

# Predictors of Cotinine Levels in US Children\*

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## Data From the Third National Health and Nutrition Examination Survey

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**Study objective:** To determine what factors predict cotinine levels in US children.

**Design:** Cross-sectional study.

**Subjects:** Nationally representative sample of 5,653 US children, both with and without reported tobacco smoke exposure in their homes.

**Methods:** We stratified the children into those with reported passive smoke exposure at home and those without this exposure. We used regression models to predict the log of the cotinine level of the participants with the following independent covariates: age; race/ethnicity; number of rooms in the home; sex; parental education; family poverty index; family size; region; and, among children with reported passive smoke exposure, the number of cigarettes smoked in the home.

**Results:** Children exposed to passive smoke had a mean cotinine level of 1.66 ng/mL, and children not exposed to passive smoke had a mean level of 0.31 ng/mL. Among children with reported smoke exposure, non-Mexican-American race/ethnicity, young age, low number of rooms in the home, low parental education, and an increasing number of cigarettes smoked in the home were predictors of increased serum cotinine levels. Among children with no reported smoke exposure, significant predictors of increased cotinine levels included black race, young age, Midwest region of the United States, low number of rooms in the home, low parental education, large family size, and low family poverty index.

**Conclusion:** While the reported number of cigarettes smoked in the home is the most important predictor of cotinine levels in children exposed to smoke and may provide an opportunity for clinical intervention, other demographic factors are important among children both with and without reported smoke exposure.

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**Key words:** children; cotinine; tobacco smoke pollution

**Abbreviations:** ETS = environmental tobacco smoke; NHANES III = Third National Health and Nutrition Examination Survey

Tobacco smoke exposure is an important and preventable cause of morbidity among children. Recent comprehensive reviews by the California Environmental Protection Agency,<sup>1</sup> and by Cook and

Strachan<sup>2</sup> in *Thorax* have concluded that environmental tobacco smoke (ETS) increases respiratory symptoms and disease and decreases lung function in children.

Most studies that have examined the health effects of ETS on children have used reported ETS exposure or the presence of smokers in the child's household to define exposure.<sup>3-5</sup> A limitation of these studies is that many children in the United States with no reported smoke exposure have cotinine, a nicotine metabolite indicating recent ETS exposure, in their blood.<sup>6,7</sup> Although the widespread exposure of children to ETS has been described previously,<sup>6</sup> factors determining cotinine levels among children, including parental education, poverty status of the family, and region of the country, have not been fully explored.

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Our study analyzed data among children aged 4 through 16 years from the Third National Health and Nutrition Examination Survey (NHANES III), a nationally representative study of the US population. We determined what factors predicted cotinine levels in US children both with and without reported tobacco smoke exposure in their homes.

## MATERIALS AND METHODS

### Study Population

NHANES III was conducted from 1988 through 1994 by the National Center for Health Statistics of the Centers for Disease Control and Prevention, Atlanta, GA,<sup>8</sup> and was approved by the National Center for Health Statistics Institutional Review Board. In this survey, a stratified, multistage, clustered probability design was used to select a representative sample of the civilian, noninstitutionalized US population. A total of 81 geographic sites were included in the final sample. Survey participants completed extensive questionnaires about household characteristics and a comprehensive physical examination, including the drawing of blood at a specially equipped mobile examination center to determine serum cotinine levels. Questionnaires for participants who were < 17 years of age were completed by a knowledgeable adult proxy (usually a parent or caretaker). Children aged  $\geq 12$  years responded to questions about their personal use of tobacco.

### Subjects and Demographics

We limited our analysis to children aged 4 to 16 years for whom serum cotinine levels were obtained (cotinine levels were not obtained for children younger than 4 years old). In addition, we excluded children who reported either current smoking, based on self-report, or who had cotinine levels  $> 15$  ng/mL, indicating the possible current use of cigarettes or spit tobacco.<sup>6</sup>

### Variable Definition

We classified the race/ethnicity of the participants as "Non-Hispanic white," "Non-Hispanic black," "Mexican-American," or "Other," as determined by self-report on the questionnaire. We determined parental education level, which was classified as < 12 years or unknown, 12 years, or  $> 12$  years, using the reference adult in the family (*ie*, one of the persons who owns the home or pays the rent). Family poverty index was classified as either below or above the poverty index level of 1, or was unknown, for the family.<sup>8</sup> This index is determined on the basis of the family income and the number of people in the household. We classified family size as four members or fewer or as five members or more, the number of rooms in the home as five or fewer or six or more (including the kitchen but excluding bathrooms), and region of the country using standard census definitions (Northeast: CT, ME, MA, NH, NJ, NY, PA, RI, and VT; Midwest: IL, IN, IA, KS, MI, MN, MO, NB, ND, OH, SD, and WI; South: AL, AR, DE, DC, FL, GE, KY, LA, MD, MS, NC, OK, SC, TE, TX, VA, and WV; West: AK, AZ, CA, CO, HI, ID, MT, NV, NM, OR, UT, WA, and WY). For most analyses, we stratified participants into the following three age strata: 4 to 6 years; 7 to 11 years; and 12 to 16 years.

The respondent for each child was asked whether anyone living in the home smoked in the home. He or she was then asked to quantify how many cigarettes each smoker smoked in the home

in an average day. We used these data to determine the total number of cigarettes smoked in each home in a typical day, and divided the exposed children into the following six strata: 1 to 9 cigarettes; 10 to 19 cigarettes; 20 to 29 cigarettes; 30 to 39 cigarettes;  $\geq 40$  cigarettes; and unknown.

### Cotinine Levels

Serum cotinine levels were determined using high-performance liquid chromatography atmospheric-pressure chemical ionization tandem mass spectrometry, as described elsewhere.<sup>6</sup> We used an estimated level of 0.035 ng/mL (*ie*, the level of detection, 0.050 ng/mL, divided by the square root of 2) for subjects with no detectable cotinine level when calculating mean exposure levels in the study subjects. Because the cotinine levels were not normally distributed, we log-transformed the values before performing any analyses.

### Analysis

We calculated all estimates using the sampling weight to represent children aged 4 to 16 years in the United States. The purpose of the sampling weight is to provide population estimates that adjust for unequal probabilities of selection and that account for nonresponses. The weights were poststratified to the US population as estimated by the Bureau of the Census. For analyses, we used computer software (SAS; SAS Institute; Cary, NC<sup>9</sup>; and SUDAAN [a program that adjusts for complex sample design when variance estimates are calculated]; Research Triangle Institute; Research Triangle Park, NC<sup>10</sup>). We developed linear regression models adjusting for age, sex, race/ethnicity, education level, income status, family size, number of rooms in the home, and, for children with reported exposure, the number of cigarettes smoked in the home daily to predict the log-transformed cotinine values in both univariate and multivariate models. The models were evaluated for evidence of collinearity, interaction, and influential observations.

## RESULTS

Of the 13,944 children aged 2 months through 16 years who participated in NHANES III, 5,643 were < 4 years old. Of the remaining 8,301 children, 2,487 did not have their serum cotinine levels obtained (either because they did not have blood drawn or the blood sample volume was not sufficient for the analysis), an additional 156 either admitted to current smoking or had cotinine levels  $> 15$  ng/mL, and data on smoke exposure in the home were not reported for 5, leaving 5,653 children available for analysis. The 2,487 children who did not have cotinine obtained were similar to the 5,653 participants with regard to sex, race, parental education, family, poverty index, reported ETS exposure, and parental history of allergy or asthma ( $p > 0.05$  for all), but they were overrepresented in the youngest age group (4 to 6 years old, 52%; 7 to 11 years old, 21%; and 12 to 16 years old, 18%;  $p < 0.01$ ).

Of the 2,189 children with reported smoke exposure, the mean cotinine level was 1.66 ng/mL, and the geometric mean level was 1.00 ng/mL, with 0.9%

of these children having serum cotinine levels  $< 0.050$  ng/mL, which is the level of detection (Fig 1, *top, A*) Of the 3,464 children with no reported smoke exposure, the mean cotinine level was 0.31 ng/mL, and the geometric mean level was 0.12 ng/mL, with 24.4% of these children having serum cotinine levels  $< 0.050$  ng/mL, which is the level of detection (Fig 1, *bottom, B*).

Among children with reported smoke exposure, the significant predictors of cotinine levels in the univariate analyses included age, region, education

level of the responding adult, race/ethnicity, family poverty index, and the number of cigarettes smoked in the home (Table 1). Among the children without reported smoke exposure in the home, the same factors (with the exception of the number of cigarettes smoked daily in the home, which was excluded by definition) along with family size and the number of rooms in the home, were significant predictors of cotinine levels (Table 2). Most factors predicted cotinine levels similarly for children both with and without smoke exposure in the home. The only

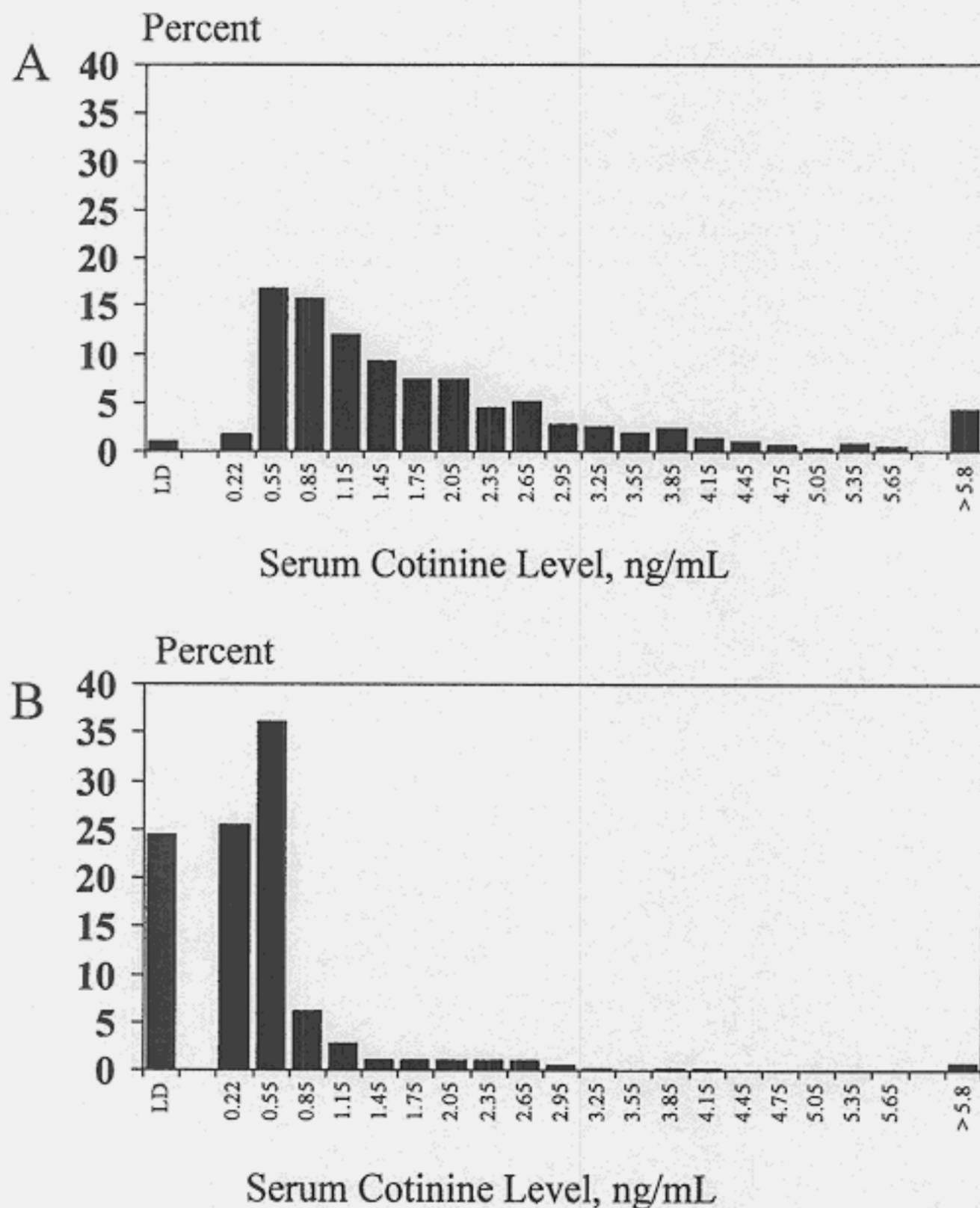


FIGURE 1. Serum cotinine concentrations in children with (*top, A*) and without (*bottom, B*) reported smoke exposure in the home. The values below the X axis represent the midpoint of the ranges of 0.3 ng/mL (eg, 0.85 = 0.71 to 1.00 ng/mL) with the exception the two lowest categories, for which LD represents all values less than the limit of detection and for which 0.22 is the midpoint of the range 0.050 to 0.4 ng/mL, and the highest category, which includes all values  $> 5.8$  ng/mL. Data from the NHANES III.

Table 1—Children With Reported Smoke Exposure in the Home\*

Category	n	Mean, ng/mL	Geometric Mean, ng/mL	F Value	p Value
Age, yr					
4-6	618	2.22	1.43	20.95	< 0.001
7-11	887	1.63	1.03		
12-16	684	1.41	0.80		
Sex					
Male	1,163	1.70	1.02	0.19	0.667
Female	1,026	1.63	0.98		
Region†					
Northeast	209	1.23	0.82	4.53	0.007
Midwest	444	1.97	1.19		
South	1,066	1.84	1.13		
West	470	1.18	0.68		
Parental education, yr					
< 12 or unknown	1,055	1.92	1.25	7.41	0.002
12	753	1.70	1.10		
> 12	381	1.32	0.68		
Race/ethnicity					
White	576	1.83	1.08	34.66	< 0.001
Black	890	1.75	1.20		
Mexican-American	634	0.87	0.47		
Other	89	0.98	0.72		
Family poverty index‡					
Below or at poverty line	939	1.96	1.28	4.75	0.013
Above poverty line	1,090	1.54	0.89		
Unknown	160	1.51	0.96		
Family size					
≤ 4	1,256	1.75	1.03	0.26	0.611
≥ 5	933	1.58	0.97		
Rooms in home					
≤ 5	519	1.83	1.20	2.54	0.117
≥ 6	1,670	1.63	0.96		
Cigarettes smoked in home					
Unknown	773	1.86	1.25	39.62	< 0.001
1-9	872	0.83	0.49		
10-19	276	1.73	1.23		
20-29	132	2.41	1.74		
30-39	41	2.78	2.05		
≥ 40	95	3.47	2.79		
Total	2,189	1.66	1.00		

\*From the NHANES III.

†States within each region are listed in the "Materials and Methods" section.

‡On the basis of family income and number of people living in household.

exception was with the variable age, in which the youngest children had the highest mean and geometric mean cotinine levels among smoke-exposed children, whereas children in the oldest age group (12 to 16 years) had the highest mean levels, but not the highest geometric mean levels, among unexposed children (Tables 1, 2).

In the multivariate analysis, significant predictors of cotinine levels among smoke-exposed children included age, education level of the responding adult, race/ethnicity, the number of rooms in the home, and the number of cigarettes smoked in the home (Table 3). The  $r^2$  value for this model was 0.36. Significant predictors of cotinine levels among unexposed children included age, region of the United

States, education level of the responding adult, race/ethnicity, the number of rooms in the home, family poverty index, and family size (Table 4). The  $r^2$  value for this model was 0.14. The  $r^2$  value for a model that included all children and set the number of cigarettes exposed to in the home to 0 for the unexposed children was 0.56 (results not shown).

## DISCUSSION

Most children in this sample, which is representative of the US population, have detectable levels of cotinine in their blood, reflecting exposure to tobacco smoke. Factors that predicted cotinine levels

Table 2—Children With No Reported Smoke Exposure in the Home\*

Category	n	Mean, ng/mL	Geometric Mean, ng/mL	F Value	p Value
Age, yr					
4-6	1,000	0.30	0.14	7.07	< 0.001
7-11	1,432	0.20	0.11		
12-16	1,032	0.43	0.13		
Sex					
Female	1,711	0.26	0.12	0.04	0.844
Male	1,753	0.35	0.12		
Region†					
Northeast	376	0.35	0.13	4.91	0.005
Midwest	545	0.38	0.14		
South	1,434	0.32	0.13		
West	1,109	0.23	0.10		
Parental education, yr					
< 12 or unknown	1,315	0.33	0.15	14.9	< 0.001
12	1,031	0.42	0.15		
> 12	1,118	0.24	0.10		
Race/ethnicity					
White	873	0.33	0.12	30.67	< 0.001
Black	1,020	0.43	0.22		
Mexican-American	1,388	0.18	0.09		
Other	183	0.19	0.10		
Family poverty index‡					
Below or at poverty line	1,181	0.48	0.18	11.32	< 0.001
Above poverty line	2,022	0.27	0.14		
Unknown	261	0.23	0.11		
Family size					
≤ 4	1,855	0.24	0.11	12.13	< 0.001
≥ 5	1,609	0.37	0.13		
Rooms in home					
≥ 5	921	0.53	0.19	22.01	< 0.001
≤ 6	2,543	0.28	0.11		
Total	3,464	0.31	0.12		

\*From the NHANES III.

†States within each region are listed in the "Materials and Methods" section.

‡On the basis of family income and number of people living in household.

were similar among children regardless of whether there was reported smoke exposure in the home, although the relative importance of the predictive factors in these two groups varied.

The age of the child was an important predictor of cotinine levels both in children exposed to smoke and in those not exposed to smoke, although the effects were in different directions in these two groups. In smoke-exposed children, the highest levels were among the youngest children; in the unexposed children, the older children had higher mean levels of cotinine, but not the highest geometric mean levels of cotinine (Tables 1, 2). Lower age has been consistently associated with higher cotinine levels among children with reported exposures.<sup>11,12</sup> Young children have higher cotinine levels than older children and adults, despite similar exposures, suggesting a higher relative nicotine dose,<sup>13</sup> or the possibility that they spend less time outdoors than older children. Younger children do not, however, appear to metabolize cotinine at a slower rate than

older children.<sup>14</sup> Our finding of higher mean cotinine levels among children 12 to 16 years old compared to those 7 to 11 years old among our subgroup of children with no reported smoke exposure in the home suggests that these children are being exposed to smoke from friends or other sources outside of the home.<sup>15</sup>

Among children with reported smoke exposure in the home, the average number of cigarettes smoked daily in the home was the best predictor of cotinine level. Although this is an expected finding, an interesting result was that children for whom the respondent could not estimate the number of cigarettes smoked daily in the home had cotinine levels suggesting that they were exposed to 10 to 20 cigarettes daily. Other researchers have found a similar relationship between cotinine levels and the number of cigarettes smoked in the home or the number of smokers in the home.<sup>11,12</sup>

Race/ethnicity is known to be associated with cotinine levels among active smokers, with blacks

**Table 3—Results of the Multivariate Linear Regression Model Predicting Change in Log Cotinine for Children With Reported Smoke Exposure in the Home \***

Category	Mean Increase in Log Cotinine, ng/mL	95% CI
Age, yr		
4-6	0.53	0.37 to 0.69
7-11	0.17	0.03 to 0.31
12-16	Referent	
Sex		
Male	-0.04	-0.16 to 0.08
Female	Referent	
Region†		
Northeast	-0.09	-0.35 to 0.17
Midwest	0.20	-0.10 to 0.50
South	0.16	-0.12 to 0.44
West	Referent	
Parental education, yr		
< 12 or unknown	0.39	0.21 to 0.58
12	0.32	0.20 to 0.44
> 12	Referent	
Race/ethnicity		
White	Referent	
Black	0.10	-0.06 to 0.26
Mexican-American	-0.73	-0.93 to -0.53
Other	-0.29	-0.61 to 0.03
Family poverty index‡		
Below or at poverty line	0.18	0.00 to 0.36
Above poverty line	Referent	
Unknown	0.14	-0.16 to 0.44
Family size		
≤ 4	0.02	-0.14 to 0.18
≥ 5	Referent	
Rooms in home		
≤ 5	0.27	0.07 to 0.47
≥ 6	Referent	
Cigarettes smoked in home		
Unknown	0.82	0.64 to 1.00
1-9	Referent	
10-19	0.86	0.62 to 1.10
20-29	1.14	0.86 to 1.32
30-39	1.33	0.87 to 1.79
≥ 40	1.55	1.25 to 1.85

\*From the NHANES III. CI = confidence interval.

†States within each region are listed in the "Materials and Methods" section.

‡On the basis of family income and number of people living in the household.

having higher levels than whites and Mexican-Americans.<sup>16,17</sup> This pattern is thought to be related to both an increased intake of nicotine from each cigarette and to decreased metabolism.<sup>17</sup> Among children exposed to ETS, the most likely explanation for the observed racial/ethnic difference is the slower metabolism of cotinine in blacks or the more rapid metabolism of cotinine in Mexican-Americans, although this hypothesis cannot be evaluated with this database.

Socioeconomic factors also are known to be related to cotinine levels. Parental education and fam-

**Table 4—Results of the Multivariate Linear Regression Model Predicting Log Cotinine Levels for Children With No Reported Smoke Exposure in the Home\***

Category	Mean Increase in Log Cotinine, ng/mL	95% CI
Age, yr		
4-6	0.07	-0.11 to 0.25
7-11	-0.20	-0.34 to -0.06
12-16	Referent	
Sex		
Female	-0.01	-0.13 to 0.11
Male	Referent	
Region†		
Northeast	0.19	-0.15 to 0.53
Midwest	0.36	0.18 to 0.54
South	0.09	-0.15 to 0.33
West	Referent	
Parental education, yr		
< 12 or unknown	0.37	0.17 to 0.57
12	0.23	0.05 to 0.41
> 12	Referent	
Race/ethnicity		
White	Referent	
Black	0.37	0.17 to 0.57
Mexican-American	-0.47	-0.63 to -0.31
Other	-0.31	-0.51 to -0.11
Family poverty index‡		
Below or at poverty line	0.37	0.13 to 0.61
Above poverty line	Referent	
Unknown	0.21	0.03 to 0.39
Family size		
≤ 4	-0.25	-0.37 to -0.13
≥ 5	Referent	
Rooms in home		
≤ 5	0.41	0.16 to 0.63
≥ 6	Referent	

\*From the NHANES III. See Table 3 for abbreviations not used in the text.

†States within each region are listed in the "Materials and Methods" section.

‡On the basis of family income and number of people living in the household.

ily income both may be indicators of the prevalence of smoking in the community in which the child lives and plays.<sup>11,12</sup> Housing characteristics also have been described previously<sup>12</sup> as being associated with cotinine levels, with smaller homes predicting higher levels among smoke-exposed children.

Finally, we found regional differences in cotinine levels. These were significant in the univariate models (Tables 1, 2) but remained significant only in the multivariate model among unexposed children for the differences between the Midwest and West. This finding may reflect differences in public smoking restrictions among states in the United States during the survey<sup>18</sup> or regional differences in housing characteristics.

These analyses and their interpretation are subject to limitations. The survey data all were reported by a

parent or caretaker of the child or by the child (for reported tobacco use) and were not verified. The survey asked about household smoking by people living in the home but not by visitors to the home. Children may spend time in more than one home, but in this survey the "primary" home was the only one asked about. Although the model for children exposed to smoke explained 36% of the variability in cotinine levels, the model for children not exposed to smoke explained only 14% of the variability, suggesting that other individual or societal factors, such as proximity of the children to the source of smoke or whether smoking was allowed in vehicles in which the children rode, may be important but could not be included in our models.

In conclusion, our findings from this nationally representative study of US children are that demographic factors such as age, race/ethnicity, poverty status, and region of the United States predict cotinine levels in children. The strongest predictor in smoke-exposed children was the reported number of cigarettes smoked in the home daily, which might offer clinicians an opportunity to interview parents about smoking in the home and to intervene. Even though parents may be able to reduce some sources of exposure, for example by eliminating smoking in the home, other factors are less amenable to parental intervention and would require community-level interventions, such as the limiting of smoking in public places.

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