Pediatric Metabolic Syndrome Predicts Adulthood Metabolic Syndrome, Subclinical Atherosclerosis, and Type 2 Diabetes Mellitus but Is No Better Than Body Mass Index Alone

The Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study

Costan G. Magnusson, PhD; Juha Koskinen, BM; Wei Chen, MD, PhD; Russell Thomson, PhD; Michael D. Schmidt, PhD; Sathanur R. Srinivasan, PhD; Mika Kivimäki, PhD; Noora Mattsson, MD; Mika Kähönen, MD, PhD; Tomi Laitinen, MD, PhD; Leena Taittonen, MD, PhD; Tapani Rönnemaa, MD, PhD; Jorma S.A. Viikari, MD, PhD; Gerald S. Berenson, MD; Markus Juonala, MD, PhD; Olli T. Raitakari, MD, PhD

Background—The clinical utility of identifying pediatric metabolic syndrome (MetS) is controversial. This study sought to determine the status of pediatric MetS as a risk factor for adult subclinical atherosclerosis (carotid intima-media thickness [cIMT]) and type 2 diabetes mellitus (T2DM) and compare and contrast this prediction with its individual components.

Methods and Results—Using data from the population-based, prospective, observational Bogalusa Heart and Cardiovascular Risk in Young Finns studies, we examined the utility of 4 categorical definitions of youth MetS and their components in predicting adult high cIMT and T2DM among 1781 participants aged 9 to 18 years at baseline (1984 to 1988) who were then examined 14 to 27 years later (2001–2007) when aged 24 to 41 years. Youth with MetS were at 2 to 3 times the risk of having high cIMT and T2DM as adults compared with those free of MetS at youth. Risk estimates with the use of high body mass index were similar to those of MetS phenotypes in predicting adult outcomes. Comparisons of area under the receiver operating characteristic curve and net reclassification index suggested that prediction of adult MetS, high cIMT, and T2DM in adulthood with the use of youth MetS was either equivalent or inferior to classification based on high body mass index or overweight and obesity.

Conclusions—Youth with MetS are at increased risk of meaningful adult outcomes; however, the simplicity of screening for high BMI or overweight and obesity in the pediatric setting offers a simpler, equally accurate alternative to identifying youth at risk of developing adult MetS, high cIMT, or T2DM. (Circulation. 2010;122:1604-1611.)

Key Words: atherosclerosis ■ diabetes mellitus ■ metabolic syndrome ■ obesity ■ pediatrics

The clinical utility of identifying pediatric metabolic syndrome (MetS) has been questioned recently because of evidence demonstrating marked short-term instability in the categorical diagnosis.1–3 Although instability of the diagnosis is an important concern, particularly in relation to considerations of pharmacotherapy in children and adolescents (herein referred to as youth), it is only 1 component in prediction. An equally important consideration concerns whether pediatric MetS identifies those at increased risk of subsequent disease later in life. Adults with MetS are at increased risk of type 2 diabetes mellitus (T2DM)4 and cardiovascular disease,4 but the evidence base for youth is not well established. For example, although some studies suggest that pediatric MetS predicts adult MetS,5–7 few studies have examined the link between MetS in youth and risk...
of future cardiovascular disease\textsuperscript{8} and T2DM in adulthood.\textsuperscript{7} Furthermore, the existing data are limited by very small case numbers and did not fully consider the contribution of each MetS component to risk prediction.\textsuperscript{9} It is therefore evident that the current understanding of youth MetS and its components and their association with adult cardiometabolic-related outcomes is in its infancy, and there is clearly a need for data from large-scale longitudinal studies on the utility of identifying pediatric MetS.

### Clinical Perspective on p 1611

The present study is based on 2 prospective cohorts, the Bogalusa Heart Study (BHS) and the Cardiovascular Risk in Young Finns Study, that both have MetS risk factor variables measured in youth (baseline) and again in adulthood (follow-up). Our aims were to determine the status of pediatric MetS as a risk factor for adult MetS, subclinical atherosclerosis (carotid intima-media thickness [cIMT]), and T2DM and compare and contrast this prediction with its individual components. A secondary aim was to determine the long-term (childhood to adulthood) stability of MetS. These aims are in accord with the directions for future research detailed in the February 2009 Scientific Statement from the American Heart Association on MetS in children and adolescents.\textsuperscript{1}

### Methods

For the BHS, youth aged 9 to 18 years who participated in either the 1984–1985 or 1987–1988 surveys and attended either the 2001–2002 or 2003–2007 adult surveys (then aged 25 to 41 years) were included in the analyses (n=374). To harmonize the study designs, we included from Young Finns those who participated in the 1986 survey when aged 9, 12, 15, or 18 years and in either the 2001 or 2007 adult follow-ups (then aged 24 to 39 years; n=1407). For individuals who participated in multiple baseline (in the case of BHS) or follow-up surveys, we used those measures that provided the longest time period between baseline and follow-up. Each study received ethical approval and obtained written informed consent from participants. Measures available at baseline and follow-up included height and weight, blood pressure, lipids and lipoproteins, glucose, and insulin. Waist circumference and ultrasound examinations of the carotid artery were collected at follow-up only. Study samples and protocols have been described in detail previously.\textsuperscript{10,11} We encourage readers to view the online-only Data Supplement for a more comprehensive description of methods.

### Classification of the MetS in Childhood

Because there is no universal definition of pediatric MetS, we took an approach used in previous reports that characterize pediatric MetS according to multiple alternate definitions.\textsuperscript{2} We used body mass index (BMI) as the measure of adiposity because waist circumference was not available for either cohort at baseline. For the first 2 definitions, we generated age-, sex-, race- (BHS), cohort-, and study year–specific Z scores of BMI, systolic and diastolic blood pressures, high-density lipoprotein cholesterol, triglycerides, and glucose. For the modified National Cholesterol Education Program (NCEP) definition, a participant was categorized as having MetS if he/she had any of the following 5 components: BMI ≥75th percentile, systolic or diastolic blood pressure ≥75th percentile, high-density lipoprotein cholesterol ≤25th percentile, triglycerides ≥75th percentile, or glucose ≥75th percentile. For the modified International Diabetes Federation (IDF) definition, the same cut points as those for the modified NCEP definition were used, but the combination of the components differed. The modified IDF required elevated BMI plus any of the remaining 4 components to be classified as having MetS. The third and fourth definitions utilized age- and sex-standardized pediatric cut points available in the literature to denote each component risk factor. For example, overweight or obesity was defined according to the Cole classification\textsuperscript{12,13}; prehypertension or hypertension was defined according to the fourth report on high blood pressure in children and adolescents from the National High Blood Pressure Education Program\textsuperscript{14}; low high-density lipoprotein cholesterol and high triglycerides were defined with the use of cut points recently proposed from growth-curve data linking youth glucose levels to adult hyperglycemia have shown levels to remain consistent in the pediatric setting.\textsuperscript{15} The pediatric NCEP definition required any 3 of these 5 criteria, whereas the pediatric IDF definition required overweight or obesity plus any 2 of the remaining 4 components. To complement the dichotomous definitions, a continuous MetS risk score (cMetS) was created with the use of the methods described by Wijndaele et al.\textsuperscript{16} Similar to previous studies in which this method was used,\textsuperscript{16,17} 2 principal components were identified (see Table I in the online-only Data Supplement). The principal components were then summed, with weights determined by the relative proportion of variance explained, to compute cMetS, where a higher score is indicative of a less favorable MetS profile.\textsuperscript{16}

### Classification of MetS in Adulthood

To classify adult MetS, we used the recent definition proposed in a joint statement of the IDF Task Force on Epidemiology and Prevention, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, and International Association for the Study of Obesity.\textsuperscript{18}

### Classification of High cIMT in Adulthood

As detailed previously,\textsuperscript{19} the most consistent cIMT measurement recorded across study centers was the maximum measurement at the far wall of the left common carotid artery. We defined high cIMT in adulthood as a maximum cIMT ≥90th percentile for age-, sex-, race- (BHS), study year–, and cohort-specific values. In sensitivity analyses, we had essentially similar results using standardized cut points corresponding to the 70th, 75th, 80th, and 85th cIMT percentiles (data not shown).

### Classification of T2DM in Adulthood

Participants were classified as having T2DM if they (1) had a fasting plasma glucose ≥7.0 mmol/L (≥125 mg/dL); or (2) reported receiving oral hypoglycemic agents and/or insulin injections and did not have type 1 diabetes mellitus; or (3) reported a history of physician-diagnosed T2DM, which is consistent with the World Health Organization definition.\textsuperscript{20} Women who reported having physician-diagnosed diabetes mellitus only during the term of their pregnancy were considered to have had gestational diabetes and were classified as not currently having T2DM provided that their plasma glucose levels were not ≥7.0 mmol/L (≥125 mg/dL).

### Statistical Analyses

#### Stability of MetS Between Youth and Adulthood

Stability of MetS definitions between youth and adulthood is presented according to 3 groups: (1) persistent MetS (MetS-positive youth who were also MetS positive as adults); (2) stable MetS (those MetS positive at baseline but MetS negative at follow-up); and (3) incident MetS (MetS-negative youth who were MetS positive as adults). The number of participants in each of these 3 groups is expressed as a proportion of the total MetS cases identified (total cases from youth and adulthood) and is presented graphically, which is consistent with previous reports.\textsuperscript{2,3}

#### Utility of Pediatric MetS in Predicting Adult Outcomes

Relative risks and 95% confidence intervals estimated with the use of log binomial regression or Poisson regression with robust standard errors were used to examine associations between MetS phenotypes (number of MetS components in youth; youth MetS status; cMetS score) and outcomes of (1) adult MetS, (2) adult high cIMT, and (3) adult T2DM. Analyses were performed for both cohort-stratified and cohort-pooled data. All estimates were adjusted for length of follow-up. We adjusted for length of follow-up to account for any within-cohort
differences observed between length of follow-up and risk of adult outcomes, as we have previously observed and detailed.

Race was also included as a covariate for BHS analyses. For pooled estimates, we included a 2-level variable for cohort. Interactions between cohort and the predictor variables were assessed by including product terms as additional covariates. The associations between each MetS component and the adult outcomes were examined with the use of 2 models. Model 1 adjusted for length of follow-up and cohort; model 2 additionally included all MetS components.

The ability of each MetS definition in youth to predict MetS, high cIMT, and T2DM in adulthood was assessed with the use of sensitivity, specificity, positive predictive value, negative predictive value, and area under receiver operating characteristic curves. Because we found high BMI in youth to be the major contributing component in the prediction of adult outcomes, we also provide these data for high BMI. In addition, to predict adult outcomes of MetS, high cIMT, and T2DM, we performed comparisons between 3 models: (1) high youth BMI (referent model); (2) modified NCEP (or pediatric NCEP) MetS definition; and (3) modified IDF (or pediatric IDF) MetS definition. Differences in area under receiver operating characteristic curves between models were estimated with the use of the DeLong algorithm. Net reclassification improvement was also calculated to determine the extent to which MetS definitions reassigned participants to a risk status that better reflected their final outcome (case or control). All statistical analyses were performed with the use of STATA 10 with statistical significance inferred at a 2-tailed $P$ value $\leq 0.05$.

Results

Participant Characteristics

Key baseline and follow-up characteristics are displayed in Table 1. Mean (SD) length of follow-up between baseline and follow-up was 24.4 (3.7) years and ranged from 14 to 27 years. The prevalence of youth MetS differed according to definition. Those with T2DM at follow-up included 25 BHS participants (2 black males, 10 black females, 4 white males, 9 white females; prevalence in blacks $= 9.5\%$, whites $= 5.3\%$, overall $= 6.7\%$) and 11 Young Finns participants (4 males and 7 females; prevalence $= 0.8\%$).

Stability of MetS Between Youth and Adulthood

The proportions of participants who had persistent MetS, incident MetS, or stable MetS diagnosis with the use of different youth MetS definitions is displayed in the Figure. Of those with MetS at either baseline or follow-up, those with persistent MetS accounted for $\sim 20\%$ based on the modified definitions and $\sim 7\%$ based on the pediatric definitions. Irrespective of the youth definition employed, the major proportion of participants with MetS had acquired it since youth.

Utility of Pediatric MetS in Predicting Adult Outcomes

Adult MetS

Pooled analyses suggested youth with MetS to have between 2.7 and 3.4 times greater risk of adult MetS compared with those without baseline MetS (all $P<0.05$; complete data not shown). The risk of adult MetS tended to increase as the number of youth MetS components increased ($P$ for trend
whereas a 1-SD increase in youth cMetS score increased the risk of adult MetS (relative risk = 1.5; 95% confidence interval, 1.4 to 1.6).

**Adult High cIMT**

Relative risks for pediatric MetS definitions in predicting high cIMT in adulthood are displayed in Table 2. Pediatric MetS definitions were associated with a 2-fold increase in risk for developing high cIMT in adulthood. The risk of high cIMT increased as the number of youth MetS components increased. As youth cMetS increased, risk of high cIMT in adulthood increased in each cohort but was stronger in the BHS than the Young Finns Study ($P$ for interaction = 0.01). In light of this interaction, the pooled estimate should be interpreted with caution. Effect estimates from pooled analyses that additionally adjusted for baseline low-density lipoprotein cholesterol and smoking were essentially similar.

**Adult T2DM**

Relative risks of T2DM in adulthood according to youth MetS are shown in Table 3. Pooled analyses showed that youth with MetS had 2 to 3 times the risk of developing T2DM in adulthood compared with those without youth MetS. There was a trend toward increased risk of T2DM as MetS components increased, but this effect was driven by Young Finns ($P$ for interaction < 0.001). A 1-SD increase in cMetS in youth was associated with 30% excess risk of T2DM in adulthood.

**Youth MetS Components in Predicting Adult Outcomes**

Table 4 displays relative risks from pooled data for predicting MetS, high cIMT, and T2DM in adulthood according to each component of youth MetS (cohort-stratified data were essentially similar; data not shown). High BMI was the only consistent component associated with increased risk of adult outcomes in multivariable models. Insulin was a multivariable predictor of adult MetS but not high cIMT or T2DM; BMI remained a strong predictor of all outcomes with the inclusion of insulin (Table II in the online-only Data Supplement). Risk estimates in which high BMI was used (Table 4) were similar to those of MetS phenotypes (Tables 2 and 3) in predicting adult outcomes.

**Comparison Between High BMI and MetS Definitions**

The prevalence of modified NCEP and modified IDF MetS among youth with BMI ≥75th percentile was 49.3%; the prevalence of pediatric NCEP and pediatric IDF MetS among youth classified as overweight or obese was 14.8%. Data that compare high BMI with MetS definitions in youth in predicting adult outcomes are displayed in Table 5 and Table III in the online-only Data Supplement. Prediction of adult outcomes by BMI in youth was either equal to or superior to the predicted outcomes by pediatric MetS definitions.

**Table 2. Relative Risks and 95% Confidence Intervals of High cIMT in Adulthood According to MetS Risk Variables in Childhood**

| No. of MetS components | Bogalusa | | Young Finns | | Pooled | |
|---|---|---|---|---|---|
| | RR | 95% CI | RR | 95% CI | RR | 95% CI |
| 0 | 1.0 | Reference | 1.0 | Reference | 1.0 | Reference |
| 1 | 3.3 | 0.7–14.8 | 1.1 | 0.7–1.7 | 1.2 | 0.8–1.9 |
| 2 | 4.8 | 1.1–21.5 | 1.2 | 0.7–1.8 | 1.4 | 0.9–2.1 |
| 3 | 7.1 | 1.6–31.7 | 1.6 | 1.0–2.7 | 2.0 | 1.3–3.2 |
| 4 | 8.7 | 1.7–45.1 | 2.5 | 1.5–4.3 | 2.9 | 1.8–4.7 |
| $P_{\text{trend}}$ | <0.001 | 0.001 | <0.001 | |

*All models are adjusted for length of follow-up; pooled estimates are additionally adjusted for cohort. Reference category for dichotomous predictor variables (modified NCEP, modified IDF, pediatric NCEP, pediatric IDF) is no MetS.

†Relative risks (RRs) and 95% confidence intervals (CIs) are expressed for a 1-SD increase in cMetS.
than the prediction provided by any of the youth MetS definitions. Substantial gains in sensitivity at relatively modest trade-offs in specificity were observed with the use of high BMI or overweight or obesity in youth, which translated to improved discrimination (area under receiver operating characteristic curves). As evidenced by negative net reclassification index values, the accuracy of classification was reduced significantly (all \( P<0.03 \)) by using either of the youth MetS definitions in place of high BMI.

**Discussion**

This study addresses 2 important areas of MetS in youth outlined in the recent Scientific Statement from the American Heart Association, as follows: (1) the long-term stability of MetS definitions from youth to adulthood and (2) whether MetS definitions are able to predict future disease.1 We found that despite instability in the diagnosis of youth MetS over a mean 24-year period, dichotomous definitions of MetS in youth predict important disease outcomes, such as adult MetS, high cIMT, and T2DM in early to middle adulthood. Our analyses also revealed that high BMI alone was as good as and in some cases superior to dichotomous pediatric MetS definitions in predicting adult MetS, high cIMT, and T2DM. These findings have important clinical implications.

MetS is a subject of controversy in both adult2,3 and pediatric settings.1 From a pediatric perspective, the American Heart Association, as follows: (1) the long-term stability of MetS definitions from youth to adulthood and (2) whether MetS definitions are able to predict future disease.1 We found that despite instability in the diagnosis of youth MetS over a mean 24-year period, dichotomous definitions of MetS in youth predict important disease outcomes, such as adult MetS, high cIMT, and T2DM in early to middle adulthood. Our analyses also revealed that high BMI alone was as good as and in some cases superior to dichotomous pediatric MetS definitions in predicting adult MetS, high cIMT, and T2DM. These findings have important clinical implications.

MetS is a subject of controversy in both adult2,3 and pediatric settings.1 From a pediatric perspective, the American Heart Association, as follows: (1) the long-term stability of MetS definitions from youth to adulthood and (2) whether MetS definitions are able to predict future disease.1 We found that despite instability in the diagnosis of youth MetS over a mean 24-year period, dichotomous definitions of MetS in youth predict important disease outcomes, such as adult MetS, high cIMT, and T2DM in early to middle adulthood. Our analyses also revealed that high BMI alone was as good as and in some cases superior to dichotomous pediatric MetS definitions in predicting adult MetS, high cIMT, and T2DM. These findings have important clinical implications.

**Table 3. Relative Risks and 95% Confidence Intervals of T2DM in Adulthood According to MetS Risk Variables in Childhood**

<table>
<thead>
<tr>
<th>MetS Risk Variable</th>
<th>Bogalusa</th>
<th>Young Finns</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of MetS components</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.0</td>
<td>Reference</td>
<td>1.0</td>
</tr>
<tr>
<td>1</td>
<td>1.2</td>
<td>0.4–4.0</td>
<td>3.1</td>
</tr>
<tr>
<td>2</td>
<td>2.3</td>
<td>0.7–7.5</td>
<td>1.2</td>
</tr>
<tr>
<td>3</td>
<td>1.7</td>
<td>0.4–6.5</td>
<td>5.0</td>
</tr>
<tr>
<td>≥4</td>
<td>3.7</td>
<td>0.9–16.0</td>
<td>12.9</td>
</tr>
<tr>
<td>( P_{\text{trend}} )</td>
<td>0.06</td>
<td>0.04</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*All models are adjusted for length of follow-up; pooled estimates are additionally adjusted for cohort. Reference category for dichotomous predictor variables (modified NCEP, modified IDF, pediatric NCEP, pediatric IDF) is no MetS.

†Relative risks (RRs) and 95% confidence intervals (CIs) are expressed for a 1-SD increase in cMetS.

**Table 4. Relative Risks and 95% Confidence Intervals of Adult MetS, High cIMT, and T2DM According to Each Component of Youth MetS Definitions**

<table>
<thead>
<tr>
<th>Component</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 1*</th>
<th>Model 2†</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI ≥75th percentile</td>
<td>3.0</td>
<td>2.5–3.7</td>
<td>2.5</td>
<td>2.1–3.1</td>
<td>2.2</td>
<td>1.7–2.9</td>
</tr>
<tr>
<td>BP ≥75th percentile</td>
<td>1.5</td>
<td>1.2–1.8</td>
<td>1.2</td>
<td>1.0–1.5</td>
<td>1.4</td>
<td>1.0–1.8</td>
</tr>
<tr>
<td>HDL cholesterol ≤25th percentile</td>
<td>1.9</td>
<td>1.6–2.4</td>
<td>1.4</td>
<td>1.2–1.8</td>
<td>1.3</td>
<td>1.0–1.8</td>
</tr>
<tr>
<td>Triglycerides ≥75th percentile</td>
<td>2.0</td>
<td>1.6–2.5</td>
<td>1.4</td>
<td>1.1–1.7</td>
<td>1.3</td>
<td>1.0–1.7</td>
</tr>
<tr>
<td>Glucose ≥75th percentile</td>
<td>1.5</td>
<td>1.2–1.9</td>
<td>1.3</td>
<td>1.0–1.6</td>
<td>1.1</td>
<td>0.8–1.6</td>
</tr>
</tbody>
</table>

Pediatric NCEP/IDF

| Overweight or obese | 2.9 | 2.4–3.6 | 2.5 | 2.0–3.1 | 2.4 | 1.8–3.2 | 2.2 | 1.6–3.0 |
| Prehypertensive or hypertensive | 1.7 | 1.4–2.1 | 1.4 | 1.1–1.8 | 1.7 | 1.2–2.3 | 1.5 | 1.1–2.0 |
| Low HDL cholesterol | 1.7 | 1.3–2.1 | 1.3 | 1.0–1.7 | 1.3 | 0.9–1.9 | 1.2 | 0.8–1.8 |
| Hypertriglyceridemia | 2.5 | 1.9–3.3 | 1.5 | 1.0–2.1 | 1.6 | 0.9–2.7 | 1.0 | 0.6–1.8 |
| Hyperglycemia | 1.3 | 0.7–2.3 | 1.2 | 0.7–2.1 | 0.9 | 0.4–2.4 | 0.9 | 0.4–2.3 |

RR indicates relative risk; CI, confidence interval; BP, blood pressure; and HDL, high-density lipoprotein.

*Model 1: adjusted for length of follow-up and cohort.
†Model 2: adjusted for length of follow-up, cohort, and all other MetS components.
Assessment of pubertal stage on a number of MetS components that stability. This finding is not surprising given the known influence of risk factor clustering, the diagnosis of MetS was stable in only 50% of cases over a 3-year period. Among obese youth aged 6 to 17 years, Gustafson et al3 found that only 30% and 45% of those with baseline MetS were confirmed after 60-day and 1.5-year follow-ups, respectively, which is striking considering the short duration of follow-up but also because we would expect that MetS in obese youth would persist into adulthood, it may be more apt to use these definitions, should they be adopted in a clinical setting, as a basis for identifying those not at risk so that further attention can be focused on those with unclear potential for developing MetS, high cIMT, or T2DM in early to middle adulthood. This interpretation appears relevant given our findings that those with youth MetS, irrespective of instability in the categorical diagnosis and poor clinical prediction, were at significantly increased risk of MetS, high cIMT, and T2DM in adulthood. However, we acknowledge that a substantially longer follow-up period is needed to judge the clinical utility with respect to T2DM given that the increase in T2DM incidence begins to rise only after age 50 years.

Perhaps the most important finding from this study was that high BMI predicts each outcome as well as or better than the categorical MetS definitions considered in this study. This finding has clinical relevance. At pediatric visits for health care, BMI can easily and accurately be determined with the use of minimum equipment, which would allow the immediate identification of youth at heightened risk (with the use of Cole’s international tables) who might benefit from therapeutic lifestyle intervention aimed at weight control. Other benefits include the need not to subject a child to a blood draw and aversion of costs and time associated with laboratory analysis. A caveat to the clinical application of these findings is that a substantial number of contemporary youth will be identified as at risk.

One explanation for why the additional measures incorporated into MetS did not improve prediction may be because 1 measurement of BMI is more accurate than 1 measurement of the laboratory components of MetS. Pediatric guidelines on blood pressure13 and lipids29 require multiple measurements before elevated levels are diagnosed owing to laboratory and biological variation. It is possible that multiple laboratory-
Based and blood pressure measures collected over a period of weeks or months may improve the observed estimates for pediatric MetS, and this is a limitation of this study. In agreement with this hypothesis, Gaziano and colleagues have recently shown a non–laboratory-based risk score (including BMI, blood pressure, smoking status, and reported diabetes mellitus status) that predicted cardiovascular disease events as accurately as a risk score that additionally included laboratory-based methods.

Another explanation may be that overweight and obesity precede the clustering of MetS components such that it may be a more sensitive marker in the pediatric setting. Although the specific cause of MetS is unknown, potential mechanisms posit obesity and insulin resistance as initiating factors. We found overweight/obesity to remain an independent predictor of adult outcomes in multivariable models, but the corresponding association with insulin disappeared. Although our study cannot establish causality, these data are consistent with reports from the BHS showing a temporal association between degree of baseline adiposity and incidence of hyperinsulinemia in youth and young adults independent of baseline insulin levels and independent of childhood obesity, but not insulin or insulin resistance, in predicting adult MetS.

**Limitations**

Several limitations need to be considered. First, because a substantial proportion of participants at baseline did not attend follow-up, bias due to differential loss to follow-up is possible. However, although we have previously shown that nonparticipants at follow-up were more likely to be younger, male, and black (BHS), baseline risk factor levels were similar between those who did and those who did not attend follow-up, suggesting that a major bias is unlikely. A second limitation is missing data on baseline waist circumference in both cohorts. The baseline surveys were performed in the 1980s before the importance of abdominal adiposity to clustering of metabolic-related risk factors was known. Although BMI is considered a reasonable alternative to waist circumference, it may be a less sensitive measure in the pediatric setting. Although our data suggest that the identification of meaningful outcomes in adulthood might be accomplished by screening for only youth BMI, we are unable to discount that other elements of youth MetS may be useful in identifying and possibly treating cardiometabolic disorders, and future research should seek to address this gap.

**Conclusions**

Accumulating evidence is increasingly coming to light on the limitations of using a dichotomous definition of MetS in the pediatric setting that incorporates rudimentary elements shown to have clinical utility in adult settings. Although our data demonstrate that multiple pediatric definitions predict clinically meaningful outcomes, these definitions do so at a level equivalent or inferior to predictions obtained from the status of high BMI in youth. The benefits of screening for only high BMI or overweight and obesity in the pediatric setting are obvious. These data thus contribute to the ongoing debate on the clinical utility of applying dichotomous MetS definitions adapted from the adult literature to the pediatric setting.

**Acknowledgments**

We thank Pronabesh Das Mahapatra, MD, MPH, from the BHS group and Ville Aalto, MSc, from the Young Finns group for assistance in compiling these data.

**Sources of Funding**

The BHS was supported financially by National Institutes of Health grants AG-16592 from the National Institute of Aging and HL-38844 from the National Heart, Lung, and Blood Institute. The Cardiovascular Risk in Young Finns study was supported financially by the Academy of Finland (grants 117797, 126925, and 121584), Social Insurance Institution of Finland, Turku University Foundation, special federal grants for Turku University Central Hospital, Juho Vainio Foundation, Finnish Foundation of Cardiovascular Research, Finnish Cultural Foundation, and Orion Farmos Research Foundation. Dr Magnussen’s contribution to this article was supported in part by the Emil and Bilda Maunulan fund. Dr Kivimäki was supported by the National Heart, Lung, and Blood Institute (R01HL036310–20A2), National Institutes of Health, and the BUPA Foundation specialist research grant. Dr Kähönen was supported by the Tampere University Hospital Medical Fund.

**Disclosures**

None.

**References**

By guest on May 1, 2017
http://circ.ahajournals.org/ Downloaded from


CLINICAL PERSPECTIVE

In a recent Scientific Statement from the American Heart Association on metabolic syndrome (MetS) in children and adolescents, the need for additional research examining the efficacy of pediatric MetS to predict adult health was highlighted. In the present analyses based on 2 population-based prospective cohorts, the Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study, we examined the utility of youth MetS and its components in predicting adult high carotid intima-media thickness and type 2 diabetes mellitus among 1781 participants aged 9 to 18 years at baseline who were reexamined 14 to 27 years later. We observed that youth with MetS were at 2 to 3 times the risk of having high carotid intima-media thickness and type 2 diabetes mellitus as adults compared with those free of MetS. However, the prediction of adult high carotid intima-media thickness and type 2 diabetes mellitus with the use of youth body mass index was either equivalent or superior to classification based on pediatric MetS. Our findings have direct clinical relevance because they suggest that in the clinical setting, efforts to identify youth with heightened future risk of meaningful outcomes can be minimally achieved with the use of body mass index only, thus avoiding cost and other barriers associated with testing and classification of youth MetS. However, clinicians who use high body mass index to identify youth at increased future risk need to keep in mind that a large proportion of contemporary youth will be classified as at risk and that our analyses are unable to discount that youth MetS may be useful in identifying and possibly treating other cardiometabolic disorders.
Pediatric Metabolic Syndrome Predicts Adulthood Metabolic Syndrome, Subclinical Atherosclerosis, and Type 2 Diabetes Mellitus but Is No Better Than Body Mass Index Alone: The Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study

Costan G. Magnussen, Juha Koskinen, Wei Chen, Russell Thomson, Michael D. Schmidt, Sathanur R. Srinivasan, Mika Kivimäki, Noora Mattsson, Mika Kähönen, Tomi Laitinen, Leena Taittonen, Tapani Rönnemaa, Jorma S.A. Viikari, Gerald S. Berenson, Markus Juonala and Olli T. Raitakari

Circulation. 2010;122:1604-1611; originally published online October 4, 2010; doi: 10.1161/CIRCULATIONAHA.110.940809

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/122/16/1604

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2010/10/04/CIRCULATIONAHA.110.940809.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/
SUPPLEMENTAL MATERIAL
Supplemental Methods

For the BHS, youth aged 9-18 years who participated in either the 1984-85 or 1987-88 surveys and participated in either the 2001-02 or 2003-07 adult surveys (then aged 25-41 years) were included in the analyses. To harmonize the study designs, we included from Young Finns those who participated in the 1986 survey when aged 9, 12, 15, or 18 years and in either the 2001 or 2007 adult follow-ups (then aged 24-39 years). We selected these baseline and follow-up samples for the following reasons: first, glucose screening only commenced in Young Finns in 1986; second, Young Finns participants in 1986 were aged from 9 years, so for consistency, we limited the baseline BHS sample to those aged 9 years or older; third, we chose the adult follow-ups because they were the most consistent time-points between the two studies and served to minimize differences in length of follow-up. For individuals that participated in multiple baseline (in the case of BHS) or follow-up surveys, we used those measures that provided the longest time-period between baseline and follow-up. For all analyses, we excluded women who were pregnant at the time of follow-up or participants with type 1 diabetes mellitus. Each study received ethical approval, and obtained written informed consent from participants. Participant numbers with available data and the measures relevant to the aims of this report follow.

United States Data: The Bogalusa Heart Study

Study sample

The Bogalusa Heart study sample has been described in detail elsewhere. For this study, 374 participants aged 9-18 years at baseline (11% of those eligible, 42% male, 34% Black) were included.

Clinic measurements
Height and weight were measured at all time points and body mass index (BMI) calculated as weight(kg)/[height(m)]². Waist circumference was only measured at adult follow-ups. Blood pressure measurements at baseline and follow-up were obtained from the right arm of seated participants by two randomly assigned nurses using mercury sphygmomanometers. The first and fifth Korotkoff sounds were used to define systolic and diastolic blood pressures, with the means of replicate readings used in all analyses. Venous blood samples were taken after a 12-hour fast. At the 1984-85 baseline survey, cholesterol and triglycerides were measured using chemical procedures with a Technicon Auto Analyzer II (Technicon Instrument Corp, Tarrytown, NY), according to the laboratory manual of the Lipid Research Clinics program.² These variables were determined by enzymatic procedures using the Hitachi 902-Automatic Analyzer (Roche Diagnostics, Indianapolis, IN) at follow-up. Serum lipoprotein cholesterols were analyzed using a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures.³ Plasma glucose was measured enzymatically using the Beckman Instant Glucose Analyzer (Beckman Instruments, Palo Alto, CA).

Carotid artery ultrasound studies
B-mode ultrasound examinations were performed according to established protocols.⁴⁶ Maximum cIMT measurements of 3 right and 3 left far walls for common carotid, carotid bifurcation, and internal carotid segments were recorded according to strict protocols.⁵ Seventy-five participants underwent repeat ultrasound examinations 10-12 days after their initial visit to determine intra-individual reproducibility. The average absolute difference and standard deviation (SD) between measurements for all cIMT segments was 0.05±0.03 mm.

Finnish Data: The Cardiovascular Risk in Young Finns Study

Study sample
The Young Finns sample is described in detail elsewhere. For this study, 1407 participants aged 9-18 years at baseline (79% of those eligible from baseline, 44% male) were included.

**Clinic measurements**

Height and weight were measured at baseline and follow-up and BMI calculated. Waist circumference was measured in 2001 and 2007 only. Blood pressure measurements were obtained from the right arm using a random zero sphygmomanometer at baseline and follow-up. The first and fifth Korotkoff sounds were used to define systolic and diastolic pressures, with the average of three measurements used in the analyses. Venous blood samples were taken after a 12-hour fast. At baseline (1986), serum cholesterol and triglycerides were measured using fully enzymatic Boehringer CHOD-PAP kits with an OLLI 3000 analyzer. Since this time, Olympus System reagent analyzer in a clinical chemistry analyzer (AU400, Olympus), was used to determine lipid levels. Serum HDL-cholesterol was measured by the dextran sulphate 500,000 method. Glucose concentration was determined using β-D-glucose: nicotinamide adenine dinucleotide oxidoreductase method in 1986 and enzymatically (Olympus, Diagnostica GmbH, Germany) at follow-up. Due to changes in determination methods and kits during study years, biochemistry for 1986 has been corrected to follow-up levels, as previously detailed.

**Carotid artery ultrasound studies**

B-mode ultrasound studies of the left carotid artery were performed at both 2001 and 2007 follow-ups using standardized protocols. At least four measurements of the far wall were taken approximately 10 mm proximal to the bifurcation to derive mean and maximum cIMT. To assess intra-individual reproducibility of ultrasound measurements, 57 subjects were re-
examined 3 months after their initial visit. The average absolute difference and SD between measurements was 0.05±0.04 mm.

Classification of the metabolic syndrome in childhood

Because there is no universal definition of pediatric MetS, we took an approach used in previous reports that characterize pediatric MetS using multiple alternate definitions. We used BMI as the measure of adiposity since waist circumference was not available for either cohort at baseline. For the first two definitions, we generated age-, sex-, race- (Bogalusa), cohort-, and study-year-specific z-scores of BMI, systolic and diastolic blood pressures, HDL-cholesterol, triglycerides, and glucose. For the modified National Cholesterol Education Program (modNCEP) definition, a participant was categorized as having MetS if he/she had any three of the following five components: BMI ≥75th percentile, systolic or diastolic blood pressure ≥75th percentile, HDL-cholesterol ≤25th percentile, triglycerides ≥75th percentile, or glucose ≥75th percentile. For the modified International Diabetes Federation (modIDF) definition, the same cut-points as those for the modNCEP definition were used but the combination of the components differed. The modIDF required elevated BMI plus any two of the remaining four components to be classified as having MetS. The third and fourth definitions utilized age- and sex-standardized pediatric cut-points available in the literature to denote each component risk factor. For example, overweight or obesity was defined according to the Cole classification, prehypertension or hypertension was defined according to the fourth report on high blood pressure in children and adolescents from the National High Blood Pressure Education Program; low HDL-cholesterol and high triglycerides were defined using cut-points recently proposed from growth-curve data that were linked to adult definitions, and hyperglycemia was defined as plasma glucose ≥5.60 mmol/L (100 mg/dL), as growth-curve data linking youth glucose levels to adult hyperglycemia have
shown levels to remain consistent in the pediatric setting.\textsuperscript{15} Pediatric NCEP (pedNCEP) definition required any three of these five criteria whereas the pediatric IDF (pedIDF) required overweight or obesity plus any two of the remaining four components. To complement the dichotomous definitions, a continuous metabolic syndrome risk score (cMetS) was created using the methods described by Wijndaele et al.\textsuperscript{16, 17} Briefly, principal component analysis with varimax rotation was applied separately by cohort to the normalized MetS components (age-, sex-, race [Bogalusa], cohort-, and study-year-specific z-scores of BMI, systolic and diastolic blood pressure, HDL-cholesterol, triglycerides, and fasting plasma glucose) to derive the principal components that account for the greater proportion (eigenvalue $\geq 1.0$) of MetS variance. Similar to previous studies using this method,\textsuperscript{16, 18} two principal components were identified (see Table I on the online-only data supplement for details). The principal components were then summed, with weights determined by the relative proportion of variance explained, in order to compute cMetS where a higher score is indicative of a less favorable MetS profile.\textsuperscript{16}

**Classification of the metabolic syndrome in adulthood**

To classify adult MetS, we used the recent definition proposed in a joint statement of the IDF Task Force on Epidemiology and Prevention, National Heart, Lung and Blood Institute (NHLBI), the AHA, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity that attempts to harmonize the multiple MetS classifications that have been proposed for adult populations in the literature into a single definition.\textsuperscript{19} MetS was therefore identified when three or more of the following five criteria were present: waist circumference $\geq 102$ cm in men or $\geq 88$ cm in women, triglycerides $\geq 1.695$ mmol/l ($\geq 150$ mg/dL, or specific drug treatment for elevated triglycerides), HDL-cholesterol $< 1.036$ mmol/l ($< 40$ mg/dL ) in men or $< 1.295$ mmol/l ($< 50$ mg/dL) in women, systolic blood pressure $\geq 130$ mmHg, and diastolic blood pressure $\geq 85$ mmHg.
mg/dL) in women (or specific drug treatment for reduced HDL-cholesterol), blood pressure \( \geq 130/\geq 85 \text{ mmHg} \) (or antihypertensive drug treatment in persons with a history of hypertension), fasting plasma glucose \( \geq 5.6 \text{ mmol/l} \) (\( \geq 100 \text{ mg/dL} \) or specific drug treatment of elevated glucose). At this stage, the joint statement concedes that further work is needed before the definition of central adiposity is finalized but suggests that either the former (lower threshold) IDF or (higher threshold) AHA/NHLBI cut-points be used. We chose the higher threshold for waist circumference in our data as these cut-points are more consistent with the thresholds generally used in the United States\textsuperscript{20} and Europe.\textsuperscript{21}

**Classification of high carotid IMT in adulthood**

As previously detailed,\textsuperscript{22} the most consistent cIMT measurement recorded across study centers was the maximum measurement at the far wall of the left common carotid artery. We defined high cIMT in adulthood as a maximum cIMT \( \geq 90^\text{th} \) percentile for age-, sex-, race- (Bogalusa), study-year-, and cohort-specific values to account for any method, secular, or cohort differences. We however acknowledge that no consensus clinical definition of high cIMT currently exists for young adults.

**Classification of type 2 diabetes in adulthood**

Participants were classified as having T2DM if they: (1) had a fasting plasma glucose \( \geq 7.0 \text{ mmol/L} \) (\( \geq 125 \text{ mg/dL} \)); or (2) reported receiving oral hypoglycaemic agents and/or insulin injections and did not have type 1 diabetes; or (3) reported a history of physician-diagnosed T2DM, which is consistent with the WHO definition.\textsuperscript{23} Women who reported having physician-diagnosed diabetes only during the term of their pregnancy were considered to have had gestational diabetes, and were classified as not currently having T2DM provided their plasma glucose levels were not \( \geq 7.0 \text{ mmol/L} \) (\( \geq 125 \text{ mg/dL} \)).
**Statistical analyses**

Data have been pooled where appropriate, but cohort stratified data have also been provided. All analyses were performed using STATA 10.

*Stability of MetS between youth and adulthood*

Stability of MetS definitions between youth and adulthood are presented according to three groups: (1) *persistent* MetS (MetS positive youth who were also MetS positive as adults); (2) *instable* (those MetS positive at baseline but MetS negative at follow-up); and (3) *incident* MetS (MetS negative youth who were MetS positive as adults). The number of participants in each of these three groups is expressed as a proportion of the total MetS cases identified (total cases from youth and adulthood) and are presented graphically, which is consistent with previous reports on short-term stability.\textsuperscript{10,24}

*Utility of pediatric MetS in predicting adult outcomes*

Relative risks and 95% confidence intervals estimated using log binomial regression or Poisson regression with robust standard errors were used to examine associations between MetS phenotypes (number of MetS components in youth; youth MetS status; cMetS score) and outcomes of: (1) adult MetS; (2) adult high cIMT; and (3) adult T2DM. Analyses were performed for both cohort-stratified and cohort-pooled data. All estimates were adjusted for length of follow-up (continuous variable determined as follow-up clinic date minus baseline clinic date expressed in days) to account for any within-cohort differences observed between length of follow-up and risk of outcome.\textsuperscript{22} Race was also included as a covariate for BHS analyses. For pooled estimates, we included a two-level variable for cohort to account for possible differences between cohorts. Because all predictor variables were standardized for
age and sex, these variables were not included as covariates. Interactions between cohort and the predictor variables were assessed by including product terms as additional covariates. The association between each MetS component (high BMI, high blood pressure, low HDL-cholesterol, high triglycerides, or high glucose) and outcomes of adult MetS, adult high cIMT, and adult T2DM were also examined in pooled data using two models. Model 1 adjusted for length of follow-up and cohort; model 2 included length of follow-up, cohort, and all MetS components in the same multivariable model. In all of the above models, pubertal status was considered as a covariate but its inclusion had minimal effect on the coefficients and as such was not retained for final models.

The ability of each MetS definition in youth to predict MetS, high cIMT, and T2DM in adulthood was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under receiver-operating characteristic curves (AUC). These statistics were calculated as follows: sensitivity = true positives/(true positives + false negatives) X 100; specificity = true negatives/(true negatives + false positives) X 100; NPV = true negatives/(true negatives + false negatives) X 100; and PPV = true positives/(true positives + false positives) X 100. The AUC was determined from the logistic model and represents an estimate of the probability that the model assigns a higher risk to those who have the outcome compared with those who do not have the outcome. The AUC has a range of 0 to 1, where a value of 0.5 represents no discrimination, and a value of 1 would indicate perfect discrimination. Because we found high BMI in youth to be the major contributing component in the prediction of adult outcomes, we also provide these data for high BMI. In addition we performed comparisons between three models: (A) high youth BMI (referent model); (B) modNCEP (or pedNCEP) MetS definition; and (C) modIDF (or pedIDF) MetS definition to predict adult outcomes of MetS, high cIMT, and T2DM. Differences in AUC between model B or model C compared with model A were estimated using the DeLong
algorithm.²⁵ Net reclassification improvement (NRI) was also calculated to determine the extent to which MetS definitions reassigned participants to a risk status that better reflected their final outcome (case or control).²⁶,²⁷ The proportions of participants reclassified to either higher- or lower-risk categories using models B, or C were compared with model A. Risk classification is improved if an individual with the outcome in adulthood (case) is placed in a higher risk category in youth or if an individual without the outcome in adulthood (control) is moved to a lower risk category in youth. The NRI is the sum of improvements for both case and control participants determined from youth BMI and MetS status.
### Supplemental Tables

eTable 1. Rotated factor loadings from principal components factor analysis to derive the continuous MetS score at baseline in the Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bogalusa (1984-5)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.539</td>
<td>0.271</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.137</td>
<td>0.827</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>-0.029</td>
<td>0.817</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>-0.794</td>
<td>0.059</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.837</td>
<td>-0.045</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.005</td>
<td>0.224</td>
</tr>
<tr>
<td>Variance explained, %</td>
<td>27.3</td>
<td>24.7</td>
</tr>
<tr>
<td>Total variance explained, %</td>
<td></td>
<td>52.0</td>
</tr>
</tbody>
</table>

<p>| <strong>Bogalusa (1987-8)</strong>           |          |          |
| BMI                             | 0.672    | 0.289    |
| Systolic BP                     | 0.097    | 0.802    |
| Diastolic BP                    | -0.099   | 0.769    |
| HDL cholesterol                 | -0.706   | 0.132    |
| Triglycerides                   | 0.697    | 0.090    |
| Glucose                         | 0.130    | 0.195    |
| Variance explained, %           | 24.5     | 23.0     |
| Total variance explained, %     |          | 47.5     |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Young Finns (1986)</th>
<th>Variance explained, %</th>
<th>Total variance explained, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.552</td>
<td>0.404</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.819</td>
<td>0.031</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0.722</td>
<td>-0.083</td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.067</td>
<td>-0.814</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.211</td>
<td>0.746</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>0.216</td>
<td>0.101</td>
<td></td>
</tr>
<tr>
<td></td>
<td>26.5</td>
<td>23.3</td>
<td>49.8</td>
</tr>
</tbody>
</table>
Table 2. Unadjusted* and adjusted† relative risks (RR) and 95% confidence intervals (95%CI) of adult MetS, high cIMT, and T2DM according to each component of the youth MetS definitions as well as insulin

<table>
<thead>
<tr>
<th></th>
<th>MetS</th>
<th>High cIMT</th>
<th>T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1*</td>
<td>Model 2†</td>
<td>Model 1*</td>
</tr>
<tr>
<td>modNCEP/IDF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI ≥75th percentile</td>
<td>3.0 (2.5-3.7)</td>
<td>2.4 (1.9-3.0)</td>
<td>2.2 (1.7-2.9)</td>
</tr>
<tr>
<td>BP ≥75th percentile</td>
<td>1.5 (1.2-1.8)</td>
<td>1.2 (1.0-1.5)</td>
<td>1.4 (1.0-1.8)</td>
</tr>
<tr>
<td>HDL-C ≤25th percentile</td>
<td>1.9 (1.6-2.4)</td>
<td>1.5 (1.2-1.8)</td>
<td>1.3 (1.0-1.8)</td>
</tr>
<tr>
<td>TG ≥75th percentile</td>
<td>2.0 (1.6-2.5)</td>
<td>1.3 (1.0-1.6)</td>
<td>1.3 (1.0-1.7)</td>
</tr>
<tr>
<td>Glucose ≥75th percentile</td>
<td>1.5 (1.2-1.9)</td>
<td>1.2 (1.0-1.5)</td>
<td>1.1 (0.8-1.6)</td>
</tr>
<tr>
<td>Insulin ≥75th percentile</td>
<td>2.0 (1.7-2.5)</td>
<td>1.3 (1.0-1.6)</td>
<td>1.4 (1.1-1.9)</td>
</tr>
</tbody>
</table>
Table 3. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under the curve (AUC), and net reclassification index (NRI) values for youth MetS definitions in predicting adult MetS, high cIMT, and T2DM

<table>
<thead>
<tr>
<th>Adult outcome</th>
<th>Child MetS definition</th>
<th>N</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>AUC (95%CI)</th>
<th>P-value</th>
<th>NRI, %</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS</td>
<td>Overweight or obese*</td>
<td>1708</td>
<td>33.7</td>
<td>88.8</td>
<td>39.6</td>
<td>86.0</td>
<td>0.612 (0.585-0.640)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>pedsNCEP</td>
<td>1708</td>
<td>8.2</td>
<td>98.6</td>
<td>56.8</td>
<td>83.1</td>
<td>0.534 (0.518-0.550)</td>
<td>&lt;0.001</td>
<td>-15.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>pedsIDF</td>
<td>1708</td>
<td>7.2</td>
<td>98.9</td>
<td>57.9</td>
<td>83.0</td>
<td>0.530 (0.515-0.545)</td>
<td>&lt;0.001</td>
<td>-15.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High cIMT</td>
<td>Overweight or obese*</td>
<td>1696</td>
<td>28.1</td>
<td>86.8</td>
<td>19.9</td>
<td>91.1</td>
<td>0.574 (0.540-0.608)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>pedsNCEP</td>
<td>1696</td>
<td>5.1</td>
<td>97.9</td>
<td>22.0</td>
<td>89.8</td>
<td>0.515 (0.498-0.531)</td>
<td>&lt;0.001</td>
<td>-19.4</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>pedsIDF</td>
<td>1696</td>
<td>3.9</td>
<td>98.2</td>
<td>20.0</td>
<td>89.7</td>
<td>0.510 (0.496-0.525)</td>
<td>&lt;0.001</td>
<td>-19.3</td>
<td>0.005</td>
</tr>
<tr>
<td>T2DM</td>
<td>Overweight or obese*</td>
<td>1720</td>
<td>48.6</td>
<td>85.5</td>
<td>6.5</td>
<td>98.8</td>
<td>0.670 (0.586-0.755)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>pedsNCEP</td>
<td>1720</td>
<td>8.6</td>
<td>97.6</td>
<td>6.8</td>
<td>98.1</td>
<td>0.531 (0.484-0.578)</td>
<td>0.001</td>
<td>-9.1</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>pedsIDF</td>
<td>1720</td>
<td>8.6</td>
<td>97.9</td>
<td>7.9</td>
<td>98.1</td>
<td>0.533 (0.485-0.580)</td>
<td>0.001</td>
<td>-9.1</td>
<td>0.23</td>
</tr>
</tbody>
</table>

*Overweight or obese according to Cole definition.11
Supplemental References


