

Prevalence of a Metabolic Syndrome Phenotype in Adolescents

Findings From the Third National Health and Nutrition Examination Survey, 1988-1994

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Background: In adults the metabolic syndrome imposes a substantial risk for type 2 diabetes mellitus and premature coronary heart disease. Even so, no national estimate is currently available of the prevalence of this syndrome in adolescents.

Objective: To estimate the prevalence and distribution of a metabolic syndrome among adolescents in the United States.

Design and Setting: Analyses of cross-sectional data obtained from the Third National Health and Nutrition Examination Survey (1988-1994), which was administered to a representative sample of the noninstitutionalized civilian population of the United States.

Participants: Male and female respondents aged 12 to 19 years (n=2430).

Main Outcome Measures: The prevalence and distribution of a metabolic syndrome among US adolescents, using the National Cholesterol Education Pro-

gram (Adult Treatment Panel III) definition modified for age.

Results: The overall prevalence of the metabolic syndrome among adolescents aged 12 to 19 years was 4.2%; 6.1% of males and 2.1% of females were affected ($P=.01$). The syndrome was present in 28.7% of overweight adolescents (body mass index [BMI], ≥ 95 th percentile) compared with 6.8% of at-risk adolescents (BMI, 85th to <95 th percentile) and 0.1% of those with a BMI below the 85th percentile ($P<.001$). Based on population-weighted estimates, approximately 910000 US adolescents have the metabolic syndrome.

Conclusions: Perhaps 4% of adolescents and nearly 30% of overweight adolescents in the United States meet these criteria for a metabolic syndrome, a constellation of metabolic derangements associated with obesity. These findings may have significant implications for both public health and clinical interventions directed at this high-risk group of mostly overweight young people.

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THE PREVALENCE of obesity and diabetes mellitus among adults in the United States has increased during the past decade.¹ Recent data indicate that 65% of the US adult population is either overweight, defined as a body mass index (BMI, calculated as the weight in kilograms divided by the height in meters squared) of 25 or more, or obese (BMI ≥ 30).² In children and adolescents, the term overweight is used in place of obese and is defined as a BMI at or above the 95th percentile on age- and sex-specific growth charts from the Centers for Disease Control and Prevention.³ Overweight tripled among US children between 1970 and 2000, and 15% of 6- to 19-year-olds are overweight according to the most recent estimates.⁴ Obesity is es-

timated to cause approximately 300000 deaths annually, and its 1-year direct and indirect costs are estimated to be \$117 billion.⁵

Leaders in the emerging field of preventive cardiology have increasingly recognized obesity's role in adult cardiovascular disease. Correspondingly, the guidelines for adult cholesterol and the primary prevention of cardiovascular disease reflect this increased recognition of obesity's role.^{6,7} The guidelines for cholesterol also target the metabolic syndrome, a constellation of metabolic derangements that predict both type 2 diabetes mellitus and premature coronary artery disease, as a newly recognized entity that warrants clinical intervention. According to the National Cholesterol Education Program (NCEP, or

Table 1. Criteria for the Metabolic Syndrome*

Criterion	Adults	Adolescents
High triglyceride level, mg/dL	≥150	≥110
Low HDL-C level, mg/dL		
Males	<40	≤40
Females	<50	≤40
Abdominal obesity, waist circumference, cm		
Males	>102	≥90th Percentile
Females	>88	≥90th Percentile
High fasting glucose level, mg/dL	≥110	≥110
High blood pressure, mm Hg	≥130/85	≥90th Percentile

Abbreviation: HDL-C, high-density lipoprotein cholesterol.

SI conversion factors: To convert triglycerides to millimoles per liter, multiply by 0.01129; HDL-C to millimoles per liter, multiply by 0.02586; glucose to millimoles per liter, multiply by 0.05551.

*For definitions of criteria, see the "Definitions" subsection of the "Methods" section.

Adult Treatment Panel III [ATP III]), persons meeting at least 3 of the following 5 criteria qualify as having the metabolic syndrome: elevated blood pressure, a low high-density lipoprotein (HDL) cholesterol level, a high triglyceride level, a high fasting glucose level, and abdominal obesity. Because of the increasing rates of adult obesity and obesity's association with insulin resistance and type 2 diabetes, the NCEP panel stated that the metabolic syndrome will soon have a greater impact on premature coronary artery disease than does tobacco.⁸ According to recent estimates, the metabolic syndrome affects 22% of the US adult population overall, including 7% of men and 6% of women in the 20- to 29-year age group.⁹

As childhood overweight increases,^{10,11} its medical complications are becoming more common and more frequently recognized.¹²⁻¹⁴ For example, the prevalence of type 2 diabetes has risen dramatically among adolescents in the past 20 years.¹³ Studies suggest that a substantial percentage of overweight children and adolescents may be afflicted with the metabolic syndrome because many have 1 or more of the following: an elevated triglyceride level, a low HDL cholesterol level, and high blood pressure.^{15,16} Many overweight children also have elevated insulin levels, indicating an increase in insulin resistance.¹⁶ When one considers that autopsy studies have revealed that overweight in adolescence is associated with accelerated coronary atherosclerosis,¹⁷ recent trends become even more troubling.

The purpose of the current study is to estimate the prevalence and distribution of a metabolic syndrome in adolescents using a nationally representative sample of the US population.

METHODS

Data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994) were examined. The NHANES III used a complex, multistage design to provide a representative sample of the noninstitutionalized civilian population of the United States. Approximately 40 000 persons aged 2 months to 65 years or older were studied. Young and old persons and ethnic minorities such as African Americans and Mexican Americans were oversampled.¹⁸ After being evaluated in a home interview to determine family medical

history, current medical conditions, and medication use, participants were randomly assigned to undergo a morning, afternoon, or evening examination at the mobile examination centers. Morning participants were asked to fast for 8 hours; afternoon and evening participants were asked to fast for 6 hours.

The details of the determination and analysis of triglyceride levels, HDL cholesterol levels, and glucose values have previously been described.^{9,19} For adolescents aged 17 years and older, 6 seated blood pressure readings were taken in 2 separate settings. The household interviewer took 3 measurements at the participant's home, and the study physician took 3 during the evaluation in the center. The first and fifth Korotkoff sounds were used to represent the systolic and diastolic values.¹⁸ We used the mean of these 6 measurements in these analyses. Adolescents aged 12 to 16 years did not have their blood pressure taken at home, and thus this age group had only the 3 measurements taken by the physician. Again, the mean was used. Height was measured in an upright position with a stadiometer, and weight was measured at a standing position using a self-zeroing scale (Mettler-Toledo, Inc, Columbus, Ohio). The waist circumference measurement was made at the midpoint between the bottom of the rib cage and above the top of the iliac crest. Measurements of waist circumference were made for each subject at minimal respiration to the nearest 0.1 cm.¹⁸ The Tanner stage of pubic hair development was used as an indicator of sexual maturity because it was obtained for both sexes.²⁰ There was standardized training for physicians performing these examinations, and photographs and written descriptions were available for reference. Pubic hair was staged from 1, representing immaturity, to 5, for full maturity.²⁰

The initial sample consisted of 3211 subjects aged 12 to 19 years, to whom the following exclusion criteria were applied: (1) had not fasted for 6 hours, (2) was currently pregnant, or (3) was taking medication classified as a blood glucose regulator, such as insulin, androgens or anabolic steroids, or adrenal corticosteroids. The final sample numbered 2430, including some individuals with 1 or more excluding factors. No children younger than 12 years were instructed to fast as part of NHANES III.

DEFINITIONS

The criteria for the metabolic syndrome in adults specified by NCEP's ATP III and the adapted definition used in this analysis for adolescents aged 12 to 19 years are shown in **Table 1**.⁷ Because these criteria have never been formally defined or applied in children or adolescents, we modified the adult criteria to the closest representative values obtainable from pediatric reference data. In developing a definition for metabolic syndrome in adolescents,²¹ we considered reference values from the NCEP Pediatric Panel report,²² the American Diabetes Association statement on type 2 diabetes in children and adolescents,²³ and the updated Task Force report on the diagnosis and management of hypertension in childhood as well as ATP III.⁸ Because no reference values for waist circumference exist for adolescents or children, we analyzed all adolescents in the data set who had a waist circumference recorded. We classified participants with a waist circumference at or above the 90th percentile value for age and sex from this sample population as having abdominal obesity. Elevated systolic or diastolic blood pressure was defined as a value at or above the 90th percentile for age, sex, and height.²¹ If subjects reported current use of any antihypertensive drugs, they were labeled as participants with elevated blood pressure. This approach of counting participants taking medications was also used for examining the prevalence of the metabolic syndrome in adults

in the same national data set.⁹ The NCEP Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents²² and a table summarizing these values in a review by Styne¹⁴ were used to establish the criteria for cholesterol level abnormalities. The range of 35 to 45 mg/dL (0.91-1.16 mmol/L) is given for borderline low HDL cholesterol levels for all sexes and ages. In children aged 10 to 19 years, a borderline high range for triglyceride levels is given as 90 to 129 mg/dL (1.02-1.46 mmol/L). Therefore the midpoint value for HDL cholesterol (≤ 40 mg/dL [≤ 1.03 mmol/L]) was used as a 10th percentile value, and the midpoint value for triglycerides (≥ 110 mg/dL [≥ 1.24 mmol/L]) was taken as the 90th percentile value for age. The reference value for elevated fasting glucose was taken from the American Diabetes Association guideline of 110 mg/dL or higher (≥ 6.1 mmol/L).²³

STATISTICAL ANALYSIS

Prevalence values were compared using the χ^2 test for proportions for those children with and without the metabolic syndrome. Comparisons of means of continuous variables were done with the *t* test. Children identified in the racial/ethnic category "other" were included in the overall sample analyzed, but this subsample was too small for meaningful analysis separately. To account for the complex sampling design, SAS²⁴ and SUDAAN²⁵ statistical software were used in the analysis, and SUDAAN was used to apply sampling weights to produce national estimates.

RESULTS

Demographic characteristics associated with the metabolic syndrome in bivariate analyses are shown in **Table 2**. The overall prevalence of the metabolic syndrome in adolescents was 4.2%. It was more common in males (6.1%) than in females (2.1%) and was more frequent in Mexican Americans (5.6%) and whites (4.8%) than black subjects (2.0%). By region of the country, the rate was highest in the West and Midwest and lowest in the Northeast. Findings for age (12-14 years vs 15-19 years), Tanner stage by pubic hair, poverty level, and parental history of diabetes and myocardial infarction were not significant. When stratified by BMI, 28.7% of overweight adolescents (BMI ≥ 95 th percentile for age and sex) met criteria for the metabolic syndrome. A comparison of the final sample with those subjects who were excluded revealed only 1 difference by demographic characteristics (BMI also did not differ): The percentage of African Americans was slightly higher in the excluded group (18.9% vs 14.6% in the overall sample; $P = .05$). The proportion of subjects with 1 or more abnormalities of the metabolic syndrome is presented in **Table 3**. In this sample, 41% of subjects had 1 or more of these risk factors, whereas 14% had 2 or more. There were no subjects who had all 5 of these risk factors.

The prevalence of the metabolic syndrome by sex and race/ethnicity is shown in the **Figure**. The prevalence among white (7.1%) and Mexican American males (7%) was nearly the same, whereas black males had the lowest rate at 2.6% ($P = .003$). Among females, Mexican Americans (4.1%) had the highest rate, whereas black females (1.4%) had the lowest rate ($P < .001$).

Table 2. Demographic Characteristics and Prevalence of the Metabolic Syndrome Among US Adolescents Aged 12 to 19 Years, NHANES III

	No. of Subjects	% of Subjects With the Metabolic Syndrome (95% CI)	P Value
Total	2430	4.2 (2.9-5.4)	
Sex			
Male	1150	6.1 (3.7-8.6)	.001
Female	1280	2.1 (0.9-3.3)	
Race/ethnicity			
White	646	4.8 (3.1-6.5)	.004
Black	824	2.0 (0.8-3.2)	
Mexican American	846	5.6 (3.6-7.5)	
Age, y			
12-14	968	4.3 (2.0-6.5)	.92
15-19	1462	4.1 (2.5-5.7)	
Poverty level			
Below	804	5.7 (1.9-9.6)	.33
At or above	1394	3.7 (2.3-5.0)	
Region			
Northeast	264	1.2 (0.0-2.9)	<.001
Midwest	443	5.3 (4.6-6.0)	
South	1116	3.9 (1.6-6.2)	
West	607	6.0 (2.5-9.5)	
Parental history of diabetes mellitus			
Yes	185	5.8 (3.3-8.4)	.23
No	2187	4.2 (2.8-5.5)	
Parental history of myocardial infarction			
Yes	410	7.3 (3.3-11.2)	.12
No	1964	3.6 (2.2-5.1)	
BMI status, percentile			
Normal (<85th)	1694	0.1 (0.0-0.1)	<.001
At risk (85th to <95th)	366	6.8 (1.6-12.0)	
Overweight (≥ 95 th)	338	28.7 (20.7-36.7)	
Tanner stage, pubic hair, 12-18 y			
1	83	3.3 (0.0-7.6)	.54
2	97	7.0 (0.0-15.4)	
3	207	7.2 (2.5-11.9)	
4	594	3.5 (0.7-6.3)	
5	893	3.4 (1.5-5.4)	

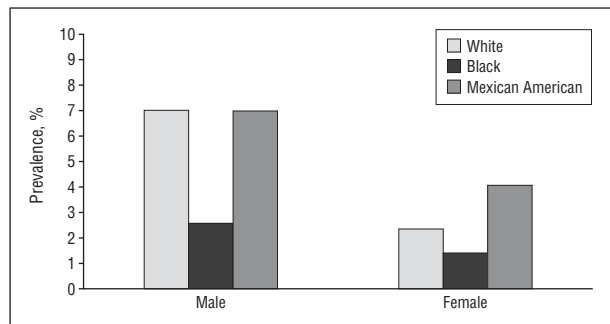
Abbreviations: BMI, body mass index; CI, confidence interval; NHANES III, Third National Health and Nutrition Examination Survey.

The distribution of each element of the metabolic syndrome is shown in **Table 4**. Overall, high triglyceride levels and low HDL cholesterol levels were most common, whereas high fasting glucose levels were the least common. White adolescents had the highest rates of high triglyceride levels (25.5%) and low HDL cholesterol levels (26.1%). Mexican American subjects had the highest rate of abdominal obesity by waist circumference (13.0%). Black adolescents had the highest proportion of elevated blood pressure (6.2%). Adolescents with the metabolic syndrome had a mean BMI of 30.1 and, on average, were at the 95.5th percentile for BMI by age and sex (data not shown). Of those adolescents who fulfilled these criteria for the metabolic syndrome, 25.2% were at risk for overweight, by BMI, and 73.9% were overweight.

Table 3. Prevalence of 1 or More Abnormalities of the Metabolic Syndrome Among 2430 US Adolescents Aged 12 to 19 Years, NHANES III

	% (95% CI)			
	≥1 Risk Factors	≥2 Risk Factors	≥3 Risk Factors	≥4 Risk Factors
Total	40.9 (37.2-44.6)	14.2 (12.0-16.4)	4.2 (2.9-5.4)	0.9 (0.2-1.7)
Sex				
Male	47.5 (42.4-52.5)	17.1 (13.6-20.5)	6.1 (3.7-8.6)	1.6 (0.2-3.0)
Female	34.2 (29.1-39.2)	11.4 (8.4-14.3)	2.1 (0.9-3.3)	0.2 (0.0-0.6)
Race/ethnicity				
White	42.9 (37.7-48.0)	16.1 (13.4-18.8)	4.8 (3.1-6.5)	1.3 (0.2-2.3)
Black	29.7 (26.0-33.5)	7.9 (5.6-10.2)	2.0 (0.8-3.2)	0.5 (0.0-1.1)
Mexican American	40.7 (35.8-45.6)	15.4 (11.3-19.5)	5.6 (3.6-7.5)	0.3 (0.1-0.5)
BMI status, percentile*				
Normal (<85th)	31.4 (27.2-35.5)	6.4 (4.9-8.0)	0.1 (0.0-0.1)	0.0 (0.0-0.0)
At risk (85th to <95th)	54.4 (43.3-65.5)	23.2 (16.3-30.0)	6.8 (1.6-12.0)	2.1 (0.0-6.2)
Overweight (≥95th)	88.5 (83.5-93.4)	56.0 (46.4-65.6)	28.7 (20.7-36.7)	5.8 (2.6-9.1)

Abbreviations: BMI, body mass index; CI, confidence interval; NHANES III, Third National Health and Nutrition Examination Survey.



Prevalence of the metabolic syndrome by sex and race/ethnicity.

COMMENT

The metabolic syndrome has been called several other names, including syndrome X, insulin resistance syndrome, dysmetabolic syndrome X, Reaven syndrome, and the metabolic cardiovascular syndrome.^{15,26} Obesity, insulin resistance, dyslipidemia, and hypertension are common to all. The World Health Organization used “metabolic syndrome” in their 1998 report on diagnosis and classification of diabetes mellitus.²⁷ Both the World Health Organization and ATP III chose this title for their consensus definitions.^{7,27} We believe that this is the first study to examine the prevalence and distribution of a metabolic syndrome in a nationally representative sample of US adolescents. Perhaps 4% of adolescents overall and nearly 30% of overweight adolescents meet the criteria for this syndrome, suggesting that almost 1 million adolescents in the United States are affected.

The metabolic syndrome affects an estimated 47 million American adults.⁹ The syndrome emerges when a person’s predisposition for insulin resistance is worsened by increasing adiposity; dyslipidemia, elevated blood pressure, and proinflammatory and prothrombotic properties result.²⁸ Adults with this syndrome frequently progress to type 2 diabetes and demonstrate markedly increased risk for morbidity and mortality from cardiovascular disease.²⁹⁻³¹ The metabolic syndrome in adults

is largely confined to the overweight population³² and represents a subgroup of obese persons who bear a level of risk for cardiovascular disease that exceeds that of the obese in general. An estimated 7% of men and 6% of women aged 20 to 29 years are affected with the metabolic syndrome,⁹ so our finding that 4% of those aged 12 to 19 years may have this syndrome should not be surprising. Four previous regional studies of children that relied on US and international samples demonstrated the clustering of the risk factors for the metabolic syndrome and reported rates from 2% to 9%.³³⁻³⁶

Overweight has important implications for the future health of our young people, especially in terms of coronary heart disease and diabetes. The Pathobiological Determinants of Atherosclerosis in Youth research group, for example, found that overweight (by BMI) in young men was associated with fatty streaks, raised lesions, and low-grade stenosis of the coronary arteries.¹⁷ In addition, studies have established that child and adolescent obesity tracks into adulthood and also predicts the metabolic syndrome in adults.³⁷⁻³⁹ Results of one of the many reports from the Bogalusa Heart Study⁴⁰ show that when insulin concentrations are increased in childhood they tend to remain elevated in adulthood, and those adults with consistently elevated insulin levels tend also to have increased rates of obesity, hypertension, and dyslipidemia. In the present study, adolescents with the metabolic syndrome had a mean BMI just above the 95th percentile; thus, they represent a fairly common clinical problem, one likely to be encountered routinely by general pediatricians.

Abdominal or centrally distributed fat is associated with type 2 diabetes and a poor cardiovascular profile in adults.⁴¹⁻⁴⁵ In children, an increased waist circumference has been shown to correlate with abnormal systolic and diastolic blood pressures and elevated serum levels of total cholesterol, low-density lipoprotein, triglyceride, lipoprotein, and insulin, as well as lower concentrations of HDL.^{36,46,47} The association between the clustering of cardiovascular risk factors and waist circumference is not only a reflection of the degree of obe-

Table 4. Prevalence of Individual Metabolic Syndrome Risk Factors Among US Adolescents Aged 12 to 19 Years, NHANES III*

	% (95% CI)				
	Abdominal Obesity	High Glucose Level	High Triglyceride Levels	Low HDL-C Level	Elevated BP
Total	9.8 (8.2-11.4)	1.5 (0.1-2.8)	23.4 (19.9-27.0)	23.3 (20.6-26.0)	4.9 (3.4-6.4)
Sex					
Male	10.2 (8.0-12.4)	2.4 (0.0-4.9)	24.7 (18.9-30.5)	31.2 (27.1-35.3)	6.7 (4.1-9.4)
Female	9.4 (6.9-11.8)	0.5 (0.2-0.8)	22.1 (17.6-26.6)	15.1 (11.9-18.3)	3.0 (1.8-4.2)
Race/ethnicity					
White	9.3 (6.9-11.7)	1.6 (0.0-3.6)	25.5 (20.7-30.3)	26.1 (22.5-29.7)	5.2 (3.1-7.3)
Black	12.2 (9.6-14.8)	1.7 (0.6-2.8)	10.5 (8.0-14.5)	11.7 (9.0-14.5)	6.2 (4.4-8.1)
Mexican American	13.0 (9.4-16.5)	1.6 (0.7-2.4)	24.7 (21.0-28.4)	20.2 (15.5-24.9)	5.1 (3.2-6.9)
BMI status, percentile					
Normal (<85th)	0.3 (0.0-0.6)	0.7 (0.0-1.4)	17.6 (13.9-21.2)	17.7 (14.7-20.8)	3.2 (2.2-4.3)
At risk (85th to <95th)	11.5 (5.4-17.8)	4.5 (0.0-9.5)	33.5 (23.9-43.0)	32.3 (24.0-40.5)	8.6 (2.8-14.4)
Overweight (\geq 95th)	74.5 (67.1-81.8)	2.6 (0.0-6.3)	51.8 (40.7-62.9)	50.0 (42.3-57.8)	11.2 (5.7-16.8)

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; NHANES III, Third National Health and Nutrition Examination Survey.

*For definitions of criteria, see the "Definitions" subsection of the "Methods" section.

sity but is also dependent on the regional distribution of the excess body fat.^{48,49} Thus, because a more central distribution of fat correlates with worse cardiovascular risk and waist circumference has been shown to be the strongest correlate of central fat distribution in children,⁵⁰ it seems appropriate to use waist circumference in a pediatric definition of metabolic syndrome. In fact, BMI is a less sensitive indicator of fatness in children and fails to account for fat distribution.⁵¹ Perhaps for these reasons, an American Heart Association statement has recommended the inclusion of waist circumference measurements in evaluating children for insulin resistance or those who manifest features resulting from insulin resistance that constitute much of the metabolic syndrome.⁴⁹

Given the growing concern about metabolic syndrome, coupled with the alarming increase in the prevalence of overweight in children and adults, it is not surprising that the American Heart Association set forth a series of guidelines for promoting cardiovascular health as part of comprehensive pediatric care.^{49,52,53} Evidence shows that obesity and insulin resistance has already started "the clock of coronary heart disease" in some adults, even before the onset of diabetes.²⁹ We cannot definitely state that this would be the case for overweight adolescents with the metabolic syndrome according to our definition, but this seems likely for many because the syndrome is a constellation of cardiovascular risk factors. Cluster-tracking studies have shown that multiple cardiovascular risk factors persist from childhood into adulthood in 25% to 60% of cases.^{54,55} One study showed that subjects who either developed or lost their risk factor clustering over time had significant changes in their adiposity and lifestyle behaviors related to nutrition and physical activity.⁵⁵

The first limitation of the data we present is to consider how to define the metabolic syndrome for pediatric patients. The intent was to create a definition for metabolic syndrome in adolescents for initial epidemiologic investigation and for possible future clinical consideration. The concept was to identify borderline high (or borderline low in the case of HDL) values for each criterion from established guidelines for children and adolescents. In some

instances, as with BMI, age- and sex-specific criteria are recommended to identify abnormal patients.^{56,57} In contrast, in the case of glucose and serum cholesterol, screening guidelines give single specific cutoff values for identifying abnormal subjects.^{23,58,59} Although the rates of abnormal cholesterol values in adolescent subjects may seem higher than expected, 30% of adults from the same data set had hypertriglyceridemia and 37% had a low HDL cholesterol value according to the ATP III criteria for the metabolic syndrome.⁹ There might also be concern that the cholesterol cutoff values used might lead to some overestimation or underestimation, but there was no difference in the prevalence of metabolic syndrome between 12- to 14-year-olds vs 15- to 19-year-olds ($P = .92$). When teenagers were stratified by Tanner stage, there was also no statistical difference in the rates of this syndrome phenotype, but rates increased among Tanner 2 and Tanner 3 individuals and decreased among Tanner 4 and 5 subjects. Although no national definition of the metabolic syndrome in adolescents currently exists, obesity treatment guidelines recommend identifying youth with medical complications of their obesity.^{56,57} Even recent scientific statements on cardiovascular disease prevention or obesity and insulin resistance in children have not presented a definition of metabolic syndrome for research or clinical application.^{49,52}

Some other limitations to consider include the cross-sectional nature of these data, which do not allow causal inferences and limit any assumptions about the duration of the existence of any of the criteria, such as blood pressure or cholesterol level. Also, since NHANES III was conducted, both obesity and type 2 diabetes have become more common among adolescents,^{13,60} which may mean that this clustering of risk factors may have a higher prevalence now than it did during data collection. Despite subjects 12 years and older being instructed to fast, just more than 700 subjects from the original sample had to be eliminated for not fasting for at least 6 hours. Although 6 hours of fasting may not be ideal, it allowed a larger sample size to be analyzed by having subjects from afternoon and evening examinations included.

What This Study Adds

Childhood overweight currently affects 15% of children, and more than 60% of adults are overweight. Recently, the metabolic syndrome has been shown to affect more than 20% of the age-adjusted adult population and is closely related to the obesity epidemic. It is a clustering of metabolic derangements that reflect or portend insulin resistance, type 2 diabetes, and premature cardiovascular disease. To date, there has been no estimate of the potential disease burden for children or adolescents.

This study suggests that the phenotype of the metabolic syndrome may affect 4% of adolescents in the United States, with nearly 80% of adolescents who meet the criteria employed for the metabolic syndrome being overweight. Almost 30% of the overweight youth in this sample have 3 or more of the risk factors for the metabolic syndrome, thus qualifying under the criteria employed. Because metabolic syndrome significantly increases the risk of type 2 diabetes and premature coronary artery disease in adults, adolescent subjects who continue to manifest this risk factor profile may constitute a subgroup of overweight teenagers to target for lifestyle behavior changes.

Finally, it should be noted that owing to the low prevalence of the metabolic syndrome, some cell sizes were small when stratified by demographic characteristics. Multiple prospective reports confirm that the clustering of risk factors for the metabolic syndrome are developing during childhood,^{16,33,40,46,61} and studies of the metabolic syndrome in adults show that its prevalence increases with age.⁹

Our findings highlight a high percentage of overweight adolescents who may bear a heightened risk for future metabolic syndrome in adulthood with subsequent increased risks for premature cardiovascular disease and type 2 diabetes. Consistent with recent commentaries that have called for better ways to define overweight in children,⁶² use of a consensus definition for the metabolic syndrome to assess overweight adolescents might be a useful strategy to target a group at increased risk. Targeting adults with glucose intolerance and other markers of the metabolic syndrome has been employed in trials to prevent type 2 diabetes in adults.⁶³⁻⁶⁵ The high prevalence of metabolic syndrome in overweight adolescents, however, emphasizes the need for effective preventive and therapeutic strategies that rely on diet, exercise, and lifestyle modification rather than medications. Otherwise, the financial burden imposed by obesity may be matched by the costs of treatment.

CONCLUSIONS

This study demonstrates that a metabolic syndrome phenotype may exist in perhaps 4% of the US adolescent population and almost 30% of overweight adolescents. Of those adolescents with metabolic syndrome, the great majority were overweight. This syndrome may affect almost 1 million adolescents in the United States. The impact of the meta-

bolic syndrome in adolescents on subsequent morbidity and mortality has not, however, been explored, nor has the potential to reduce these risks by weight loss, increased activity, or pharmacological alteration of associated metabolic derangements. Nonetheless, these data indicate that a substantial percentage of US adolescents may be at significantly heightened risk for the metabolic syndrome in adulthood and the subsequent risks for type 2 diabetes and premature coronary artery disease. Perhaps they should be considered candidates for aggressive therapeutic interventions to maintain healthy lifestyle into and throughout adulthood.

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REFERENCES

1. Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. *JAMA*. 2001;286:1195-1200.
2. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288:1723-1727.
3. Kuczmarski RJ, Ogden CL, Guo SS, et al. *2000 CDC Growth Charts for the United States: Methods and Development*. Hyattsville, Md: National Center for Health Statistics; 2002. Vital and Health Statistics Series 11, No. 246. DHHS Publication PHS 2002-1696.
4. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA*. 2002;288:1728-1732.
5. US Department of Health and Human Services. *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity 2001*. Rockville, Md: Public Health Service, Office of the Surgeon General; 2001.
6. Pearson TA, Blair SN, Daniels SR, et al. AHA guidelines for primary prevention of cardiovascular disease and stroke: 2002 update: consensus panel guide to comprehensive risk reduction for adult patients without coronary or other atherosclerotic vascular diseases; American Heart Association Science Advisory and Coordinating Committee. *Circulation*. 2002;106:388-391.
7. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-2497.
8. National Cholesterol Education Program. *Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): Full Report*. Bethesda, Md: National Institutes of Health; 2001. NIH publication No. 01-3670.
9. Ford ES. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA*. 2002;287:356-359.
10. Troiano RP, Flegal KM, Kuczmarski RJ, Campbell SM, Johnson CL. Overweight prevalence and trends for children and adolescents: the National Health and Nutrition Examination Surveys, 1963 to 1991. *Arch Pediatr Adolesc Med*. 1995;149:1085-1091.
11. Troiano RP, Flegal KM. Overweight children and adolescents: description, epidemiology, and demographics. *Pediatrics*. 1998;101(suppl 3):497-504.
12. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics*. 1998;101(suppl 3):518-525.
13. Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. *J Pediatr*. 1996;128(5 pt 1):608-615.
14. Styne DM. Childhood and adolescent obesity: prevalence and significance. *Pediatr Clin North Am*. 2001;48:823-854.
15. Falkner B, Hassink S, Ross J, Gidding S. Dysmetabolic syndrome: multiple risk factors for premature adult disease in an adolescent girl. *Pediatrics*. 2002;110(1 pt 1):e14. Available at: <http://www.pediatrics.org/cgi/content/full/110/1/e14>. Accessed August 5, 2002.
16. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. *Pediatrics*. 1999;103(6 pt 1):1175-1182.
17. McGill HC Jr, McMahan CA, Herderick EE, et al. Obesity accelerates the progres-

- sion of coronary atherosclerosis in young men. *Circulation*. 2002;105:2712-2718.
18. US Department of Health and Human Services. *Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988-94*. Hyattsville, Md: National Center for Health Statistics; 1994. Vital and Health Statistics Series 1, No. 32. DHHS Publication PHS 94-1308.
 19. Fagot-Campagna A, Saaddine JB, Flegal KM, Beckles GL. Diabetes, impaired fasting glucose, and elevated HbA1c in US adolescents: the Third National Health and Nutrition Examination Survey. *Diabetes Care*. 2001;24:834-837.
 20. Sun SS, Schubert CM, Chumlea WC, et al. National estimates of the timing of sexual maturation and racial differences among US children. *Pediatrics*. 2002;110:911-919.
 21. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. *Pediatrics*. 1996;98(4 pt 1):649-658.
 22. National Cholesterol Education Panel. *Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents*. Bethesda, Md: National Institutes of Health; 1991. NIH Publication No. 91-2732.
 23. Type 2 diabetes in children and adolescents. *Diabetes Care*. 2000;23:381-389.
 24. *SAS, Version 8.2* [computer program]. Cary, NC: SAS Institute Inc; 1999.
 25. Shah BV, Barnwell BG, Bieler GS. *SUDAAN User's Manual, Release 7.5*. Research Triangle Park, NC: Research Triangle Institute; 1997.
 26. Hjermann I. The metabolic cardiovascular syndrome: syndrome X, Reaven's syndrome, insulin resistance syndrome, atherothrombotic syndrome. *J Cardiovasc Pharmacol*. 1992;20(suppl 8):S5-S10.
 27. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications, part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998;15:539-553.
 28. Grundy SM. Obesity, metabolic syndrome, and coronary atherosclerosis. *Circulation*. 2002;105:2696-2698.
 29. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals: does the clock for coronary heart disease start ticking before the onset of clinical diabetes? *JAMA*. 1990;263:2893-2898.
 30. Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin-resistance syndrome (syndrome X). *Diabetes*. 1992;41:715-722.
 31. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001;24:683-689.
 32. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*. 2003;163:427-436.
 33. Chen W, Srinivasan SR, Elkasabany A, Berenson GS. Cardiovascular risk factors clustering features of insulin resistance syndrome (syndrome X) in a biracial (black-white) population of children, adolescents, and young adults: the Bogalusa Heart Study. *Am J Epidemiol*. 1999;150:667-674.
 34. Csabi G, Torok K, Jeges S, Molnar D. Presence of metabolic cardiovascular syndrome in obese children. *Eur J Pediatr*. 2000;159:91-94.
 35. Dwyer T, Blizzard L, Venn A, Stankovich JM, Ponsonby AL, Morley R. Syndrome X in 8-y-old Australian children: stronger associations with current body fatness than with infant size or growth. *Int J Obes Relat Metab Disord*. 2002;26:1301-1309.
 36. Maffei C, Pietrobelli A, Grezzani A, Provera S, Tato L. Waist circumference and cardiovascular risk factors in prepubertal children. *Obes Res*. 2001;9:179-187.
 37. Guo SS, Roche AF, Chumlea WC, Gardner JD, Siervogel RM. The predictive value of childhood body mass index values for overweight at age 35 y. *Am J Clin Nutr*. 1994;59:810-819.
 38. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med*. 1997;337:869-873.
 39. Vanhala M, Vanhala P, Kumpusalo E, Halonen P, Takala J. Relation between obesity from childhood to adulthood and the metabolic syndrome: population based study. *BMJ*. 1998;317:319-320.
 40. Bao W, Srinivasan SR, Berenson GS. Persistent elevation of plasma insulin levels is associated with increased cardiovascular risk in children and young adults: the Bogalusa Heart Study. *Circulation*. 1996;93:54-59.
 41. Dobbela CJ, Joffres MR, MacLean DR, Flowerdew G. A comparative evaluation of waist circumference, waist-to-hip ratio and body mass index as indicators of cardiovascular risk factors: the Canadian Heart Health Surveys. *Int J Obes Relat Metab Disord*. 2001;25:652-661.
 42. Janssen I, Katzmarzyk PT, Ross R. Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. *Arch Intern Med*. 2002;162:2074-2079.
 43. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. *Am J Clin Nutr*. 2002;75:683-688.
 44. Thompson CJ, Ryu JE, Craven TE, Kahl FR, Crouse JR. Central adipose distribution is related to coronary atherosclerosis. *Arterioscler Thromb*. 1991;11:327-333.
 45. Van Pelt RE, Evans EM, Schechtman KB, Ehsani AA, Kohrt WM. Waist circumference vs body mass index for prediction of disease risk in postmenopausal women. *Int J Obes Relat Metab Disord*. 2001;25:1183-1188.
 46. Freedman DS, Serdula MK, Srinivasan SR, Berenson GS. Relation of circumferences and skinfold thickness to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. *Am J Clin Nutr*. 1999;69:308-317.
 47. Savva SC, Tornaritis M, Savva ME, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. *Int J Obes Relat Metab Disord*. 2000;24:1453-1458.
 48. Kissebah AH, Krakower GR. Regional adiposity and morbidity. *Physiol Rev*. 1994;74:761-811.
 49. Steinberger J, Daniels SR. Obesity, insulin resistance, diabetes, and cardiovascular risk in children: an American Heart Association scientific statement. *Circulation*. 2003;107:1448-1453.
 50. Daniels SR, Khoury PR, Morrison JA. Utility of different measures of body fat distribution in children and adolescents. *Am J Epidemiol*. 2000;152:1179-1184.
 51. Reilly JJ, Dorosty AR, Emmett PM. Identification of the obese child: adequacy of the body mass index for clinical practice and epidemiology. *Int J Obes Relat Metab Disord*. 2000;24:1623-1627.
 52. Kavey RE, Daniels SR, Lauer RM, et al. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. *Circulation*. 2003;107:1562-1566.
 53. Williams CL, Hayman LL, Daniels SR, et al. Cardiovascular health in childhood: a statement for health professionals from the Committee on Atherosclerosis, Hypertension, and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation*. 2002;106:143-160.
 54. Guo S, Beckett L, Chumlea WC, Roche AF, Siervogel RM. Serial analysis of plasma lipids and lipoproteins from individuals 9-21 y of age. *Am J Clin Nutr*. 1993;58:61-67.
 55. Raitakari OT, Porkka KV, Rasanen L, Ronnema T, Viikari JS. Clustering and 6 year cluster-tracking of serum total cholesterol, HDL-cholesterol and diastolic blood pressure in children and young adults: the Cardiovascular Risk in Young Finn Study. *J Clin Epidemiol*. 1994;47:1085-1093.
 56. Barlow SE, Dietz WH. Obesity evaluation and treatment: Expert Committee recommendations. *Pediatrics*. 1998;102:e29. Available at: <http://www.pediatrics.org/cgi/content/full/102/3/e29>. Accessed August 5, 2002.
 57. Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services: recommendations from an expert committee: the Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services. *Am J Clin Nutr*. 1994;59:307-316.
 58. American Academy of Pediatrics. National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. *Pediatrics*. 1992;89(3 pt 2):525-584.
 59. American Academy of Pediatrics Committee on Nutrition. Cholesterol in childhood. *Pediatrics*. 1998;101(1 pt 1):141-147.
 60. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA*. 2002;288:1728-1732.
 61. Freedman DS, Bowman BA, Otvos JD, Srinivasan SR, Berenson GS. Differences in the relation of obesity to serum triacylglycerol and VLDL subclass concentrations between black and white children: the Bogalusa Heart Study. *Am J Clin Nutr*. 2002;75:827-833.
 62. Kimm SY, Obarzanek E. Childhood obesity: a new pandemic of the new millennium. *Pediatrics*. 2002;110:1003-1007.
 63. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403.
 64. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20:537-544.
 65. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344:1343-1350.