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Tobacco Smoke Exposure Is Associated With the Metabolic Syndrome in Adolescents

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Background—The metabolic syndrome predicts future coronary artery disease and type II diabetes and often emerges in childhood. Tobacco smoke potentially contributes to insulin resistance in this syndrome. This study evaluates the association of environmental tobacco smoke (ETS) exposure and active smoking with the prevalence of the metabolic syndrome in US adolescents.

Methods and Results—Data from 2273 subjects 12 to 19 years of age were examined from the National Health and Nutrition Examination Survey III (NHANES III, 1988 to 1994). Serum cotinine levels, presence of household smokers, and self-report of smoking were used to determine ETS exposure and active smoking. The metabolic syndrome was defined as having ≥3 criteria from the National Cholesterol Education Panel definition. Bivariate and multivariable analyses were conducted. Among adolescents, 5.6% met the criteria for metabolic syndrome, and prevalence increased with tobacco exposure: 1.2% for nonexposed, 5.4% for those exposed to ETS, and 8.7% for active smokers ($P<0.001$). In adolescents at risk for overweight and overweight adolescents (body mass index above the 85th percentile), a similar relationship was observed: 5.6% for nonexposed, 19.6% for those exposed to ETS, and 23.6% for active smokers ($P=0.01$). In multivariable logistic regression analyses among all adolescents, ETS exposure was independently associated with the metabolic syndrome (ETS exposure: odds ratio, 4.7, 95% CI, 1.7 to 12.9; active smoking: odds ratio, 6.1; 95% CI, 2.8 to 13.4).

Conclusions—Considering that tobacco and obesity are the 2 leading causes of preventable death in the United States, these findings of a dose-response, cotinine-confirmed relationship between tobacco smoke and metabolic syndrome among adolescents may have profound implications for the future health of the public. **(*Circulation*. 2005;112:862-869.)**

Key Words: adolescent ■ metabolic syndrome ■ obesity ■ smoking ■ tobacco

Obesity is poised to overtake tobacco as the No. 1 cause of preventable death in the United States.[1] According to the most recent estimates from the Centers for Disease Control, obesity was responsible for 400 000 deaths, just shy of tobacco's death toll of 435 000, in the year 2000.[2] Exacerbated by a modern lifestyle of poor nutrition and physical inactivity, the rising trend of obesity has affected Americans of all ages. The percentage of children who are overweight (body mass index [BMI] >95th percentile for age and gender) has tripled in the last 2 decades to current estimates of 15% among those 6 to 19 years of age.[3] The Surgeon General's Report states that the health problems resulting from obesity threaten to reverse the major improvements in health accomplished in the 20th century.[1]

The emergence of the obesity epidemic is especially important to the development of the metabolic syndrome, a clinical entity defined by the clustering of cardiovascular risk factors that include central obesity, dyslipidemia, hyperglycemia, and hypertension. The metabolic syndrome is especially important because it often develops in childhood,[4,5] has a substantially higher prevalence in overweight children,[6] increases directly with the degree of obesity,[7] and presages type II diabetes[8,9] and adult cardiovascular disease,[10,11] currently America's No. 1 cause of mortality.[12] Recent estimates of the prevalence of the metabolic syndrome in US adolescents (4%) compared with adults (23.7%) obfuscate its growing prevalence among overweight adolescents. We recently reported that in normal-weight adolescents 12 to 19 years of age (BMI <85th percentile) nationwide, the metabolic syndrome is rare, with a prevalence of 0.1%.[6] In comparison, the metabolic syndrome was found to occur in 6.1% of those at risk for overweight (BMI ≥85th percentile

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but ≤95th percentile) and in 28.7% of those overweight (BMI >95th percentile). Eighty percent of adolescents with the metabolic syndrome are overweight, signifying the unique vulnerability of a growing segment of the nation's youth to the development of this syndrome and to subsequent premature cardiovascular disease and type II diabetes.

A growing body of evidence also indicates that tobacco smoke is independently associated with insulin resistance and that the insulin resistant condition may contribute to the accelerated atherosclerosis that leads to excessive cardiovascular disease in adult smokers.[13] Tobacco smoke is clearly associated with dyslipidemias (increased LDL and decreased HDL),[14,15] endothelial dysfunction, and a hypercoagulable state,[16] all of which are also components of the metabolic syndrome. Additionally, a dose-response relationship exists with cigarette smoking and the development of type II diabetes in adults.[17] These findings suggest that because both tobacco smoke and the metabolic syndrome are individually associated with insulin resistance, these 2 entities may be linked through this common pathophysiology and that overweight children and youth may be especially susceptible to the impact of tobacco smoke on cardiovascular health, considering that tobacco smoke and obesity both predispose to the constellation of cardiovascular risk factors seen in the metabolic syndrome.

The present study sought to investigate the association between both active smoking and environmental tobacco smoke (ETS), also known as secondhand smoke, exposure, and the metabolic syndrome among adolescents in the United States. We hypothesized that tobacco smoke exposure is associated in a dose-dependant manner with the metabolic syndrome in adolescents.

Methods

Data from 3211 subjects 12 to 19 years of age from the National Health and Nutrition Examination Survey (NHANES III, 1988 to 1994) were examined. The response rate for this age range participating in the examination component of the survey was 83%. NHANES III is a cross-sectional health survey that used a complex, multistage design to achieve a nationally representative sample of the noninstitutionalized civilian population in the United States. Participants were evaluated with a home interview to determine family medical history, current medical conditions, medication use, self-report of the presence of any smokers in the household, and socioeconomic and demographic information. Additionally, each person was randomly assigned to undergo a morning, afternoon, or evening examination at a mobile examination center consisting of physical exams and laboratory testing using blood and urine samples. Morning participants were asked to fast for 8 hours; afternoon and evening participants were asked to fast for 6 hours.

Further details about the determination and analysis of serum triglycerides, HDL cholesterol, and glucose levels have been described elsewhere.[3] Blood pressure measurements for adolescents ≥17 years of age were averaged from 3 measurements taken at the participant's home and 3 taken at the examination center. The first and fifth Korotkoff sounds were used for the systolic and diastolic values. For adolescents 12 to 16 years of age, only the 3 blood pressure measurements at the examination center were taken, and the average of those 3 measurements was used. Measurements for height were taken with a stadiometer in subjects in an upright posture; weight was measured with a self-zeroing scale. Waist circumference measurements were made to the nearest 0.1 cm, with the patient at minimal respiration.[18] The point of measurement was between the bottom of the ribcage and the top of the iliac crest. The sample numbered 2273 after the following exclusion criteria were applied: (1) had not fasted for 6 hours; (2) was currently pregnant; (3) was taking medication classified as a blood glucose regulator such as insulin, androgens or anabolic steroids, or adrenal corticosteroids; or (4) had no serum cotinine level available. In the regression analysis, we included 2006 subjects who had complete data for all covariates in the final model.

TABLE 1. Potential Components of the Metabolic Syndrome in Adolescents

Criterion	
High triglyceride level, mg/dL	≥110
Low HDL-C level, mg/dL	≤40
Abdominal obesity, waist circumference, percentile	≥90th*
High blood pressure, percentile	≥90th†
High fasting plasma glucose, mg/dL	≥100

*90th percentile for age and sex.

†90th percentile for age, sex, and height or current use of antihypertensive medication.

Definitions

At Risk for Overweight and Overweight

Weight status was assessed with age- and gender-specific BMI. Those with a BMI <85th percentile were classified as normal weight; those with a BMI ≥85th but <95th percentile were classified as at risk for overweight; those with a BMI ≥95th percentile were considered overweight; and all those with a BMI ≥85th percentile were classified as at risk for overweight and overweight.[19]

Metabolic Syndrome

Although no universally accepted definition for the metabolic syndrome in adolescents has been formulated, previously developed criteria[6] have been used in the literature that are based on values from national references for cholesterol, blood pressure, and glucose for children and adolescents.[16,20–22] Adolescents who had a waist circumference ≥90th percentile for age and gender from this sample population were classified as having abdominal obesity. Systolic and diastolic hypertension was defined by having blood pressure values ≥90th percentile for age, sex, and height[22] or currently using antihypertensive medication. Participants were classified with hypertriglyceridemia if they had ≥110 mg/dL, low HDL if they had values ≤40 mg/dL, and elevated fasting glucose if they had serum glucose values ≥100 mg/dL.[23] Those with the metabolic syndrome were defined as individuals with ≥3 of these abnormalities (Table 1).

Active Smoking and ETS Exposure

Cotinine, a metabolite of nicotine, was used as a biomarker for both active smoking and exposure to ETS. In addition to cotinine, NHANES III includes adolescent self-report of smoking status and parent/guardian report of the presence of any smokers in the household. Active smokers were defined as those with cotinine levels >15 ng/mL[24] or those who reported smoking in the past 5 days. Those with serum cotinine levels that were detectable but ≤15 ng/mL and who did not report smoking in the past 5 days were defined as exposed to ETS.[24] A cotinine level of <0.05 ng/mL was below the detection limit. Those with undetectable serum cotinine levels, no reported smoking in the home, and no self-reported smoking were defined as nonexposed. We used parental report of smoking in the home to verify that the mean cotinine levels of those living in households reported to contain a smoker were in fact higher than the levels among those reported as living in a household without a smoker. Before separating the ETS exposure group into terciles for a secondary dose-response analysis, we excluded those adolescents whose parents did not report the presence of any smokers in the household to yield a group more enriched for true ETS exposure. Thus, for the analysis involving this enriched group in ETS by

TABLE 2. Definitions of Smoking Status

Smoking Status	Definition
For general analysis	
Active smoker	Cotinine >15 ng/mL or self-report of smoking in the past 5 d
Exposed to ETS	Cotinine ≥0.0 5ng/mL and ≤15 ng/mL and did not report smoking in past 5 d
Nonexposed	Undetectable serum cotinine and no self-report of smoking and no reported smoking in the home
For subanalysis of ETS with smokers in the home*	
Active smoker	Cotinine >15n g/mL or self-report of smoking in the past 5 d
Exposed to ETS with smokers in the home	Cotinine ≥0.05 ng/mL and ≤15 ng/mL and adult guardian report of smoker in the home and did not report smoking in past 5 d
Nonexposed	Undetectable serum cotinine and no self-report of smoking and no reported smoking in the home

*See definitions in Methods for rationale of tercile analysis.

terciles, ETS exposure is defined as detectable cotinine ≤15 ng/mL, no self-report of smoking in past 5 days, and adult guardian report of smoker in the home. The definitions for active smoking and nonexposed are identical to those described above for the initial analysis. All definitions for smoke exposure categories are illustrated in Table 2.

Statistical Analyses

We used χ^2 tests for bivariate analyses to determine the statistical significance of associations of independent variables investigated with the metabolic syndrome and its components. Student's *t* tests were used to compare the mean serum cotinine levels and the geometric mean of cotinine levels of those who were reported to live in households with smokers with those who were reported not to live in households with smokers. The Cochran-Armitage trend test was used to test for trends. Variables found to be statistically significant in bivariate analyses at $P<0.10$ or thought to be associated with the metabolic syndrome were included in multivariable logistic regression analyses to determine independent associations with the metabolic syndrome. Variables in the logistic regression models were screened for colinearity by examining correlation coefficients in bivariate analyses, and no colinearity was found. Two additional analyses were performed: one on overweight teens and one on teens from households with reported smokers in the home. All analyses were conducted with SAS,[25] and SUDAAN statistical software was used to account for the complex sample design of the NHANES and to apply sampling weights to produce national estimates by adjusting for the oversampling of young children, older adults, Mexican Americans, and blacks.[26]

Results

The overall rate of nonexposure to tobacco (cotinine <0.05 ng/mL, no self-report of active smoking, and no report of household members smoking) was 11.8%, ETS exposure (cotinine 0.05 to 15 ng/mL and no self-report of active smoking) was 67.0%, and active smoking (cotinine >15 ng/mL or self-report of smoking in the past 5 days) was 21.2%. When self-reported data alone were used, 52.3% of adolescents reported no exposure to tobacco (neither household exposure nor actively smoking), 42.5% of adolescents reported any household exposure (with or without actively smoking), and 19.1% of adolescents reported actively smoking. Serum cotinine levels were higher among adolescents for whom the presence of a smoker in the home was reported (1.7 versus 0.4 ng/mL, $P<0.001$; and 1.1 versus 0.2 ng/mL when geometric mean cotinine levels were compared, $P<0.001$). There were no adolescents with cotinine levels <0.05 ng/mL who reported smoking in the last 5 days.

The metabolic syndrome was present in 5.6% of US adolescents overall: 8.1% of boys and 2.9% of girls ($P=0.001$), 6.5% of whites, 3.1% of blacks, and 6.7% of Mexican Americans ($P=0.003$) (Table 3). Age, poverty status, parental history of diabetes or heart attack, and reported presence of a smoker in the home were not statistically associated with increased rates of occurrence. In contrast, the rate increased with increasing BMI and level of tobacco smoke exposure: 1.2% of nonexposed teens, 5.4% of those exposed to ETS, and 8.7% of actively smoking teens ($P<0.001$).

In multivariable logistic regression analyses conducted among all those 12 to 19 years of age, the following characteristics were independently associated with the metabolic syndrome after adjustment for gender, age, race/ethnicity, poverty status, region, and parental history of diabetes or heart attack: male gender (odds ratio [OR], 3.3; 95% CI, 1.6 to 6.6), black race (OR, 0.3; 95% CI, 0.1 to 0.6), ETS exposure (OR, 4.7; 95% CI, 1.7 to 12.9), and active smoking (OR, 6.1; 95% CI, 2.8 to 13.4) (Table 4). To control for possible confounding of BMI with components of the metabolic syndrome, identical multivariable analyses were conducted among youth with a BMI ≥85th percentile. Male gender, black race, ETS exposure, and active smoking again were independently associated with the risk of metabolic syndrome, with ORs similar to those of the entire adolescent sample (Table 4). To test for the interaction between race/ethnicity and poverty status and the metabolic syndrome, an interaction term was added to the model, and the multivariable analysis was repeated. Black race remained associated (OR, 0.4), but there was no statistically significant association between poverty or the interaction term and the metabolic syndrome.

To assess the potential burden of smoke exposure on at risk for overweight and overweight teens, analyses were performed on teens with BMIs ≥85th percentile, thus examining the impact of the 2 most prevalent cardiac risk factors in adults. In bivariate analyses among adolescents with a BMI ≥85th percentile, the metabolic syndrome was present in 5.6% of those who were nonexposed, 19.6% of those exposed to ETS, and 23.6% of active smokers (test for trend, $P=0.01$) (Table 5). Among those who were overweight (BMI >95th percentile; n=318), the respective rates were 23.8%, 32.3%,

TABLE 3. Rates of Occurrence of the Metabolic Syndrome Among Adolescents 12 to 19 Years of Age in the United States, NHANES III, 1988–1994

	n	With Metabolic Syndrome, %	P
Overall	2273	5.6	
Gender			0.001
Male	1077	8.1	
Female	1196	2.9	
Race/ethnicity			0.003
White	608	6.5	
Black	766	3.1	
Mexican American	792	6.7	
Other	107	1.8	
Age, y			0.53
12–14	896	6.2	
15–19	1377	5.2	
Poverty status			0.35
Below poverty	751	7.4	
At or above poverty	1303	5.1	
Region			0.004
Northeast	236	1.5	
Midwest	425	8.1	
South	1056	5.5	
West	556	6.4	
Parental history of diabetes			0.32
Yes	170	7.3	
No	2048	5.7	
Parental history of heart attack			0.13
Yes	382	8.7	
No	1839	5.1	
BMI category			<0.001
Normal	1581	0.7	
At risk	346	9.1	
Overweight	318	34.6	
Reported household smoke exposure			0.55
Yes	942	6.2	
No	1331	5.1	
Tobacco			<0.001
Nonexposed* (11.8%)	255	1.2	
Exposed to ETS† (67.0%)	1647	5.4	
Active Smokers‡ (21.2%)	371	8.7	

n=2273.

*Nonexposed defined as having a cotinine level <0.05 ng/mL, no self-report of smoking in the past 5 days, and no report of household members smoking in the house.

†ETS as evidenced by serum cotinine level ≤15 ng/mL and no self-report of smoking in the past 5 days.

‡Active smoking defined as having a cotinine level >15 ng/mL or self-report of smoking in the past 5 days.

and 40.4% (test for trend, $P=0.08$). Similar trends were found for the following components of the syndrome: high triglycerides, low HDL, and high waist circumference (each statistically significant at $P=0.001$ or less). Elevated fasting glucose occurred in 11.6% of nonexposed, 14.1% of ETS exposed, and 9.6% of actively smoking youth ($P=0.19$). In contrast, rates of elevated blood pressure were lowest among actively smoking youth (6.2%), intermediate among those exposed to ETS (9.8%), and highest among those nonexposed (17.6%) ($P=0.01$). Limitations of sample size would not allow statistical reliability for multivariable analyses on this subset; thus, they were not performed.

To examine a purer subset of adolescents exposed to passive tobacco smoke, analyses were performed on only those teens with a reported smoker in the home because subjects would be less likely to lie about positive household smoking. To assess for the possibility of a dose-response relationship between metabolic syndrome and level of tobacco smoke exposure, cotinine levels for ETS-exposed adolescents were categorized by tercile among youth in households with reported smokers present. Adolescents who had cotinine values in the ETS range but whose parents did not report smokers in the home were excluded to provide a group with optimal true ETS exposure. A linear relationship was found between intensity of tobacco smoke exposure and rates of the metabolic syndrome (the Figure). This apparent dose-response relationship persisted in multivariable analyses (Table 6).

Discussion

This study demonstrates a dose-response, cotinine-confirmed relationship between tobacco smoke and the metabolic syndrome among adolescents in the United States. Data come from a large, nationally representative sample with objective biochemical rather than exclusive self-report measures of smoking status. The findings indicate that exposure to tobacco smoke, whether by active smoking or exposure to ETS, is associated with at least a 4-fold increase in the risk of the metabolic syndrome among adolescents who are overweight and at risk for overweight. These findings may have profound implications in light of the still-increasing rates of overweight and persistently high rates of active smoking and exposure to ETS among adolescents in the United States.

Both smoking and the metabolic syndrome have individually been recognized as independent risk factors for cardiovascular disease and type II diabetes for some time, and at least 2 previous studies have reported increased rates of the metabolic syndrome among adult smokers.[27,28] Never before, to the best of our knowledge, have these associations been investigated using a biological marker of smoking and ETS in adolescents. Furthermore, although previous work has explored ETS by cotinine studies in adults, only individual cardiovascular risk factors[15] or coronary artery disease deaths[29] were examined, not the cluster of the adverse physiological changes of the metabolic syndrome, as demonstrated here.

The mechanisms underlying the development of the metabolic derangements that occur in the metabolic syndrome are not fully understood. The most widely accepted hypothesis posits a complex interaction between insulin resistance and obesity that is modified by social, environmental, racial/ethnic, and genetic factors.[30–32] Although it is not possible to conclusively establish an etiological role for tobacco smoke

TABLE 4. Independent Associations With the Metabolic Syndrome, NHANES III, 1988–1994, for Adolescents 12 to 19 Years of Age*

	All Adolescents 12–19 y of Age (n=2006)			At Risk or Overweight Adolescents 12–19 y of Age (n=584)		
	OR	95% CI	*P*	OR	95% CI	*P*
Tobacco						
Nonexposed† (referent)	1.0			1.0		
Exposed to ETS‡	4.7	1.7–12.9	0.003	4.1	1.4–12.6	0.01
Active smokers§	6.1	2.8–13.4	<0.001	4.4	1.4–14.0	0.01
Gender						
Male	3.3	1.6–6.6	0.001	4.2	1.9–9.2	0.001
Female (referent)	1.0			1.0		
Age, y						
12–14 y	1.2	0.7–2.3	0.48	1.1	0.5–2.5	0.76
15–19 y (referent)	1.0			1.0		
Race/ethnicity						
White (referent)	1.0			1.0		
Black	0.3	0.1–0.6	0.003	0.2	0.1–0.6	0.004
Mexican American	0.7	0.3–1.6	0.39	0.7	0.3–1.8	0.47
Other	0.4	0.1–2.3	0.29	0.5	0.1–2.8	0.45
Poverty status						
Below poverty	1.9	0.8–4.5	0.14	2.2	0.9–5.1	0.08
At or above poverty (referent)	1.0			1.0		
Region						
Northeast (referent)	1.0			1.0		
Midwest	4.2	0.9–21.1	0.08	5.3	0.9–30.0	0.06
South	4.0	0.8–21.2	0.10	4.1	0.7–23.0	0.11
West	5.4	0.9–31.6	0.06	5.9	0.8–42.1	0.07
Parental history of diabetes						
Yes	1.3	0.7–2.4	0.41	0.9	0.5–1.8	0.83
No (referent)	1.0			1.0		
Parental history of heart attack						
Yes	1.3	0.6–2.5	0.50	1.2	0.6–2.7	0.57
No (referent)	1.0			1.0		

*Adolescents with a valid response for each covariate were included in the regression model.

†Nonexposed defined as having a cotinine level <0.05 ng/mL, no self-report of smoking in the past 5 days, and no report of household members smoking in the house.

‡ETS as evidenced by serum cotinine level ≤15 ng/mL and no self-report of smoking in the past 5 days.

§Active smoking defined as cotinine level >15 ng/mL or self-report of smoking in the past 5 days.

in the development of the metabolic syndrome in youth from this one cross-sectional observational study, a plausible biological basis exists for this association. The fact that diverse and complex individual components of the metabolic syndrome (eg, abdominal obesity, hyperglycemia, and dyslipidemia) cluster together more often than would be expected by chance alone has long suggested that a common biological pathway might explain the frequent emergence of this constellation of risk factors.[31] There is evidence in studies of children to suggest that insulin resistance mediates the deleterious effects of excess adiposity on blood pressure and lipids in the metabolic syndrome and that insulin resistance operates independently of the degree of obesity.[33,34] Additionally, studies have shown that smoking is associated with increased insulin resistance in adults and may be a primary defect leading to endothelial dysfunction, abnormal lipid metabolism, and accelerated cardiovascular disease.[13,35,36] If this formulation is correct, then smoking and ETS exposure may be causally related to insulin resistance, which in turn may cause, contribute to, and/or trigger the metabolic abnormalities in overweight individuals that result in the metabolic syndrome. In the present study, there are lower rates of hyperglycemia in the exposed and active smoking groups. This finding is difficult to explain; however, fasting glucose has been shown to be highly insensitive for detecting diabetes compared with other methods of assessing insulin resistance such as glucose tolerance testing, insulin, proinsulin, or c peptide. Unfortunately, these other measures are not available

TABLE 5. Prevalence of the Metabolic Syndrome and its Components by Smoke Exposure Status for At-Risk or Overweight (BMI ≥85th Percentile) Adolescents, Unadjusted Data from NHANES III, 1988–1994

	Nonexposed* (n=65), %	ETS Exposed,† % (n=479)	Actively Smoking,‡ % (n=120)	Test for Trend *P*
Metabolic syndrome	5.6	19.6	23.6	0.01
Overweight (BMI ≥95th percentile)	23.8	32.3	40.4	0.08
High triglycerides (≥110 mg/dL)	17.1	40.2	51.6	<0.001
Low HDL (≤40 mg/dL)	16.7	37.8	52.3	<0.001
High fasting glucose (≥100 mg/dL)	11.6	14.1	9.6	0.19
High blood pressure (≥90th percentile)	17.6	9.8	6.2	0.01
High waist circumference (≥90th percentile)	28.3	32.9	47.3	0.001

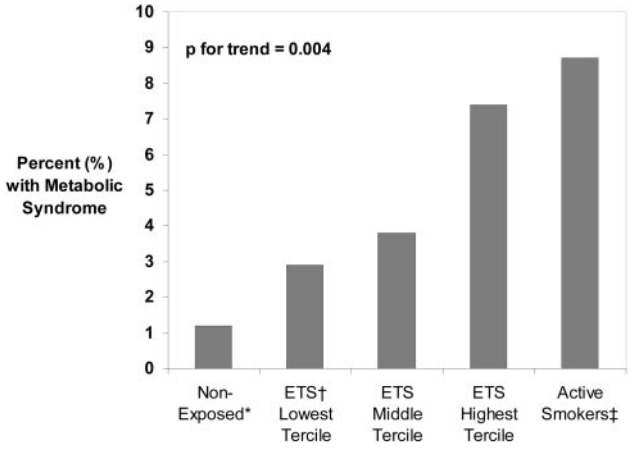
n=664.

*Nonexposed defined as having a cotinine level <0.05 ng/mL, no self-report of smoking in the past 5 days, and no report of household members smoking in the house.

†ETS as evidenced by serum cotinine level of ≤15 ng/mL and no self-report of smoking in the past 5 days.

‡Active smoking defined as cotinine level >15 ng/mL or self-report of smoking in the past 5 days.

in NHANES III. Because it is well accepted that insulin resistance is an underlying force driving the metabolic syndrome and its components, we can only state that we were unable to find a statistical difference related to hyperglycemia in the study population. Although hyperglycemia, the least common of the metabolic syndrome components, does not trend in the direction one might expect, one cannot discount the possibility that tobacco exposure plays a role in insulin resistance. An insulin resistance–centered model would also have significant clinical implications. Reaven and Tsao[36] have suggested that, given the difficulty of making behavior changes to alter both weight and smoking habits, drug therapy targeting insulin resistance might significantly enhance the ability of practitioners to clinically treat the adverse health effects of obesity and smoking.



Rates of occurrence of metabolic syndrome by active smoking or ETS with smokers in the home among adolescents 12 to 19 years of age in United States. Unadjusted data are from NHANES III, 1988 to 1994. n=1325. *Nonexposed defined as having cotinine level <0.05 ng/mL, no self-report of smoking in past 5 days, and no report of household members smoking in the house. †ETS as evidenced by serum cotinine level of ≤15 ng/mL, no self-report of smoking in past 5 days, and positive report of household members smoking in the house. ‡Active smoking defined as cotinine level >15 ng/mL or self-report of smoking in the past 5 days.

The findings reported here of both ETS exposure and active smoking being associated with decreased rates of hypertension are consistent with a number of studies in adults showing that active smoking is associated with decreased blood pressure.[37–40] The literature on passive exposure to ETS and blood pressure is still more limited and unclear, and we could find no prior published studies of either the association of ETS exposure or active smoking with blood pressure among adolescents.

These data also reveal pronounced differences in rates of the metabolic syndrome by gender and race, consistent with other studies.[7,41,42] These differences may at least in part be a consequence of a lack of a universally accepted definition of the metabolic syndrome in adolescents or, perhaps more importantly, of the differences across gender and race in the normal values for the various components of this syndrome. For example, there is evidence that white children have significantly higher serum triglyceride levels than black

TABLE 6. Association in Multivariable Analysis of Tobacco Use With Metabolic Syndrome Among Adolescents 12 to 19 Years of Age in the United States, NHANES III, 1988–1994*

	Odds Ratio	95% CI	*P*
Nonexposed† (referent)	1.0		
ETS‡ lowest tercile (≤0.540 ng/mL)	2.5	0.7–9.1	0.15
ETS middle tercile (0.541–1.35 ng/mL)	2.9	0.9–9.1	0.08
ETS highest tercile (1.36–15 ng/mL)	6.7	1.5–29.7	0.01
Active smokers§	6.9	3.4–14.4	<0.001

n=1109.

*Adolescents with a valid response for each covariate were included in the regression model. Results were adjusted for gender, age, race/ethnicity, poverty status, region, and parental history of diabetes and heart attack.

†Nonexposed defined as cotinine level <0.05 ng/mL, no self-report of smoking in the past 5 days, and no report of household members smoking in the house.

‡ETS as evidenced by serum cotinine level ≤15 ng/mL, no self-report of smoking in the past 5 days, and positive report of household members smoking in the house.

§Active smoking defined as cotinine level >15 ng/mL or self-report of smoking in the past 5 days.

children[43] and have a stronger correlation between weight and triglyceride concentrations.[44] Similarly, Weiss et al[7] found that use of race- and ethnicity-specific cutoff points for serum lipid levels might account for the differences between both the prevalence of the metabolic syndrome and the effect of obesity, among blacks versus whites and Hispanics.

Although NHANES III (1988 to 1994) data were used, there is no biologically plausible reason to believe that such an association would not exist today. More important limitations include the cross-sectional nature of the data, limiting causal inferences and the possibility that part or all of the observed associations between tobacco smoke exposure and increased rates of the metabolic syndrome are due to some unmeasured confounder or confounders. One such confounder may be physical activity, which is difficult to assess in this population using NHANES III because questions about physical activity were asked differently to children $<$16 years of age compared with children $>$16 years of age in this survey. Because, unlike in adults, the metabolic syndrome is found almost exclusively in youth at risk for overweight or overweight adolescents,[6] analyses for the association of tobacco exposure with the metabolic syndrome were investigated among those adolescents who were at risk for overweight or overweight. It is possible that even after adjustment for weight, adolescent smokers and those passively exposed to ETS may differ in diets, which may account for some of the associations found in the present study between the metabolic syndrome and tobacco exposure. Furthermore, it is difficult to tell whether those reporting active smoking with cotinine levels $<$15 ng/mL and those with cotinine levels $\geq$15 ng/mL were also exposed to ETS; thus, we cannot estimate the exclusive contribution of ETS exposure to the increased risk of the metabolic syndrome among those classified as active smokers. We also do not know every source of ETS exposure such as in public settings where ETS exposure could be reduced by bans on smoking. In an effort to correctly classify active smokers, a cotinine level of $>$15 ng/mL was used as a marker for active smoking. This level, previously used in the literature on ETS exposure,[24] is low enough to include infrequent smokers. Other studies use levels as high as 25 ng/mL[45]; thus, a more conservative measure was applied in the present study. In our analysis of dose response, we were not able to eliminate misclassification bias entirely. Adolescents who are actually smoking but deny smoking by self-report may still exist in the "ETS exposed" group. However, parents who do report presence of smokers in the household are likely to be telling the truth, yielding a group that is more enriched for true ETS exposure, as opposed to transient exposure in public locations or a misclassification of exposure based on the temporally dependent cotinine measure itself.[46] Therefore, by excluding those adolescents whose parents do not report the presence of other smokers in the home, we have probably reduced the number of adolescent active smokers who are lying about their use in our ETS exposed group. This differential reporting phenomenon probably is due to normative beliefs by the adolescent about what constitutes acceptable/reportable behavior in the context of smoking and nonsmoking households.[47]

In summary, this is the first study to demonstrate a dose-responsive, cotinine-confirmed relationship between tobacco smoke and the metabolic syndrome and the first that we are aware of to demonstrate any association between tobacco smoke and the metabolic syndrome in adolescents. Although there may be reason to celebrate decreasing rates of active and passive exposure to tobacco smoke, 1 in 5 adolescents are still actively smoking, and an additional two thirds of all adolescents are exposed to tobacco smoke as measured by biological markers. Exposure to tobacco smoke, whether by active or passive smoking, is associated with an $\approx$4-fold increase in the risk of the metabolic syndrome among adolescents who are overweight and at risk for overweight. Considering that tobacco and obesity are individually the 2 leading causes of preventable death in the United States, these findings may have profound implications for the future health of the public.

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