75.52 (34.58) | 85.86 (52.88) | 85.80 (42.99) | 93.06 (55.42) | 89.45 (43.28) |
| ***Mean BMI and components (SD)*** | | | | | | |
| BMI ($kg/m^2$) | 17.21 (2.72) | 17.42 (3.49) | 19.53 (3.96) | 18.74 (3.96) | 20.74 (3.22) | 22.61 (4.86) |
| FFM index ($kg/m^2$) | 13.32 (1.40) | 12.90 (1.52) | 14.57 (1.93) | 13.66 (1.58) | 16.67 (1.74) | 15.56 (1.48) |
| FM index ($kg/m^2$) | 3.86 (2.04) | 4.52 (2.42) | 4.96 (2.69) | 4.84 (2.33) | 3.83 (2.08) | 6.17 (2.34) |

FFM: Fat-free mass; FM: Fat mass; SD: Standard deviation.

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**Table 2**

Pearson partial correlation coefficients among BMI and its components and with lipid measures, adjusted for age by sex, Project HeartBeat!, 1991–1995.

| | FFM index | FM index | Total cholesterol | LDL-C | HDL-C | Triglycerides |
|---|---|---|---|---|---|---|
| ***Males*** | | | | | | |
| BMI (kg/m$^2$) | 0.71 | 0.87 | 0.16 | 0.19 | −0.24 | 0.28 |
| FFM index (kg/m$^2$) | – | 0.27 | 0.01$^\dagger$ | 0.06$^\dagger$ | −0.15 | 0.08$^\dagger$ |
| FM index (kg/m$^2$) | – | – | 0.22 | 0.23 | −0.22 | 0.33 |
| ***Females*** | | | | | | |
| BMI (kg/m$^2$) | 0.79 | 0.93 | 0.06$^\dagger$ | 0.12 | −0.23 | 0.13 |
| FFM index (kg/m$^2$) | – | 0.51 | −0.05$^\dagger$ | 0.00$^\dagger$ | −0.11 | −0.02$^\dagger$ |
| FM index (kg/m$^2$) | – | – | 0.06$^\dagger$ | 0.11 | −0.22 | 0.16 |

$^\dagger$All estimates are statistically signifcant ($p \leq 0.05$), except for those marked, which are nonsignificant.

FFM: Fat-free mass; FM: Fat mass.

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**Table 3**

Multilevel regression models for plasma lipids: estimates (regression coefficients) and standard errors for BMI and its componants, adjusted for sex, age and race, Project HeartBeat!, 1991–1995.

| | Total cholesterol | | LDL-C | | HDL-C | | Triglycerides | |
|---|---|---|---|---|---|---|---|---|
| | *Estimate* | *SE* | *Estimate* | *SE* | *Estimate* | *SE* | *Estimate* | *SE* |
| ***Lipid models on BMI*** | | | | | | | | |
| BMI | 1.539 | 0.216 | 1.472 | 0.186 | −0.777 | 0.079 | 4.308 | 0.469 |
| BMI × sex | – | – | – | – | – | – | – | – |
| BMI × race | – | – | – | – | – | – | −2.900 | 0.921 |
| ***Lipid models on FFM index*** | | | | | | | | |
| FFM index | −0.606 † | 0.323 | −0.409 † | 0.291 | −0.628 | 0.129 | 2.575 | 0.605 |
| FFM index × sex | – | – | – | – | – | – | – | – |
| FFM index × race | – | – | – | – | – | – | – | – |
| ***Lipid models on FM index*** | | | | | | | | |
| FM index | 3.649 | 0.361 | 3.343 | 0.321 | −0.936 | 0.102 | 5.885 | 0.542 |
| FM index × sex | −1.606 | 0.522 | −1.387 | 0.464 | – | – | – | – |
| FM index × race | – | – | – | – | – | – | −3.420 | 1.048 |
| ***Lipid models on FM index and FFM index*** | | | | | | | | |
| FM index | 3.743 | 0.357 | 3.321 | 0.318 | −0.897 | 0.102 | 5.365 | 0.556 |
| FM index × sex | −1.661 | 0.513 | −1.335 | 0.460 | – | – | – | – |
| FM index × race | – | – | – | – | – | – | −2.653 | 1.155 |
| FFM index | −0.855 | 0.278 | −0.574 | 0.255 | −0.537 | 0.127 | 2.128 | 0.610 |
| FFM index × sex | – | – | – | – | – | – | – | – |
| FFM index × race | – | – | – | – | – | – | −2.273 † | 1.169 |

† All estimates are statistically signifcant ($p \leq 0.05$), except for those marked, which are nonsignifcant.

FFM: Fat-free mass; FM: Fat mass; SE: Standard error.

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**Table 4**

Multilevel regression models for plasma lipids: estimates (regression coefficients) and standard errors of BMI and components, adjusted for sex, age, race, energy intake, sedentary behavior, physical activity and Tanner stage, Project HeartBeat!, 1991–1995.

| | Total cholesterol | | LDL-C | | HDL-C | | Triglycerides | |
|---|---|---|---|---|---|---|---|---|
| | *Estimate* | *SE* | *Estimate* | *SE* | *Estimate* | *SE* | *Estimate* | *SE* |
| ***Lipid models on BMI*** | | | | | | | | |
| BMI | 1.393 | 0.282 | 1.376 | 0.220 | −0.788 | 0.100 | 5.495 | 0.592 |
| BMI × sex | – | – | – | – | – | – | −1.633 | 0.791 |
| BMI × race | – | – | – | – | – | – | −3.576 | 0.793 |
| ***Lipid models on FFM index*** | | | | | | | | |
| FFM index | 0.270† | 0.498 | 0.868 | 0.425 | −1.031 | 0.208 | 5.905 | 1.038 |
| FFM index × sex | – | – | – | – | – | – | – | – |
| FFM index × race | – | – | – | – | – | – | −4.845 | 1.735 |
| ***Lipid models on FM index*** | | | | | | | | |
| FM index | 3.825 | 0.600 | 3.065 | 0.466 | −1.169 | 0.159 | 8.471 | 0.933 |
| FM index × sex | −1.567† | 0.827 | −0.868† | 0.690 | – | – | −2.822 | 1.277 |
| FM index × race | −1.417† | 0.926 | – | – | – | – | −6.123 | 1.363 |
| ***Lipid models on FM index and FFM index*** | | | | | | | | |
| FM index | 4.042 | 0.604 | 3.110 | 0.463 | −1.015 | 0.173 | 7.908 | 0.972 |
| FM index × sex | −1.567† | 0.822 | −0.372† | 0.634 | – | – | −2.854 | 1.273 |
| FM index × race | −1.145† | 0.927 | – | – | – | – | −6.631 | 1.383 |
| FFM index | −1.094 | 0.545 | −1.073 | 0.482 | −0.513 | 0.229 | 2.004 | 1.012 |
| FFM index × sex | – | – | – | – | – | – | – | – |
| FFM index × race | – | – | – | – | – | – | – | – |

†All estimates are statistically signifcant ($p \leq 0.05$), except for those marked, which are nonsignifcant.

FFM: Fat-free mass; FM: Fat mass; SE: Standard error.