

# Development of Age-Specific Adolescent Metabolic Syndrome Criteria That Are Linked to the Adult Treatment Panel III and International Diabetes Federation Criteria

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- Objectives** The study objectives were to develop age-specific adolescent metabolic syndrome (MetS) criteria that were linked to the health-based Adult Treatment Panel III (ATP) and International Diabetes Federation (IDF) adult criteria.
- Background** There has been no consistency in the criteria used to diagnose the MetS in adolescents. Studies have either applied adult criteria or arbitrarily chosen adolescent high-risk cut-points.
- Methods** The adolescent (12 to 19 years old) MetS criteria developed in this study were linked to the ATP and IDF adult criteria with LMS growth curve modeling for each MetS component (waist circumference, systolic and diastolic blood pressure, high-density lipoprotein cholesterol, triglycerides, and glucose). Nationally representative data from the National Health and Nutrition Examination Surveys were used to develop the growth curves.
- Results** The growth curves for each MetS component passed through the ATP and IDF cut-points at 20 years of age such that adolescent cut-points were linked to the adult values. Age- and gender-specific cut-points for each MetS component were developed that can be used to define high-risk values in 12- to 19-year-olds. The prevalence of MetS in adolescents nearly doubled over the last decade and was 7.6% on the basis of the newly developed ATP adolescent criteria and 9.6% on the basis of the newly developed IDF adolescent criteria.
- Conclusions** These new criteria should provide improved and age-appropriate approaches for diagnosing MetS among adolescents. (J Am Coll Cardiol 2007;49:891-8) © 2007 by the American College of Cardiology Foundation

The metabolic syndrome (MetS), a constellation of cardiovascular (CVD) risk factors present in approximately 25% of adult Americans (1), is a strong risk factor for atherosclerotic CVD and type 2 diabetes (2-4). In light of this evidence; the National Heart, Lung, and Blood Institute (NHLBI) has recently published a scientific statement indicating that it is important to diagnose and treat the MetS in clinical settings (5).

Several adult MetS criteria have been developed (6-9). The World Health Organization and European Group for the Study of Insulin Resistance criteria include glucose tolerance, insulin resistance, and microalbuminuria components, all of which are not routine clinical measures (6,7). Conversely, the National Cholesterol Education Program

Adult Treatment Panel III (ATP) and International Diabetes Federation (IDF) criteria are clinically appropriate, because all of the risk factor components can be easily and routinely measured (8,9). The clinical-friendly nature of the ATP and IDF criteria has facilitated the widespread measurement of the MetS in adults.

Alarming, CVD risk factor clustering has also been documented among adolescents (10-12). The CVD risk factor clustering in adolescents tracks into adulthood, suggesting that the early diagnosis of MetS might identify adolescents at increased and premature cardiovascular risk and in need of risk factor management (13-15). However, consistent and objective MetS criteria do not exist for youth. Many different MetS criteria have been employed in adolescents, and the components and cut-points used to diagnose the MetS have varied considerably among studies (11,16-20). Furthermore, the adolescent cut-points used to define high-risk values have been arbitrarily chosen and have no health basis. For instance, some studies have used the 90th age-specific percentile to define elevated blood

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**Abbreviations and Acronyms**

- ATP** = Adult Treatment Panel
- BMI** = body mass index
- CVD** = cardiovascular disease
- DBP** = diastolic blood pressure
- HDL-C** = high-density lipoprotein cholesterol
- IDF** = International Diabetes Federation
- MetS** = metabolic syndrome
- NHANES** = National Health and Nutrition Examination Survey
- NHLBI** = National Heart, Lung, and Blood Institute
- SBP** = systolic blood pressure
- TG** = triglycerides
- WC** = waist circumference

pressure (11,17,19); but why not use the 85th percentile instead? From a clinical perspective it is more appropriate to have cut-points that are on the basis of health risk, such as the adult ATP and IDF cut-points.

The study objective was to develop age-specific cut-points and MetS criteria for adolescents that were linked to the health-based ATP and IDF adult criteria that are widely employed in clinical and research settings.

**Methods**

**Criteria used to define MetS in adolescents.** The adolescent MetS criteria developed in this study were linked to the adult ATP (5,8) and IDF (9) criteria. The ATP defines MetS as having at least 3 of the following: high waist circumference (WC)

( $\geq 102$  cm in men,  $\geq 88$  cm in women), high systolic blood pressure (SBP) or diastolic blood pressure (DBP) ( $\geq 130/85$  mm Hg), low high-density lipoprotein cholesterol (HDL-C) ( $< 1.03$  mmol/l in men,  $< 1.30$  mmol/l in women), high triglycerides (TG) ( $\geq 1.7$  mmol/l), and high blood glucose ( $\geq 5.6$  mmol/l). The IDF requires the presence of a high WC ( $\geq 94$  cm in men,  $\geq 80$  cm in women) in addition to 2 of the remaining 4 components, with the cut-points for these 4 components being identical to those of ATP. The IDF also uses different WC cut-points on the basis of race and country of origin (9). In this study, however, WC cut-points of 94 cm (men) and 80 cm (women) as recommended for Europids (people of European ancestry) was used for all National Health and Nutrition Examination Survey (NHANES) subjects (9).

**Data set and study population.** The MetS component cut-points were developed with data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1994) and the 1999 to 2000 and 2001 to 2002 NHANES surveys. The NHANES are nationally representative cross-sectional surveys conducted with a stratified multistage probability design of the U.S. population. Detailed descriptions of each survey are found elsewhere (21). Data from the 3 surveys were combined to maximize the sample in this study. The NHANES underwent institutional review board-approval by the National Center for Health Statistics, and consent was obtained from all participants and their parents/guardian if under the age of majority.

The analysis was limited to 12- to 20-year-old adolescents who completed the home interview and mobile examination center exam (21). Furthermore, analysis was

limited to those who had fasting measurements ( $\geq 6$  h as per NHANES protocol) of HDL-C, TG, and glucose (note: subjects who did not fast were comparable to subjects who fasted for other characteristics including age, body mass index [BMI], WC, and blood pressure). Although WC and blood pressure were measured in every participant, analyses were limited to those who fasted in order to obtain similarly matched groups for each MetS component. This resulted in 2,921 male and 3,146 female participants.

**Measurement of the MetS components.** The SBP and DBP were recorded as the average of 3 or 4 measurements with a mercury sphygmomanometer and standard protocols (21). The WC was measured to the nearest 0.1 cm at the level of the iliac crest with standard protocols (21,22).

Lipoproteins were analyzed at the Johns Hopkins Lipoprotein Analytical Laboratory, and glucose was analyzed at the University of Missouri-Columbia as detailed in the NHANES Laboratory Procedures Manuals (21). The HDL-C was measured in all subjects participating in the mobile examination center exam; however, TG and glucose were only measured in the morning subsample.

**Development of MetS cut-points for adolescents.** Age- and gender-specific growth curves were developed with the Lambda Mu Sigma method (23). The distribution of each MetS component were summarized by Lambda (L), Mu (M), and Sigma (S) curves that describe the skewness, median, and coefficient of variance of the distribution at each age.

Each MetS component growth curve was linked to the respective adult ATP and IDF cut-point. The first step in creating a growth curve for a given MetS component involved defining the z-score (or percentile) that corresponded to the adult cut-point at 20 years of age with the following equation:

**Table 1** MetS Component Values for Male and Female Participants

	n	Mean (SD)
<b>WC, cm</b>		
Males	2,906	79.6 (12.5)
Females	3,116	78.8 (11.7)
<b>SBP, mm Hg</b>		
Males	2,876	111.7 (9.4)
Females	3,094	106.1 (7.9)
<b>DBP, mm Hg</b>		
Males	2,876	62.7 (11.3)
Females	3,094	62.8 (8.9)
<b>HDL-C, mmol/l</b>		
Males	2,833	1.22 (0.4)
Females	3,044	1.32 (0.39)
<b>TG, mmol/l</b>		
Males	1,920	1.06 (1.3)
Females	2,089	1.04 (0.73)
<b>Glucose, mmol/l</b>		
Males	1,921	5.15 (0.78)
Females	2,083	5.02 (1.9)

DBP = diastolic blood pressure; HDL-C = high-density lipoprotein cholesterol; MetS = metabolic syndrome; SBP = systolic blood pressure; TG = triglycerides; WC = waist circumference.

$$Z \text{ score} = [(Y/M)^L - 1] / (LS)$$

where Y was the adult cut-point and L, M, and S were the respective values at 20 years (23). The second step involved calculating points on the growth curve at each age by regressing the previously defined z-score through the adolescent distribution as follows:

$$\text{point on curve} = M(1 + LSz)^{1/L}$$

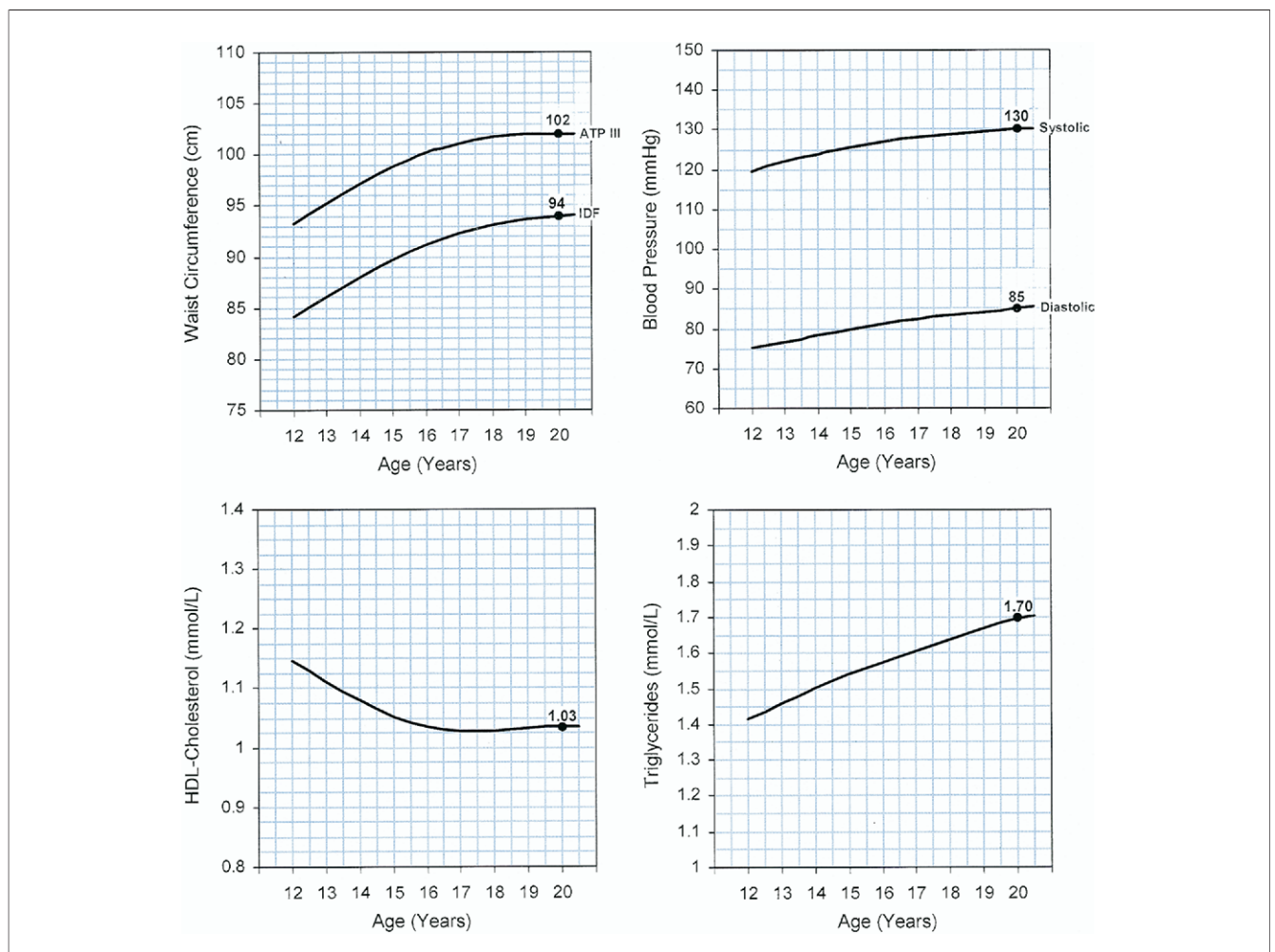
where L, M, and S are the respective age-specific values and z is the z-score that corresponded to the adult cut-point (23). Thus, by defining the percentile that corresponded to the adult cut-point and regressing it backward into adolescence, the adolescent cut-points were linked to those of adults.

**Statistical analysis.** The datasets were managed in SAS version 8.02 (SAS Institute, Cary, North Carolina). Descriptive and chi-square analyses were performed with Stata version 7.0 (Stata Corp., College Station, Texas), which accounted for the weighted and clustered nature of the

NHANES sample. Stata and other survey statistical packages do not have the capability of creating the smoothed growth curves needed for the present study, and subsequently we used the LMS Pro version 1.16 (Institute of Child Health, London). The LMS software took into consideration the weighting of the NHANES survey but was not able to account for the clustered nature of the survey. Further discussion concerning this limitation and presenting a more extensive description of the samples and weighting methodology can be found in the Appendix.

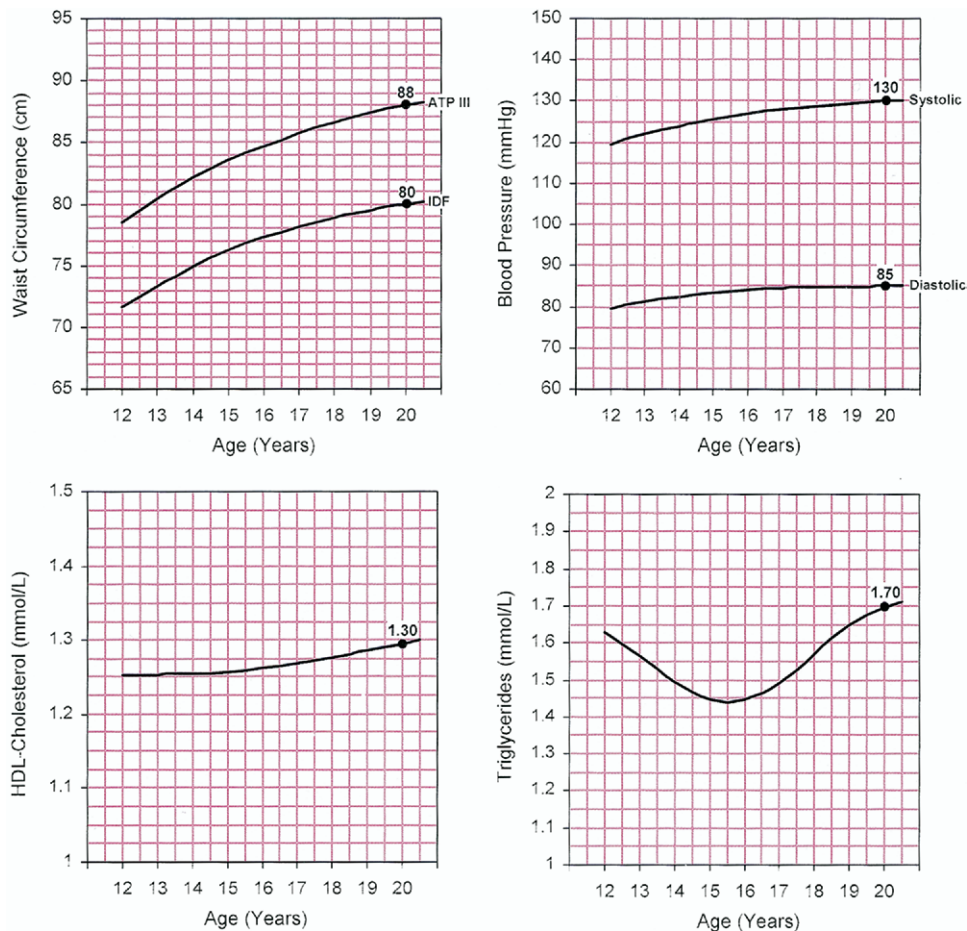
## Results

Table 1 lists the mean values of the MetS components and the number of subjects used to develop each growth curve. The growth curves corresponding to the MetS cut-points for WC (ATP and IDF), blood pressure, HDL-C, and TG are illustrated in Figures 1 and 2 for males and females, respectively. Fasting glucose is not illustrated in the figures, because it remained constant (at 5.6 mmol/l or 100 mg/dl)



**Figure 1. Metabolic Syndrome Component Growth Curves for Males**

Cut-points at age 20 correspond to the Adult Treatment Panel (ATP III) and International Diabetes Federation (IDF) adult cut-points. To convert high-density lipoprotein (HDL)-cholesterol to mg/dl, multiply by 38.67. To convert triglycerides to mg/dl, multiply by 88.5.



**Figure 2** Metabolic Syndrome Component Growth Curves for Females

Cut-points at age 20 correspond to the ATP III and IDF adult cut-points. To convert HDL-cholesterol to mg/dl, multiply by 38.67. To convert triglycerides to mg/dl, multiply by 88.5. Abbreviations as in Figure 1.

from 12 to 20 years. Therefore, a glucose cut-point of 5.6 mmol/l can be used at all ages during adolescence. As an alternative to the growth curves, Tables 2 and 3 list the cut-points in 1-year increments for each MetS component. Each cut-point reflects the midpoint of a given year (i.e., cut-point for age 12 represents 12.5 years) and can be applied to all individuals within the 1-year age range (i.e., 12.0 to 12.9 years).

Two WC curves were developed to reflect the different adult ATP and IDF cut-points. The ATP and IDF curves represented the 92nd and 83rd percentiles for males (Fig. 1A) and the 72nd and 50th percentiles for females (Fig. 2A), respectively. The adult IDF MetS criteria indicates that a high WC can be assumed for those with a BMI  $\geq 30$  kg/m<sup>2</sup> (9). Thus, age- and gender-specific adolescent BMI cut-points linked to a BMI of 30 kg/m<sup>2</sup> were also created as shown in Figure 3 and Table 4.

The SBP and DBP curves were linked to the adult ATP and IDF cut-points such that the curves pass through 130 and 85 mm Hg at 20.0 years of age (Figs. 1B and 2B). The

male and female curves followed similar trajectories. The SBP curves represented the 92nd and 93rd percentiles for males and females, respectively, whereas the DBP curves represented the 97th and 99th percentiles.

Whereas the HDL-C cut-points for males declined slightly until age 16 (Fig. 1C), the female cut-points increased marginally after age 15 (Fig. 2C). The curves were linked to the adult cut-points (1.03 mmol/l for males, 1.30 mmol/l for females) and represented the 26th and 43rd percentiles, respectively.

The male (Fig. 1D) and female (Fig. 2D) TG curves followed different trajectories. Whereas the male curve increased with age in a linear manner, the female curve declined during early adolescence before increasing to approach adult concentrations. The TG curves represent the 89th percentile for both genders.

The prevalences of MetS (in NHANES 1999 to 2002) in adolescents by gender, age, and race with the 2 criteria developed in this study are presented in Table 5. The prevalence of MetS in the total sample was 7.6% according

**Table 2** Age-Specific MetS Cut-Points and Corresponding Percentiles for Males

Age* (yrs)	WC (cm)		BP (mm Hg)		HDL-C (mmol/l)§ (26th)	TG (mmol/l)§ (89th)	Glucose (mmol/l)§
	NCEP ATP† (92nd)	IDF‡ (83rd)	SBP (92nd)	DBP (97th)			
12	94.2	85.1	121	76	1.13	1.44	5.6
13	96.2	87.0	123	78	1.10	1.48	5.6
14	98.0	88.9	125	79	1.07	1.52	5.6
15	99.5	90.5	126	81	1.04	1.56	5.6
16	100.6	91.8	128	82	1.03	1.59	5.6
17	101.4	92.7	128	83	1.03	1.62	5.6
18	101.8	93.4	129	84	1.03	1.65	5.6
19	102.0	93.8	130	85	1.03	1.68	5.6
20.0	102.0	94.0	130	85	1.03	1.70	5.6

\*MetS cut-point values represent the midpoint of a 1-year increment (i.e., the values for age 12 years represent the values at 12.5 years) and can be used for individuals within the 1-year age range (i.e., 12.0 to 12.9 years). †MetS defined as 3 of the 5 criteria. ‡MetS defined as having elevated WC and 2 of the remaining 4 criteria. Note that elevated WC can be assumed if body mass index values above thresholds presented in Table 3. §To convert HDL-C in mmol/l to mg/dl, multiply by 38.67. To convert TG in mmol/l to mg/dl, multiply by 88.5. To convert glucose in mmol/l to mg/dl, multiply by 18.03. ATP = Adult Treatment Panel; BP = blood pressure; IDF = International Diabetes Federation; NCEP = National Cholesterol Education Program; other abbreviations as in Table 1.

to the adolescent ATP criteria and 9.6% according to the adolescent IDF criteria. Prevalences did not differ by gender or age ( $p > 0.2$ ). However, the prevalence of IDF-MetS was lower in non-Hispanic blacks than non-Hispanic whites and Hispanics ( $p < 0.05$ ). Changes in the prevalence of MetS from NHANES III (1988 to 1994) to NHANES 1999 to 2002 were also examined. The prevalence increased from 4.7% to 7.6% on the basis of the adolescent ATP criteria and from 5.3% to 9.6% on the basis of the adolescent IDF criteria ( $p < 0.01$ ).

**Discussion**

The study objective was to develop adolescent MetS criteria that are linked to the commonly used ATP and IDF adult criteria. Our goals were to provide age-appropriate and health-based MetS component cut-points for adolescents and adolescent MetS definitions that could be used consistently in clinical and research settings. Most clinicians will be familiar with the growth curve approach for identifying high-risk values (Figs. 1 and 2), because this approach is similar to that currently used to monitor height, weight, and BMI growth in youth (24). Tables 1 and 2 present age-

specific thresholds that are an alternative to the growth curves. As with any newly developed classification system, studies are needed to validate the adolescent MetS criteria developed in this study, which could be done with intermediate CVD and metabolic outcomes (i.e., atherosclerotic lesions, endothelial function).

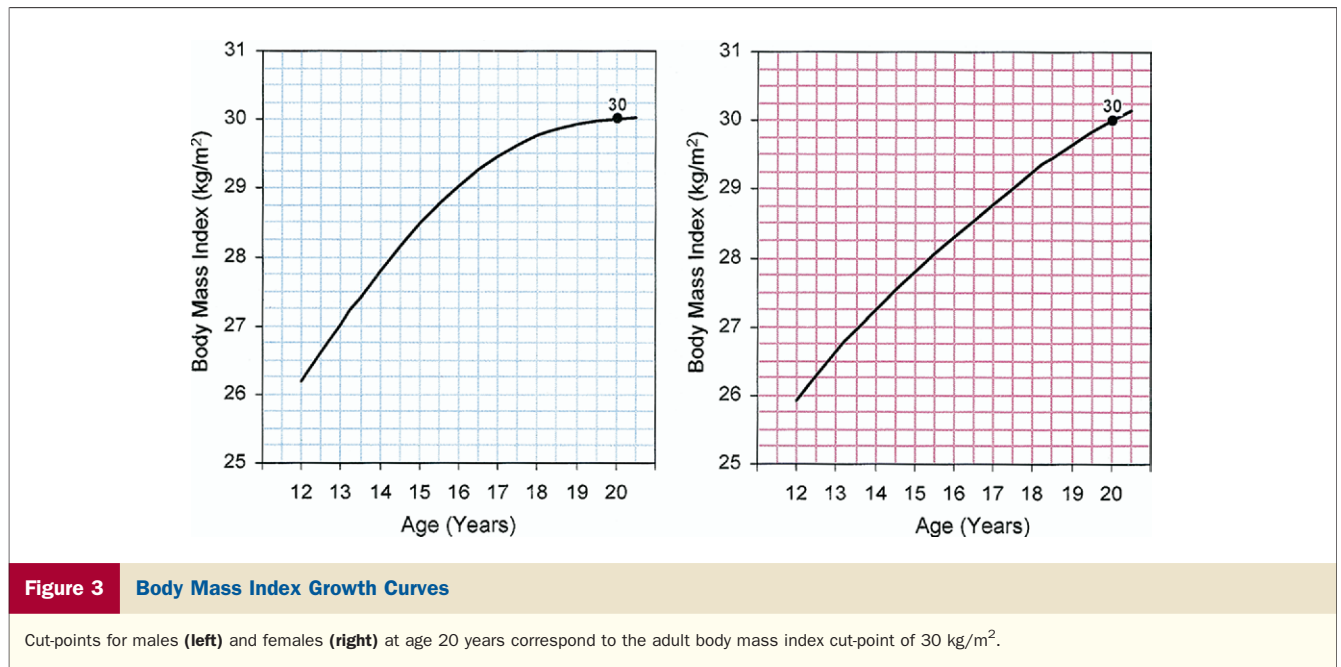
In adults, MetS is a clear predictor of atherosclerotic CVD and type 2 diabetes (5), and the NHLBI has strongly urged its diagnosis and management in the clinical setting in adults to help reduce chronic disease risk (5). In light of the increasing prevalence of obesity and other MetS indicators in the pediatric population (25,26), it seems as urgent to address this problem in this age group. There is not a recognized consistent method of diagnosing MetS in youth (16), and a major goal of this study was to provide criteria that might resolve this issue.

Although the NHLBI has emphasized the importance of diagnosing and managing the MetS, others have argued that the MetS is not a useful diagnostic tool (27-29). A common argument is that the MetS does not incur additional health risk beyond its individual components (27,30) or beyond global risk factor assessment tools such as the Framingham

**Table 3** Age-Specific MetS Cut-Points and Corresponding Percentiles for Females

Age* (yrs)	WC (cm)		BP (mm Hg)		HDL-C (mmol/l)§ (43rd)	TG (mmol/l)§ (89th)	Glucose (mmol/l)§
	NCEP ATP† (72nd)	IDF‡ (50th)	SBP (93rd)	DBP (99th)			
12	79.5	72.5	121	80	1.25	1.60	5.6
13	81.3	74.2	123	82	1.25	1.53	5.6
14	82.9	75.7	125	83	1.26	1.46	5.6
15	84.2	76.8	126	84	1.26	1.44	5.6
16	85.2	77.7	128	84	1.27	1.46	5.6
17	86.2	78.5	128	85	1.27	1.53	5.6
18	87.0	79.2	129	85	1.28	1.61	5.6
19	87.7	79.8	130	85	1.29	1.68	5.6
20.0	88.0	80.0	130	85	1.3	1.7	5.6

\*MetS cut-point values represent the midpoint of a 1-year increment (i.e., the values for age 12 years represent the values at 12.5 years) and can be used for individuals within the 1-year age range (i.e., 12.0 to 12.9 years). †MetS defined as 3 of the 5 criteria. ‡MetS defined as having elevated WC and 2 of the remaining 4 criteria. Note that elevated WC can be assumed if body mass index values above thresholds presented in Table 3. §To convert HDL-C in mmol/l to mg/dl, multiply by 38.67. To convert TG in mmol/l to mg/dl, multiply by 88.5. To convert glucose in mmol/l to mg/dl, multiply by 18.03. Abbreviations as in Tables 1 and 2.



Heart Score (5,31). Furthermore, some do not consider the MetS to be a therapeutic target, given that each MetS component is treated individually. The purpose of this study was not to debate the utility of diagnosing and treating the MetS. Rather, we developed adolescent MetS classification systems to facilitate the comparison of results across studies and to provide clinicians and researchers with objective criteria if they choose to use it as a diagnostic or research tool in adolescents.

The MetS classification systems developed in this study have several other benefits. Foremost, the adolescent cut-points were linked to the ATP and IDF adult cut-points, which themselves are based on CVD and diabetes risk. This eliminates some of the arbitrariness inherent in the percentile approach used in the existing youth MetS criteria and should provide a more accurate assessment of risk status. Second, the new MetS cut-points reflect the fluctuations in WC, blood pressure, and plasma lipoproteins that occur naturally with age (32-34), which should help avoid potential misclassification that is due to age-related changes.

**Table 4** Age-Specific BMI Cut-Points (kg/m<sup>2</sup>) and Corresponding Percentiles for Males and Females

Age (yrs)	Males (89th)	Females (84th)
12	26.62	26.28
13	27.42	26.96
14	28.15	27.54
15	28.77	28.05
16	29.27	28.54
17	29.63	29.02
18	29.86	29.46
19	29.97	29.83
20	30.00	30.00

BMI = body mass index.

With the ATP- and IDF-linked MetS criteria developed in this study, the prevalence of MetS in U.S. adolescents in 1999 to 2002 were 7.6% and 9.6%, respectively. Prevalence estimates were similar among genders and among younger and older adolescents (Table 5). These results are consistent with some studies (17,18) and inconsistent with others (11,19,35). The problem has been that consistent adolescent MetS criteria have been unavailable, and thus MetS criteria and prevalence estimates vary considerably between studies.

Of interest was the racial difference in the prevalence of MetS, which was lower in non-Hispanic black adolescents than non-Hispanic whites and Hispanics (Table 5). This could be explained by the more favorable lipoprotein profiles of non-Hispanic blacks (1,36). Of further interest was the almost 2-fold increase in the prevalence of MetS among

**Table 5** Prevalence of MetS in 12- to 19-Year Olds by Gender, Age, and Race in NHANES, 1999-2002

Subgroup	n	Prevalence of MetS, % (SE)	
		ATP	IDF
All	1,820	7.6 (1.1)	9.6 (1.2)
Gender			
Male	926	8.2 (1.5)	9.4 (1.6)
Female	894	7.0 (1.6)	9.7 (1.9)
Age			
12-15 yrs	891	7.7 (1.4)	9.0 (1.4)
16-19 yrs	918	7.7 (1.3)	10.2 (1.5)
Race			
Non-Hispanic white	480	8.0 (1.7)	10.2 (1.8)*
Non-Hispanic black	500	6.4 (1.3)	6.9 (1.4)
Hispanic	760	8.0 (1.1)	10.1 (0.1)*

\*Significantly different from non-Hispanic black (p < 0.05).

NHANES = National Health and Nutrition Examination Survey; other abbreviations as in Tables 1 and 2.

adolescents from 1988 to 1994 and 1999 to 2002. This increase was most likely driven by the 50% increase in adolescent obesity during this time period (37).

An important limitation to note is the limited age span for which the MetS classification systems were developed (12 to 19 years). Ideally we would have included the entire pediatric age range in our analysis; however, requesting fasting blood samples from young children is rarely performed in research settings and was not performed in individuals under 12 years in NHANES. Furthermore, a measure of sexual maturation was not incorporated into the analysis, and thus the growth curves represent age-related rather than maturation-related changes. Furthermore, although using cross-sectional data to develop growth curves is a common practice, cross-sectional comparisons between ages might not completely represent changes over time in a given individual, owing to individual differences in growth velocity.

It is possible that race-specific MetS cut-points would provide a more accurate assessment of risk status. However, because the ATP and IDF adult cut-points are not race-specific (exception of IDF WC cut-points) and because we wanted to link the adolescent criteria to those used in adults, we did not develop race-specific growth curves. Another limitation to consider is that it would have been ideal to directly link the adolescent cut-points to CVD and diabetes risk. However, because CVD and type 2 diabetes are chronic diseases, usually of late onset, it is very difficult to establish a direct link between adolescent risk factor values and disease outcomes without having an exceptionally long follow-up period. Finally, a variety of methods are available for creating smoothed growth curves. There is no method that is clearly the best, and it is likely that a number of methods would have worked as well and produced results comparable to those of the LMS method used here (38).

## Conclusions

This study presents the first attempt to create classification systems for MetS in adolescents that are linked to adult health-based values. We have developed 2 MetS criteria to reflect the adult definitions most commonly applied in the clinical and research settings. Future studies are needed to validate the adolescent MetS criteria developed here.

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 **APPENDIX**

**For a more extensive description of the samples and weighting methodology, please see the online version of this article.**