Prevalence and Trends of a Metabolic Syndrome Phenotype Among U.S. Adolescents, 1999–2000

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OBJECTIVE — To determine the prevalence of a metabolic syndrome phenotype among U.S. adolescents using the most recent national data and to examine trends in metabolic syndrome prevalence.

RESEARCH DESIGN AND METHODS — Analysis of data on 991 adolescents (aged 12–19 years) who had fasted for at least 6 h, from the National Health and Nutrition Examination Survey (NHANES 1999–2000). The metabolic syndrome was determined using the National Cholesterol Education Program (Adult Treatment Panel III) definition modified for age.

RESULTS — The overall prevalence of a metabolic syndrome phenotype among U.S. adolescents increased from 4.2% in NHANES III (1988–1992) to 6.4% in NHANES 1999–2000 ($P < 0.001$). The syndrome was more prevalent ($P < 0.01$) in male than female adolescents (9.1 vs. 3.7%) and was found in 32.1% of overweight adolescents (BMI ≥95th percentile for age and sex), compared with 7.1% of adolescents at risk for overweight (BMI between 85th and 95th percentiles) ($P < 0.001$). Based on population-weighted estimates, >2 million U.S. adolescents currently have a metabolic syndrome phenotype.

CONCLUSIONS — The prevalence of a metabolic syndrome phenotype has increased significantly over the past decade among U.S. adolescents and is particularly prevalent (>30%) in overweight adolescents. These findings have important implications for public health because of the well-known health risks associated with the metabolic syndrome in adults.

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An association between obesity, high fasting triglycerides, elevated fasting plasma insulin, impaired glucose tolerance, hypertension, and cardiovascular disease (CVD) has been recognized since the early 1960s. These major risk factors tend to cluster together in many individuals, suggesting a common etiology, which has been variously termed Syndrome X, the insulin resistance syndrome, and the metabolic syndrome. The Third Report of the National Cholesterol Education Program (Adult Treatment Panel III [ATP III]) recognized the clustering of these major CVD risk factors, which was termed the metabolic syndrome, as a secondary target of risk-reduction therapy (1). Current estimates indicate that the age-adjusted prevalence of the metabolic syndrome is roughly 24% among U.S. adults (2). The metabolic syndrome is largely confined to overweight and obese adults, with prevalence estimates of ~22% among adults with a BMI ≥25 and <30 kg/m^2 and 60% among adults with a BMI ≥30 kg/m^2 (3). In adults free of diabetes, having the metabolic syndrome independently predicts incident type 2 diabetes (4). The metabolic syndrome is also related to an increased risk of all-cause and CVD mortality in adults with (5) and without (6,7) type 2 diabetes, independent of other risk factors.

Although it has been studied extensively in adults, much less is known about the metabolic syndrome in youth. Current estimates indicate that roughly 4% of U.S. adolescents have a metabolic syndrome phenotype, based on an age-modified definition of the ATP III criteria established for adults (8). When stratified by BMI category, roughly 29% of overweight adolescents (BMI ≥95th percentile for age and sex) have a metabolic syndrome phenotype, compared with 7% of at-risk-for-overweight adolescents (BMI ≥85th and <95th percentile for age and sex) and <1% of normal-weight adolescents (BMI <85th percentile for age and sex) (8). Because the prevalence of overweight has continued to increase substantially over the past several decades among children and adolescents in the U.S. (9), it is also likely that the prevalence of the metabolic syndrome phenotype has increased among U.S. youth. This work presents the most recent national estimates of the prevalence of a metabolic syndrome phenotype in U.S. adolescents, based on data from the 1999–2000 National Health and Nutrition Examination Survey (NHANES). These results are compared with previous estimates (8) based on data from NHANES III (1988–1992).

RESEARCH DESIGN AND METHODS

— The NHANES survey design is a stratified, multistage, probability sample of the civilian noninstitutionalized U.S. population. The current

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Abbreviations: ATP III, National Cholesterol Education Program (Adult Treatment Panel III); CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

NHANES includes oversampling of low-income individuals, adolescents 12–19 years, adults aged ≥60 years, African Americans, and Mexican Americans to improve estimates for these groups. Approximately 9,965 individuals aged 2 months to 85 years were studied in NHANES 1999–2000. Over 3,000 individuals were invited to attend a morning examination after having fasted overnight. The NHANES protocol was reviewed and approved by the National Center for Health Statistic's Institutional Review Board. Fully informed consent and assent, where applicable, were obtained from all participants before any testing.

Details of the NHANES protocol and all laboratory procedures are available elsewhere. Briefly, height was measured in an upright position with a stadiometer, and weight was measured at a standing position on a self-zeroing scale. The waist circumference measurement was made at the midpoint between the bottom of the rib cage and above the top of the iliac crest during minimal respiration. Blood pressure measurements were performed by trained technicians using a standardized protocol. Three and sometimes four measurements were made on all subjects with a mercury sphygmomanometer, and the first and fifth Korotkoff sounds were recorded to represent the systolic and diastolic pressures. We used the average of three recorded measurements in all data analyses. Blood analytes were stored frozen and shipped to a central laboratory for analysis. Plasma glucose and serum or plasma triglycerides and HDL cholesterol were all measured using fully enzymatic techniques.

The initial sample consisted of 2,165 subjects aged 12–19 years who had a fasting plasma glucose value recorded. Only subjects who had complete data were included in this study. Subjects who had not fasted for at least 6 h, who were pregnant, or who were taking medications to regulate blood glucose (e.g., insulin or an oral hypoglycemic agent) were excluded from the analysis. The final sample consisted of 991 adolescent subjects.

Metabolic syndrome and overweight definitions

To allow for statistical comparisons between NHANES III and NHANES 1999–2000, we used the age-modified standards of the ATP III metabolic syndrome criteria published previously (8). We established the abdominal obesity criterion by analyzing all adolescents in the current dataset who had a waist circumference recorded. Subjects with a value ≥90th percentile for age and sex from this sample population were classified as having abdominal obesity. The blood pressure criterion was defined as a value ≥90th percentile for age, sex, and height, based on published reference data (10). The blood glucose (≥110 mg/dl), triglyceride (≥110 mg/dl), and HDL cholesterol (≤40 mg/dl) standards in the present study were identical to the cut points used previously (8). Subjects who met at least three of the five criteria were classified as having a metabolic syndrome phenotype.

Overweight among adolescents was a statistical definition based on the 2000 Centers for Disease Control and Prevention growth charts for the U.S. (9), defined as ≥95th percentile of BMI for age and sex. At risk for overweight was defined as ≥85th but <95th percentile of BMI for age and sex and normal weight as <85th percentile of BMI for age and sex.

Statistical analysis

Data were analyzed using STATA with survey replication package SVR (version 7; STATA, College Station, TX). All analyses were completed using the morning subsample weights to estimate means and 95% CIs, and the jackknife replication weights were used to estimate the SEs of those means using the delete-one-jackknife method (11). Prevalence values for those subjects with and without the metabolic syndrome were compared using the χ^2 test for proportions. Differences between surveys for the metabolic syndrome phenotype overall, by sex, and by race/ethnic group were tested univariately using the *t* test for independent samples. Statistical significance was established at $\alpha = 0.05$ a priori, and all multiple comparisons were adjusted using the Bonferroni method.

RESULTS — The prevalence of a metabolic syndrome phenotype was 6.4% (95% CI 3.8–8.9) among U.S. adolescents. Based on population-weighted estimates, ~2,070,950 U.S. adolescents have a metabolic syndrome phenotype. The syndrome was more common in male (9.1%, 4.8–13.4) than in female (3.7%, 0.2–7.1) adolescents ($P < 0.01$); however, there was no difference ($P = 0.3$) in the prevalence when examined by race/ethnic group (8.5% in Mexican Americans, 7.2% in non-Hispanic whites, and 5.1% in non-Hispanic blacks). When examined by BMI category, 32.1% of overweight adolescents had the syndrome compared with 7.1% of adolescents at risk for overweight and with <1% of adolescents with normal weight ($P < 0.001$).

The proportion of subjects with one or more abnormalities of the adolescent metabolic syndrome phenotype is presented in Table 1. In this sample, roughly 43% of subjects had one or more risk factors, nearly 17% had two or more risk factors, and ~1% had four or more risk factors. We also examined the proportion of subjects with one or more abnormalities using a fasting plasma glucose cut point ≥100 mg/dl (5.6 mmol/l) (12). By doing so, the proportion of subjects with the metabolic syndrome phenotype increased slightly to 6.7%. The proportion of subjects who had one or more individual risk factors increased to 45.9%, whereas 18.9% had two or more risk factors and 1.8% had four or more risk factors.

The distribution of the individual components of the metabolic syndrome phenotype is shown in Table 2. Overall, high fasting triglycerides and low HDL cholesterol were the most commonly satisfied criteria (23.2 and 23.4%, respectively), whereas high fasting glucose was the least common (1.1%). However, lowering the fasting plasma glucose cut point from 110 to 100 mg/dl (6.1 to 5.6 mmol/l) increased the proportion of subjects who met this standard to 7.6%.

The overall prevalence of a metabolic syndrome phenotype increased significantly ($P < 0.001$) from 4.2% in NHANES III (1988–1992) to 6.4% in NHANES 1999–2000 (Fig. 1). When examined by sex, the prevalence increased from 6.1 to 9.1% in male adolescents and from 2.1 to 3.7% in female adolescents ($P < 0.001$) (Fig. 1). When examined by race/ethnic group, the prevalence increased from 5.6 to 8.5% in Mexican Americans, from 4.8 to 7.2% in non-Hispanic whites, and from 2.0 to 5.1% in non-Hispanic blacks ($P < 0.001$) (Fig. 2).

CONCLUSIONS — The major new finding from this study is that the prevalence of a metabolic syndrome phenotype has increased significantly over the past decade among U.S. adolescents. Based on population-weighted estimates, >2 mil-

Table 1—*Prevalence of one or more risk factors of the metabolic syndrome among 991 U.S. adolescents aged 12–19 years: NHANES 1999–2000*

	Number of risk factors			
	≥1	≥2	≥3	≥4
≥110-mg/dl FPG cut point				
Total	43.2 (38.5–47.9)	16.6 (12.9–20.2)	6.4 (3.8–8.9)	0.7 (0.0–1.5)
Sex				
Male	46.1 (38.7–53.7)	20.0 (14.3–25.7)	9.1 (4.8–13.4)	1.3 (0.0–2.9)
Female	40.4 (32.9–48.0)	13.2 (7.6–18.7)	3.7 (0.2–7.1)	0.2 (0.0–0.3)
Race/ethnicity				
Non-Hispanic white	44.0 (37.8–50.1)	16.8 (11.9–21.7)	7.2 (3.5–10.9)	0.9 (0.0–2.0)
Non-Hispanic black	39.1 (31.2–47.1)	15.5 (9.5–21.4)	5.1 (0.9–9.4)	0.6 (0.0–1.9)
Mexican American	49.1 (42.3–55.9)	20.0 (14.6–25.4)	8.5 (5.6–11.4)	0.8 (0.0–1.7)
BMI status (percentile)				
Normal (<85th)	32.5 (27.4–37.6)	6.5 (3.2–9.7)	0.0 (0.0–0.0)	0.0 (0.0–0.0)
At risk (85th to <95th)	49.6 (35.5–63.7)	22.5 (8.8–36.2)	7.1 (0.0–18.1)	0.0 (0.0–0.0)
Overweight (≥95th)	82.2 (73.2–91.2)	52.8 (41.0–64.6)	32.1 (22.1–42.1)	4.4 (0.0–9.5)
≥100-mg/dl FPG cut point				
Total	45.9 (41.4–50.4)	18.9 (14.7–23.2)	6.7 (4.1–9.2)	1.8 (0.5–3.1)
Sex				
Male	49.4 (41.7–57.1)	23.1 (16.9–29.3)	9.6 (5.3–13.9)	3.2 (0.6–5.9)
Female	42.5 (35.1–50.0)	14.9 (9.2–20.5)	3.8 (0.3–7.2)	0.3 (0.0–0.7)
Race/ethnicity				
Non-Hispanic white	46.9 (40.9–52.8)	19.6 (13.4–25.7)	7.2 (3.5–10.9)	1.6 (0.0–3.5)
Non-Hispanic black	40.2 (32.4–48.0)	15.5 (9.5–21.4)	5.9 (1.2–9.7)	2.1 (0.0–4.3)
Mexican American	55.3 (49.1–61.5)	23.6 (19.2–28.0)	10.4 (6.8–14.0)	2.5 (0.0–4.3)
BMI status (percentile)				
Normal (<85th)	35.2 (30.3–40.2)	8.7 (3.7–13.7)	0.1 (0.0–0.2)	0.0 (0.0–0.0)
At risk (85th to <95th)	51.0 (37.1–64.8)	23.5 (9.6–37.5)	7.9 (0.0–18.9)	0.2 (0.0–0.5)
Overweight (≥95th)	86.1 (77.5–94.7)	57.3 (45.5–68.9)	32.8 (22.7–42.9)	10.7 (2.9–18.5)

Data are percent (95% CI). FPG, fasting plasma glucose.

lion U.S. adolescents currently have a metabolic syndrome phenotype. The trend for increasing metabolic syndrome prevalence was evident in both sexes and in all three major race/ethnic groups analyzed in this study.

A metabolic syndrome phenotype was most common in overweight adolescents, with a prevalence of 32.1%, compared with only 7.1% of at-risk-for-overweight adolescents. The difference in metabolic syndrome prevalence among overweight compared with at-risk-for-overweight adolescents was striking and further underscores the importance of small amounts of weight loss in potentially avoiding the development of the metabolic syndrome and related sequelae. These findings are consistent with published results (8), in which 28.1 and 6.8% of overweight and at-risk-for-

Table 2—*Prevalence of individual risk factors of the metabolic syndrome among 991 U.S. adolescents aged 12–19 years: NHANES 1999–2000*

	Risk factor					
	Abdominal obesity	High glucose (mg/dl)		High triglycerides	Low HDL cholesterol	Elevated blood pressure
		≥100	≥110			
Total	11.8 (8.6–15.1)	7.6 (4.8–10.4)	1.1 (0.0–0.2)	23.2 (18.6–27.9)	23.4 (19.3–27.6)	8.0 (5.3–10.6)
Sex						
Male	12.1 (7.7–16.5)	10.0 (6.2–13.7)	0.8 (0.0–2.0)	25.5 (19.7–31.4)	27.3 (20.3–34.5)	10.8 (6.8–14.7)
Female	11.6 (6.5–16.7)	5.3 (1.4–9.2)	1.3 (0.0–3.0)	20.9 (14.6–27.2)	19.3 (12.2–26.4)	5.1 (1.7–8.5)
Race/ethnicity						
Non-Hispanic white	9.3 (4.9–13.6)	8.1 (3.7–12.5)	1.4 (0.0–3.0)	26.0 (19.4–32.6)	25.0 (19.5–30.5)	7.5 (3.2–11.8)
Non-Hispanic black	15.6 (10.0–21.2)	4.0 (1.8–6.2)	1.1 (0.0–2.5)	13.9 (8.4–19.0)	17.6 (10.3–24.8)	12.7 (8.5–16.9)
Mexican American	14.6 (11.1–18.1)	13.5 (8.9–18.1)	0.4 (0.0–1.1)	25.2 (21.3–29.1)	26.0 (20.2–31.8)	11.3 (7.7–14.9)
BMI status (percentile)						
Normal (<85th)	0.4 (0.0–1.4)	5.5 (2.0–9.0)	0.6 (0.0–1.5)	17.1 (11.4–22.8)	18.6 (13.6–23.6)	4.4 (1.0–7.8)
At risk (85th to <95th)	12.1 (1.3–22.8)	7.3 (1.5–13.0)	4.0 (0.0–9.5)	27.8 (15.5–40.1)	29.1 (17.1–41.2)	6.0 (0.5–11.4)
Overweight (≥95th)	61.5 (49.5–73.4)	17.2 (6.9–27.6)	0.1 (0.0–0.3)	45.5 (35.1–55.8)	39.1 (29.1–49.1)	25.6 (14.5–36.7)

Data are percent (95% CI).

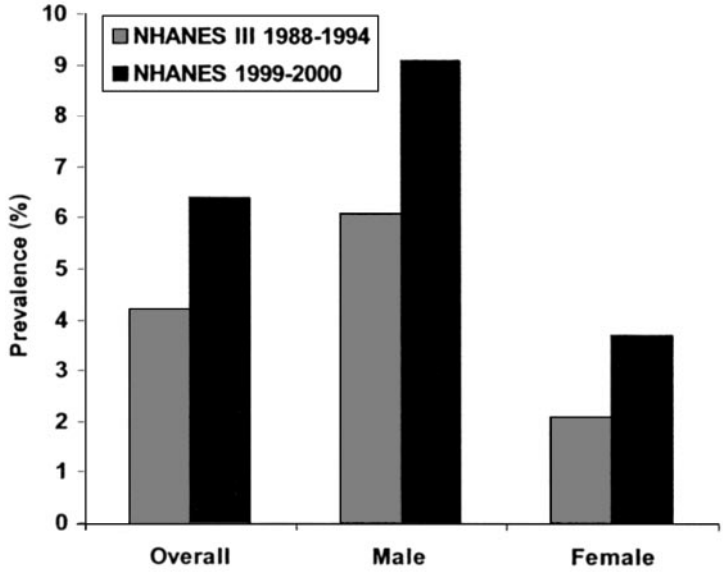

Figure 1—*Prevalence of a metabolic syndrome phenotype among U.S. adolescents aged 12–19 years. Differences shown are between NHANES III (1988–1994) and NHANES 1999–2000, overall and by sex. All comparisons between surveys are significant at* $P < 0.001$.

overweight adolescents, respectively, had a metabolic syndrome phenotype based on data from NHANES III (1988–1992). Together, these studies indicate that a metabolic syndrome phenotype is likely present in at least 30% of all U.S. adolescents who are overweight. It is not entirely surprising that this syndrome has increased over the past decade among U.S. adolescents because overweight per se has also increased in the same time period in this group (9) and the metabolic syndrome phenotype is largely confined to overweight adolescents. This is consistent with findings in adults, in whom the metabolic syndrome was found in roughly 5, 22, and 60% of normal-weight, overweight, and obese men and women, respectively (3).

In adults, older age, postmenopausal status, Mexican-American ethnicity, higher BMI, current smoking, low household income, high carbohydrate intake, no alcohol consumption, and physical inactivity are associated with an increased risk of developing the metabolic syndrome (3). Central adiposity, and specifically a high level of visceral fat, is a hallmark feature of the metabolic syndrome in adults (13–16). Furthermore, central obesity appears to be the major discriminating factor when comparing metabolic syndrome prevalence differences in various populations (17). Adults with the metabolic syndrome are also characterized by low levels of cardiorespiratory fitness ($V_{O_{2max}}$) (18–21) and abnormalities in several inflammatory biomarkers (14–16,22,23).

Although it has been studied extensively in adults, much less is known about the metabolic syndrome in youth. A clustering of risk factors related to the metabolic syndrome, including total and HDL cholesterol, triglycerides, insulin, and blood pressure, were investigated in a large group of Danish boys and girls (aged 9–15 years). In this study (24), 5.4% of the sample had four or five risk factors, and in these individuals, $V_{O_{2max}}$ was 1.2 SDs lower and BMI 1.6 SDs higher than the mean levels for these variables in the sample population. A population-based study (25) of factors leading to the metabolic syndrome demonstrated that one-half of the obese children sampled at age 7 years had become obese adults at follow-up and had a high risk of developing the metabolic syndrome; this risk was significantly lower among the obese adults who had not been obese as children compared with the obese adults who had also been obese as children. In adults, it is well established that the progression from normal to impaired glucose tolerance, and subsequently to type 2 diabetes, is characterized by peripheral insulin resistance and defects in β-cell function (26,27). Insulin resistance is thought to be the major underlying feature of the metabolic syndrome (28). Along these same lines, a recent study (29) demonstrated that obese children and adolescents with impaired glucose tolerance had high levels of visceral and intramyocellular fat, and this altered fat partitioning was closely linked to severe peripheral insulin resistance. Thus, the factors leading to the development of the metabolic syndrome in adults are also likely operating in youth, includ-

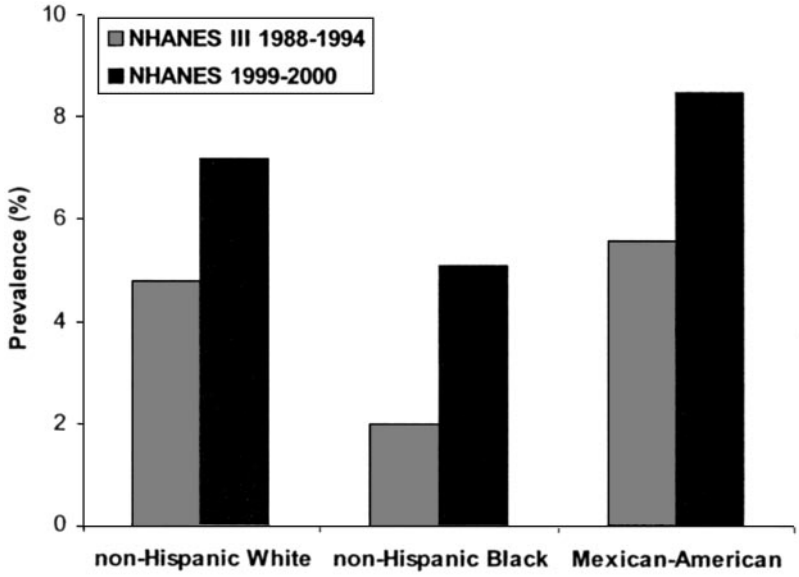

Figure 2—*Prevalence of a metabolic syndrome phenotype among U.S. adolescents aged 12–19 years. Differences shown are between NHANES III (1988–1994) and NHANES 1999–2000, by race/ethnic group. All comparisons between surveys are significant at* $P < 0.001$.

ing increased BMI, visceral fat accumulation, and low cardiorespiratory fitness.

Because overweight adolescents are particularly at risk for developing the metabolic syndrome, they are also more likely to develop the metabolic complications of overweight in adulthood. This notion is supported by findings from cluster-tracking studies (30,31) demonstrating that overweight in youth persists into adulthood and may be associated with subsequent adverse health outcomes in later life. Similarly, several population-based studies have demonstrated that elevated blood lipid (32–37) and blood pressure (35–37) levels in childhood are associated with elevated levels in adulthood. Together, these studies demonstrate that risk factors related to the metabolic syndrome tend to track from childhood to adulthood, increasing the risk for adverse health outcomes in later life. For example, in adults who do not have diabetes, having the metabolic syndrome predicts incident type 2 diabetes independent of age, sex, ethnicity, family history of type 2 diabetes, impaired glucose tolerance, and fasting insulin levels (4). In adults who have type 2 diabetes, the presence of the metabolic syndrome is associated with a fivefold increase in CVD risk independent of age, sex, smoking status, and HbA_{1c} (5). However, the risk of developing type 2 diabetes and CVD in youth who have the metabolic syndrome is unknown.

The number of U.S. adolescents who had one or more abnormalities of the syndrome also increased from previous findings. In the present study, roughly 43% of subjects had at least one risk factor, nearly 17% had two or more risk factors, and 6.4% had three or more risk factors (i.e., metabolic syndrome) (Table 1). In NHANES III, ~ 41% had at least one risk factor, 14% had two or more risk factors, and 4.2% had three or more risk factors (8). When we used a fasting plasma glucose cut point of ≥100 mg/dl (5.6 mmol/l) to establish the high glucose level threshold, the proportion of subjects who had one or more individual risk factors increased to ~46%, two or more risk factors to 19%, and three or more risk factors to 6.7% (Table 1). Although the high glucose level standard was least common, whereas high fasting triglycerides and low HDL cholesterol were most common (Table 2), lowering the fasting plasma glucose cut point from 110 to 100 mg/dl (6.1 to 5.6 mmol/l) increased the proportion of subjects who met this standard to 7.6%. Closer inspection of our data reveals that the major cause of the shifts noted above was a large proportion of Mexican-American and non-Hispanic white subjects who met the new glucose standard. For example, the proportion of Mexican-American adolescents who met the different glucose standards increased from 0.4 to 13.5% for the 110- and 100-mg/dl thresholds, whereas the proportion of non-Hispanic white youth meeting these standards increased from 1.4 to 8.1%. Thus, these groups of adolescents appear to be particularly prone to abnormalities in glucose metabolism.

Although no national definition of the metabolic syndrome in youth currently exists, we chose to use methods identical to those used previously in order to make statistical comparisons between NHANES III (1988–1992) and NHANES 1999–2000. This allowed us to estimate the current prevalence of a metabolic syndrome phenotype in adolescents and to determine trends for this condition over the past decade. The cross-sectional nature of the NHANES surveys does not allow us to make causal inferences as to the underlying relationship between developing overweight and the metabolic syndrome in youth. However, because both conditions have continued to increase in parallel over relatively short periods in genetically stable populations, our findings point to major changes in lifestyle, such as poor diet and physical inactivity, as major contributors to the increasing prevalence of a metabolic syndrome phenotype in youth. Our findings provide evidence of an emerging public health problem that cuts across both sexes and all major ethnic/racial groups and further underscores the importance of early intervention to prevent overweight in youth. Elucidating the precursors of the metabolic syndrome in youth may lead to effective therapies to prevent its development or to mitigate its consequences later in life.

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