Obesity affects at least 1 in 6 children and adolescents in this country and should be considered the most common chronic disease in childhood. The complications of obesity also represent a group of chronic conditions that pediatricians must face and should be identified by their persistence over time and not at a single visit. Guidelines for hypertension, another complication of obesity, recommend that a diagnosis should be made after multiple elevated measurements taken over at least 3 visits. Diabetes mellitus guidelines also recommend repeat testing for confirmation of elevated fasting blood glucose in asymptomatic patients.

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Expert recommendations for identification and management of childhood obesity endorse regular tracking of body mass index (BMI) and medical assessment for complications of obesity. They recommend the collection of information on history, symptoms, and physical findings, as well as a screening for abnormalities in lipids, glucose, insulin, and liver enzymes. The ubiquitous nature of childhood obesity (17%) contrasts with the rarity of severe complications such as type 2 diabetes mellitus (<0.5%), which suggests that a group of obese youth exists with additional abnormalities that elevate their risk for future cardiovascular disease (CVD) and/or type 2 diabetes mellitus. Obese youth who persistently have multiple, moderately abnormal cardiovascular risk factors should be identified for aggressive lifestyle counseling as an essential part of primordial prevention.

Pediatric studies have modeled the adult metabolic syndrome (MetS) definition to describe the epidemiology and generate hypotheses for obese children, and the studies have found associations with other adult CVD risk factors such as C-reactive protein and smoking. A recent article by Jolliffe et al used a statistical technique on a national database of adolescents to develop a growth curve approach for MetS. This definition has an advantage over previous definitions because it translates abnormal adult values into age- and gender-specific values for teenage subjects. Jolliffe et al showed that waist circumference and blood pressure values progressively increased with age, whereas glucose remained constant at 100 mg/dL. This technique revealed noticeable trends in lipid values by age and gender. These lipid values are different from the single cut-offs applied previously and represent progress in the identification of risk factors by age and gender.

In this issue of Circulation, an article by Goodman et al reports on the stability and instability found with different methods to identify the MetS in adolescents. The authors point out that MetS as a ≥3 factors, yes/no, clinical diagnosis is premature for pediatric populations. This is consistent with adult studies that suggest that a dichotomous approach excludes far too much clinically important information. However, if 1 risk factor is identified, this should prompt a search for others. A number of research questions remain unanswered about the syndrome and how it is defined, such as the need to identify an underlying cause or causes of CVD risk-factor clustering, to determine which combinations of components signify a higher risk, to assess CVD risk in subjects with combinations of abnormal components with or without insulin resistance, and to evaluate the need to add other CVD risk factors to the definition (eg, age, family history, and direct measure of insulin resistance). The pediatric research community has a unique role, especially in helping to describe the emergence of cardiovascular risk factors in childhood.

The article by Goodman et al uses principle component analysis as a method to study the tracking of CVD risk factors in adolescents. This unique statistical tool helps describe the linear relationships among variables to create a smaller number of summary factors and optimize the explained variance in these variables. As has been pointed out with factor analysis, it is not a standardized technique; factors can be defined differently, standardization of variables is not consistent (systolic blood pressure or mean arterial pressure), and various methods for rotation for factor loading can be applied. One example can be found from a previous report on this cohort that used factor analysis to describe both a 3-factor model (adiposity, cholesterol, and metabolism) and a 4-factor model (the 3 original factors plus blood pressure). These models accounted for about 68% of the explained variance in the measured variables, but they also included total cholesterol, low-density lipoprotein cholesterol, and fibrinogen, variables not included in this article by Goodman and colleagues. A recent report from national data on adolescents used confirmatory factor analysis to test a single underlying factor model for MetS in adolescents made up of 4 phenotypic variables; waist circumference, triglycerides, insulin, and systolic blood pressure. This model was generalized to males and females, as well as whites, blacks and Hispanics. Thus, factor analysis is a useful method for describing the relationships between these factors, but it may be difficult to...
determine which factors go into the construction of the models. Factor analysis allows researchers to look at the relationships among variables across the distribution of all individuals. A study by Chen et al tracked youth with multiple risk factors at low (protective) levels into adulthood and found lower rates of a family history for CVD and lower values for risk factors in adulthood. Therefore, this tool has a useful role in the future study of cardiovascular risk factors and obesity through childhood and into adulthood.

The authors suggest that the 3-factor model is stable between the baseline and follow-up visit. The total explained variance went from 62% to 65%, but 2 factors changed their composition and 2 variables had noticeable changes between the 2 visits. For example, glucose loaded on the metabolic factor at baseline, then switched and loaded on the fat factor at follow-up. Additionally, insulin, which is a potentially key underlying factor, loaded on the metabolic and fat factors at baseline but then only on the fat factor at follow-up. The blood pressure factor appears to be the only factor that is virtually identical at baseline and follow-up. The authors stated that “overall, these differences were minor and suggest that the factor structure is stable.” However, because changes occurred in the number of variables in each factor, and stability of factors clearly were noted, and no test of confirmation of stability was reported, we would suggest some caution with this interpretation.

The concern of instability in the categorical definitions of MetS was also highlighted. In this study, rather small samples are presented in each of these categorical groups (eg, 19 persistent adult MetS cases). Therefore, only a few subjects changing categories could produce a noticeable change in proportions, as is demonstrated by the overlapping confidence intervals of baseline and the cumulative and follow-up prevalence. A number of reasons could exist for changes in cardiovascular risk factors that necessitate the confirmation of elevated risk factors. Studies that track youth cholesterol levels demonstrate that some regression toward the mean occurs with measurements repeated on a monthly or yearly basis as well as elevations in lipids after acute infection.

A number of studies have shown that changes in risk factor clustering can be explained by changes in lifestyle behaviors. The Beaver County study looked at cholesterol screening patterns in childhood and their ability to predict hypercholesterolemia in adulthood. They described “false positives” as adults who were in the top quintile for cholesterol in childhood but were in a normal cholesterol range during adulthood, analogous to the baseline-only cases reported by Goodman et al. The “false negatives” had normal cholesterol levels during childhood but were found to have hypercholesterolemia in adulthood, similar to the incident MetS cases. They showed that subjects who crossed categories also had changes in diet, exercise, smoking status, and birth control use that would lead to improved or worsening cholesterol profiles. The Young Finns study described the cluster of total cholesterol, high-density lipoprotein, and diastolic blood pressure over 6 years and the “false positives” and “false negatives” at follow up. They too described lifestyle behaviors among these youth and how they changed over time. “False positives” showed improvements in their weight, decreased total and saturated fat intake, increased physical activity, and less incidence of smoking. At the same time, the “false negatives” showed worse diet and exercise patterns, and they also increased weight. In a recent article, a nonclinical sample of girls was tracked over 8 years with 5 visits to describe risk profiles for MetS. They tracked the 6 clinical measurements (blood pressure, waist circumference, glucose, triglycerides, and high-density lipoprotein) also tested by Goodman et al. Ventura et al measured dietary and physical activity and discovered 4 patterns over time; a lower metabolic risk group, a lower dyslipidemia risk group, a lower hypertension risk group, and a higher MetS risk group. The higher MetS risk group had greater increases in BMI and fat mass, higher intake of sweetened beverages, and significantly more family history of type 2 diabetes mellitus and obesity. Also, the lower MetS group had the highest fitness level at the final follow-up. Thus, changes in cardiovascular risk factor clustering are modifiable by lifestyle behaviors.

The baseline, incident, and persistent MetS cases presented by Goodman et al experienced changes to their anthropometric and insulin measures differently. All 3 cases have high BMIs and waist circumferences. However, the incident and persistent cases had large increases in BMI (>5 kg/m²) and waist circumference (>14 cm) over the 2.7 years of follow-up. The baseline cases had very minimal increases in BMI (1 kg/m²) and waist circumference (8 cm) over the same time, whereas the entire cohort only increased their BMI by 1.7 kg/m² and waist circumference by 6 cm over the same time.

The changes in insulin values were also different: the baseline subjects insulin levels dropped by 83 pM/L, whereas the incident cases increased 13.9 pM/L. This suggests that insulin resistance may have improved with baseline cases and worsened with the incident cases. These alterations can be influenced by changes in weight, pubertal status, and exercise. The children with persistent MetS also experienced a drop in insulin levels by 62 pM/L over the same time. For these children, changes did not appear to be the result of improvements in diet or fitness level, as other CVD risk factors and measures of adiposity worsened. This fall in insulin might be a warning for a decrease in β cell function, especially because these subjects had the highest BMI. Although this was entirely an observational study, it is possible that participation in this study had some effect on the subjects and their families. This study was conducted during the current era of childhood obesity and heightened media attention. The baseline measurements may have raised a concern with the parents, who then sought out their child’s pediatrician for advice on their child’s weight.

Although a label of “metabolic syndrome” among obese youth should not be a green light for pharmacotherapy, and nor should a diagnosis be made on 1 set of measurements, multiple abnormal risk factors in obese youth should still trigger concern for other complications as well as counseling and treatment efforts for persistently affected youth and their families. The American Heart Association and the American Diabetes Association have pointed out that patients with CVD risk factors above normal cut points should receive counseling for lifestyle modification. Because a number of
these factors are modifiable by fitness improvement, smoking cessation, and diet changes, these must be the areas of focus of the primary care providers and, if available, of more intensive lifestyle programs.

Disclosures
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