Biomarker Evidence of Tobacco Smoke Exposure in Children Participating in Lead Screening

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Objectives. We assessed tobacco smoke exposure (TSE), defined according to detection of cotinine, in dried blood spots collected from children for lead screening.

Methods. Dried blood spots collected from a national sample of 1541 Black and White children and submitted to a commercial laboratory for lead analysis were analyzed for cotinine. We used an anonymous administrative data set including information on children's characteristics to conduct univariate and multivariate analyses.

Results. Cotinine was detected in 61% of dried blood spots; 17% of samples had cotinine levels above 3 nanograms per gram. Median cotinine levels were significantly higher among Black than White children (0.66 ng/g vs 0.30 ng/g) and among Medicaid recipients (0.94 ng/g vs < 0.3 ng/g). In multivariate analyses, significant increases in cotinine levels were associated with Black (vs White) race, older age, Medicaid coverage, higher state smoking rate, and higher average winter temperature. Detectable cotinine levels were significantly associated with higher lead levels.

Conclusions. TSE is highly prevalent among children undergoing lead screening, and exposure levels are greater among Black children and children on Medicaid. TSE may contribute to lead exposure. Concurrent lead screening and biological screening for TSE may be a feasible approach to increasing childhood TSE detection. (*Am J Public Health.* 2013;103:e54–e59. doi:10.2105/AJPH.2013.301315)

Tobacco smoke exposure (TSE) is responsible for an estimated 60 000 deaths per year among nonsmokers,[1] including more than 5000 deaths in children (3 times the number of deaths from all childhood cancers combined).[2,3] Notably, levels of cotinine—a metabolite of nicotine and a well-established biomarker of TSE levels—are highest in the youngest children and those below the poverty level.[4]

Screening for TSE is recommended at all pediatric visits[5] because of its important health consequences.[6,7] Although parent reports suggest that 24% of children are exposed to tobacco smoke, data from the National Health and Nutrition Examination Survey (NHANES) show a much higher rate: in 2008, 54% of children aged 3 to 11 years were exposed to TSE, determined by the presence of cotinine in urine or blood.[8,9] Parents may underreport childhood TSE because of lack of awareness, social desirability bias, or fear of consequences.[9] Requirements for parents to disclose their child's TSE are an important barrier to delivering interventions to help parents quit smoking and implement smoke-free policies for the home and car.

Extant childhood screening programs for lead—another environmental toxin—provide an obvious yet currently untapped opportunity to detect TSE by measuring biomarkers of tobacco exposure in children at well-child visits. The Centers for Disease Control and Prevention and the American Academy of Pediatrics recommend that all US children have blood lead concentrations measured at 1 and 2 years of age. Lead screening is a requirement for all Medicaid-eligible children and is now performed routinely in both high- and low-risk groups.[10–12] Because health care providers already screen children for lead exposure as part of their routine practice,[10] a similar tactic of measuring cotinine in children might institutionalize management of TSE in a comparable fashion. The detrimental health effects of lead exposure[10] and TSE[6] have been well described. Childhood exposure to these toxins is highly prevalent, and the likelihood of exposure is more common in children of lower socioeconomic status.[6,10]

No studies of which we are aware have demonstrated the feasibility of large-scale biological screening for TSE in very young children. We assessed rates of TSE (determined according to detection of cotinine) from an analysis of dried blood spots collected for lead screening from very young children (less than 48 months old), an age group generally excluded from population-based TSE biomarker surveys. We hypothesized that TSE would vary significantly according to race and Medicaid coverage. We also postulated that the level of cotinine in dried blood spots would be positively correlated with lead levels owing to shared socioeconomic risk factors for both of these environmental exposures and examined whether TSE might predict lead exposure in small children.

METHODS

In a cross-sectional study, we examined cotinine levels in dried blood spots and administrative data from a national sample of children whose blood had been collected in clinical settings and submitted for lead analysis to MEDTOX Laboratories, a commercial laboratory facility in St. Paul, Minnesota.

Study Design, Setting, and Data Sources

We requested discarded dried blood spots from MEDTOX Laboratories after lead analyses had been completed (dried blood spots are typically destroyed after a waiting period of approximately 2 weeks to determine whether test results require confirmation). We included an unselected series of dried blood spots collected during the months of November and December 2010 and January, February, June, and July 2011. Samples were collected from approximately equal numbers of Black and

TABLE 1—Results of Univariate Analysis of Cotinine Levels by Child Characteristics, Black and White Children With Lead Levels of ≤ 9 μg/dL: United States, 2011–2012

Characteristic	No. of Children	Cotinine Level, ng/g, Median (Range)	*P*
Race[a]			< .001[b]
Black	723	0.66 (< 0.3–35)	
White	815	0.30 (< 0.3–41)	
Age, mo[c]			< .001[d]
≤12	205	< 0.3 (< 0.3–24)	
13–24	665	0.49 (< 0.3–41)	
25–36	471	0.48 (< 0.3–28)	
>36	179	0.76 (< 0.3–34)	
Gender[e]			.728[b]
Female	747	0.46 (< 0.3–35)	
Male	768	0.51 (< 0.3–41)	
Collection month			.004[b]
June or July	525	0.59 (< 0.3–41)	
November, December, January, or February	1010	0.40 (< 0.3–34)	
State smoking rate, %[f]			< .001
≤ 17.5	319	< 0.3 (< 0.3–25)	
17.6–20.0	507	0.30 (< 0.3–41)	
20.1–22.5	483	0.72 (< 0.3–27)	
> 22.5	193	1.05 (< 0.3–34)	
Medicaid recipient			< .001[b]
No	954	< 0.3 (< 0.3–41)	
Yes	585	0.94 (< 0.3–34)	
Average winter temperature, °F[g]			< .001
< 32	562	< 0.3 (< 0.3–25)	
≥ 32	940	0.63 (< 0.3–41)	
Average summer temperature, °F[h]			< .001
< 74.9	746	0.30 (< 0.3–34)	
≥ 75	756	0.67 (< 0.3–41)	
Lead level, μg/dL[i]			< .001[d]
< 1	306	< 0.3 (< 0.3–34)	
1	611	0.37 (< 0.3–35)	
2	314	0.76 (< 0.3–26)	
3	161	0.92 (< 0.3–28)	
4	70	1.07 (< 0.3–22)	
5	34	1.36 (< 0.3–24)	
6	16	0.40 (< 0.3–41)	
7	13	0.97 (< 0.3–3)	
8	7	5.06 (< 0.3–11)	
9	7	0.97 (< 0.3–4)	
Total	1541	0.48 (< 0.3–41)	

[a]One child was of mixed race and was not included in the race breakdown, and data on race were missing for 2 children.
[b]Based on nonparametric Wilcoxon rank sum test.
[c]Data on age were missing for 21 children. Age ranged from 0.4–47.9 months.
[d]Derived from nonparametric Spearman correlation.
[e]Data on gender were missing for 26 children.
[f]The state smoking rate range is 9.8%–25.6%. The nonparametric correlation between cotinine and the state smoking prevalence is 0.23. Data on collection month were missing for 6 children.
[g]The average winter temperature range is 12.1–59.4 °F. The nonparametric correlation between cotinine and state winter temperature is 0.14. Data on average winter temperature were missing for 39 children.
[h]The average summer temperature range is 63.7–81.1 °F. The nonparametric correlation between cotinine and state summer temperature is 0.12. Data on average summer temperature were missing for 39 children.
[i]Data on lead level were missing for 2 children.

White children 7 to 48 months old whose lead levels were 9 micrograms per deciliter or less (n = 1541). In 1991, the Centers for Disease Control and Prevention established blood levels of 10 micrograms per deciliter or above as concentrations of concern in children.[13] Thus, we performed a separate analysis of dried blood spots from children of all races whose lead level was above 9 micrograms per deciliter (n = 118).

MEDTOX Laboratories supplied an anonymous administrative data set to accompany the dried blood spots. The data provided included the child's month of birth, race, gender, month of dried blood spot collection, first 3 digits of zip code of residence, Medicaid eligibility status, and lead level.

As a means of analyzing cotinine in dried blood spots, three 4.8-millimeter punches were extracted and then analyzed for cotinine levels (expressed in ng/g) via solid phase extraction, followed by liquid chromatography tandem mass spectrometry. This method of analyzing the presence of cotinine in dried blood spots has been demonstrated to be accurate and valid, and it correlates closely with plasma cotinine concentrations among both smokers and individuals exposed to secondhand smoke.[14] The lower limit of quantitation was 0.3 nanograms per gram. The MEDTOX Laboratories protocol for analyzing lead in dried blood spots is to remove a pair of 0.19-inch (0.48-cm) punches from the sample, solvate them in 3 milliliters of 5% nitric acid containing bismuth as an internal standard, and analyze them via inductively coupled plasma mass spectrometry.

Statistical Analysis

Cotinine levels measured from the dried blood spots were examined according to children's characteristics, including age in months, gender, race, Medicaid status, month of dried blood spot collection, average winter and average summer temperatures in the state of collection[15] (because weather conditions may influence the amount of time children spend indoors), state smoking prevalence,[16] and lead level. We used nonparametric methods in our univariate analysis of the influence of these variables on cotinine levels. Wilcoxon rank sum tests were conducted, and Spearman correlation coefficients were calculated.

A large proportion of cotinine levels in the dried blood spots fell below the lower limit of quantitation (39.5%). Thus, we used the Tobit model,[17] a parametric model for left-censored data that assumes a normally distributed error term, in our multivariate analysis. Cotinine (the response variable) had a log-normal distribution. We used maximum likelihood (Proc LIFEREG, SAS version 9.3, SAS Institute Inc, Cary, NC) to estimate the model regression parameters. The regression coefficients and confidence intervals (CIs) for the log-transformed biomarkers were exponentiated so that the results could be interpreted on their original scale as the ratios of the biomarker medians between levels of the risk factors.

Because the correlation between average winter and summer temperatures was very high ($r > .90$), only average winter temperature was selected for the regression model. We included all other variables in the multivariate model with the exception of lead because of the possibility that lead exposure might be a consequence of TSE.[18]

In a separate Tobit analysis with lead levels of 9 micrograms per deciliter or less as the dependent variable, the same child characteristics were used as the covariates in addition to cotinine as a categorical variable (above or not above the limit of detection). We evaluated 2-way interactions between all significant main effects. *P* values less than .05 were considered statistically significant.

RESULTS

The 1541 dried blood spots came from 37 states, with representation from all US regions. Overall, detectable levels of cotinine (> 0.3 ng/g) were quantified in 61% (932 of 1541) of the dried blood spots analyzed; 17% of samples had cotinine levels above 3 nanograms per gram (equivalent to approximately 2 ng/mL plasma, roughly the 90th percentile for children aged 3–11 years according to 2008 NHANES data[19]). The median level was 0.48 nanograms per gram, and levels ranged from less than 0.3 nanograms per gram to 41 nanograms per gram.

Results of the univariate analyses are shown in Table 1. Median cotinine levels were higher in Black children than White children (0.66 ng/g vs 0.30 ng/g; $P < .001$) and higher in children on Medicaid than those not on Medicaid (0.94 ng/g vs < 0.3 ng/g; $P < .001$). There were small but significant associations between cotinine level and age ($P < .001$), month of dried blood spot collection ($P = .004$), state smoking rate ($r = 0.23$; $P < .001$), average winter temperature ($r = 0.14$; $P < .001$), average summer temperature ($r = 0.12$; $P < .001$), and lead level ($P < .001$). There were no significant differences between male and female children. Among children with lead levels of 9 micrograms per deciliter or higher (analyzed separately), the correlation with cotinine was not significant ($r = -0.08$, $P = .37$).

After adjustment for covariates, multivariate analyses showed that median cotinine ratios were significantly greater than 1.0 for Black (vs White) children, older children, children with (vs without) Medicaid coverage, states with a higher smoking rate, and higher average winter temperatures (Table 2). However, because the model revealed significant interactions between race and age and between race and Medicaid status, we conducted a separate multivariate analysis of cotinine levels among Black children and White children (Table 3).

The results of this multivariate analysis showed no significant predictors of cotinine level among Black children. Among White children, however, median cotinine levels were significantly higher for a 6-month increase in age (cotinine ratio = 1.16; 95% CI = 1.07, 1.27; $P = .001$) and for Medicaid recipients (cotinine ratio = 3.32; 95% CI = 2.35, 4.70; $P < .001$). Also, there were significant effects among White children for state smoking rates ($P < .001$), average winter temperatures ($P = .019$), and the interaction between these 2 variables ($P = .016$). Specifically, the impact of increased smoking rates on elevated cotinine levels was greater in colder states than in warmer states (Table 3).

In a separate multivariate model, we found that the following variables were significant predictors of median lead levels: 6-month increase in age (lead ratio = 1.07, 95% CI = 1.05, 1.09; $P < .001$), female gender (lead ratio = 0.92; 95% CI = 0.86, 0.98; $P = .013$), summer collection month (vs collection in other months of the year; lead ratio = 1.20; 95% CI = 1.11, 1.31; $P < .001$), and detectable cotinine (vs cotinine below the lower limit of quantitation; lead ratio = 1.21; 95% CI = 1.13, 1.30; $P < .001$; Table 4). There were no significant 2-way interactions between the significant main effects.

DISCUSSION

Our analysis documents that more than half of children (61%) who undergo lead screening have been exposed to tobacco smoke, as indicated by measurable cotinine levels in dried blood spots. The level of exposure was significantly higher among Black than White children, among children on Medicaid versus those

TABLE 2—Estimated Cotinine Ratios by Child Characteristics, Black and White Children With Lead Levels of ≤ 9 µg/dL: United States, 2011–2012

Variable	Cotinine Ratio (95% CI)
Black race	3.06 (1.91, 4.89)
Age: 6-mo increase	1.16 (1.07, 1.26)
Female gender	1.03 (0.85, 1.24)
Summer month of collection	1.05 (0.83, 1.32)
Medicaid recipient	3.38 (2.50, 4.55)
State smoking rate: 1% increase	1.56 (1.34, 1.82)
State average winter temperature: 1°F increase	1.18 (1.09, 1.26)
Black race × age interaction	0.88 (0.79, 0.98)
Black race × Medicaid interaction	0.39 (0.27, 0.58)
Smoking rate × winter temperature interaction	0.99 (0.99, 1.00)

Note. CI = confidence interval. Data were derived from a multivariate analysis with left censored data. Dried blood spots for which any of the corresponding child characteristics were missing were excluded from this analysis (n = 81). The sample size was n = 1460.

TABLE 3—Race-Specific Estimated Cotinine Ratios by Child Characteristics, Black and White Children With Lead Levels ≤ 9 μg/dL: United States, 2011–2012

Variable	Cotinine Ratio (95% CI)
Black children (n = 681)	
Age: 6-mo increase	1.03 (0.96, 1.10)
Female gender	1.13 (0.88, 1.45)
Summer month of collection	0.99 (0.77, 1.28)
Medicaid recipient	1.27 (0.92, 1.75)
State smoking rate: 1% increase	1.04 (0.98, 1.11)
State average winter temperature: 1°F increase	1.00 (0.99, 1.01)
White children (n = 779)	
Age: 6-mo increase	1.16 (1.07, 1.27)
Female gender	0.92 (0.69, 1.21)
Summer month of collection	1.21 (0.76, 1.92)
Medicaid recipient	3.32 (2.35, 4.70)
State smoking rate: 1% increase	1.52 (1.24, 1.87)
State average winter temperature: 1° increase	1.14 (1.02, 1.27)
Smoking rate × winter temperature interaction	0.99 (0.99, 100)

Note. CI = confidence interval. Data were derived from a multivariate analysis with left censored data. Dried blood spots for which any of the corresponding child characteristics were missing were excluded from this analysis (n = 81). The sample size was n = 1460.

not on Medicaid, and among children living in states with a higher prevalence of smoking. Although there were no significant predictors of cotinine levels among Black children, older age, Medicaid coverage, higher state smoking rate, and colder average winter temperature predicted elevated cotinine levels among Whites. There was a significant correlation between lead and cotinine among children with lead levels below 9 micrograms per deciliter but not among children with higher lead levels.

The TSE levels that we measured in children younger than 48 months were comparable to levels in the top 90th percentile of children aged 3 to 11 years surveyed for NHANES during 2006 to 2008.[4] The cohort for our study was unique in that it was clinic based and included children younger than those involved in previously reported TSE studies. Another recent study collected cotinine and lead data from 496 infants and children receiving preventive care at pediatrics clinics in California, and the results showed measurable cotinine in 55% of the sample but no correlation with lead levels.[20] However, blood lead levels in that smaller study were low relative to those found in our study and to national exposure data; only 70 of the 496 participants had lead levels of 2 micrograms per deciliter or above.

Consistent with studies of older children,[4,21] we observed dramatic differences in the prevalence and level of TSE between Black and White children. The higher prevalence of TSE in Black than White children might be explained by socioeconomic factors not fully captured by Medicaid status. Another possibility is differences in nicotine metabolism between Black and White children, as suggested in other studies.[18]

The correlation of lead levels with cotinine at lower lead concentrations suggests that TSE is a significant source of lead exposure in young children. Tobacco and tobacco smoke contain lead, which comes from environmental lead contaminating tobacco plants, and several studies have reported a significant correlation between TSE and blood lead levels.[18,22–26] Children in the highest quartile of serum cotinine levels who participated in NHANES from 1998 to 1994 and from 1999 to 2004 had significantly higher blood lead levels than those in the lower cotinine quartiles.[18,23] These data and the data from our study suggest that elimination of TSE among young children might reduce lead exposures. The lack of a correlation between cotinine and lead among children with high lead levels suggests that other environmental sources of lead are dominant in these children, masking the relationship of lead to TSE.

Limitations

This cross-sectional study involved several limitations. The sample was not random, and because children of other races were not included, it is impossible to fully document the prevalence of TSE in children who undergo lead screening. Despite the recommendation that lead screening be universally implemented, children of lower socioeconomic status are probably more likely to be

TABLE 4—Estimated Lead Ratios by Child Characteristics, Black and White Children With Lead Levels of 9 μg/dL or Below: United States, 2011–2012 (n = 1460)

Variable	Lead Ratio (95% Confidence Interval)
Black race	1.06 (0.97, 1.15)
Age: 6-mo increase	1.07 (1.05, 1.09)
Female gender	0.92 (0.86, 0.98)
Summer month of collection	1.20 (1.11, 1.31)
Medicaid recipient	1.04 (0.96, 1.13)
State smoking rate: 1% increase	1.00 (0.98, 1.02)
State average winter temperature: 1° increase	1.00 (1.00, 1.01)
Cotinine level ≥ 0.3 ng/g	1.21 (1.13, 1.30)

Note. Data were derived from a multivariate analysis with left censored data. Dried blood spots for which any of the corresponding child characteristics were missing were excluded from this analysis (n = 81).

screened because of their higher-than-average risk of exposure. The TSE detection limit of 0.3 nanograms per gram is well above that associated with childhood health effects.[27] A cotinine test would therefore be most useful as a screening tool to identify children at highest TSE risk, to identify unknown exposure sources, and to motivate and direct cessation support for those who smoke and need assistance in quitting.

Nevertheless, our experience using extant dried blood spots in biological screening for TSE suggests the feasibility of implementing routine screening at well-child visits. Tanski et al. have reported on a series of national surveys that describe current practices and provider and parent attitudes toward childhood screening and subsequent interventions targeting tobacco use and exposure.[28] In one national survey of 477 parents, 60% believed that children should be tested for TSE at their doctor visit. Among the parental smokers sampled, 62% believed that children should be tested. Majority support for testing persisted across all sociodemographic, geographic, and practitioner categories. Also, 74% of parents who smoked and 70% those who did not would accept testing if it was added to an existing blood test.[29]

Future Directions

Potential clinical applications of our findings include the possibility of coupling cotinine screening with lead and hemoglobin screening at 12- or 24-month visits as a means of accurately identifying children with TSE rather than relying on parents' reports. This practice would be backed by the considerable infrastructure that exists to support existing screening practices, including blood draws and remediation for abnormal values. Screening results could be applied to direct interventions targeting children at high risk of health consequences from TSE. Such interventions should include recommendations to implement strict smoke-free home and car policies and comprehensive tobacco treatment of parents who smoke, including behavioral and pharmacological therapy. This might be accomplished through pediatric practices, referral of parents to their primary care providers, or referrals to other existing tobacco treatment services such as quit lines.

Collection of biomarker data from a child might personalize the risks of tobacco use and increase parents' motivation to participate in tobacco treatment, as well as increasing their success rates. Another possibility is screening newborns for tobacco exposure at birth because this practice would identify populations at high risk for continuing exposure. In either case, parents might be motivated to take part in tobacco treatment if the risk of TSE is personalized through laboratory evidence of exposure in their own child. ■

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Contributors

A. Joseph jointly designed the study with L. Spector and S. Murphy, obtained and interpreted the cotinine and lead data, and contributed to writing the article. L. Spector interpreted the data and edited the article. K. Wickham performed cotinine analyses, interpreted data, and edited the article. G. Janis supervised the conduct of lead analyses and edited the article. J. Winickoff contributed to the study design, interpreted data, and edited the article. B. Lindgren contributed to the study design, conducted statistical analyses, and contributed to writing the article. S. Murphy analyzed the cotinine data, interpreted the lead and cotinine data, and contributed to writing the article.

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Human Participant Protection

This study was approved by the University of Minnesota institutional review board. The requirement for informed consent was waived because all of the data were anonymous.

References

1. Glantz SA, Parmley WW. Passive smoking and heart disease: mechanisms and risk. *JAMA.* 1995;273(13):1047–1053.

2. *Cancer Facts and Figures 2004.* Atlanta, GA: American Cancer Society; 2004.

3. Aligne CA, Stoddard JJ. Tobacco and children: an economic evaluation of the medical effects of parental smoking. *Arch Pediatr Adolesc Med.* 1997;151(7):648–653.

4. Centers for Disease Control and Prevention. Vital signs: nonsmokers' exposure to secondhand smoke—United States, 1999–2008. *MMWR Morb Mortal Wkly Rep.* 2010;59(35):1141–1146.

5. Winickoff JP, Berkowitz AB, Brooks K, et al. State-of-the-art interventions for office-based parental tobacco control. *Pediatrics.* 2005;115(3):750–760.

6. *Children and Secondhand Smoke Exposure.* Atlanta, GA: Centers for Disease Control and Prevention; 2007.

7. Burke H, Leonardi-Bee J, Hashim A, et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics.* 2012;129(4):735–744.

8. Centers for Disease Control and Prevention. Disparities in secondhand smoke exposure—United States, 1988–1994 and 1999–2004. *MMWR Morb Mortal Wkly Rep.* 2008;57(27):744–747.

9. Winickoff JP, Joseph A. Toward a population free of tobacco smoke exposure. *Arch Pediatr Adolesc Med.* 2012;166(9):871–872.

10. American Academy of Pediatrics. Lead exposure in children: prevention, detection, and management. *Pediatrics.* 2005;116(4):1036–1046.

11. Advisory Committee on Childhood Lead Poisoning Prevention. Recommendations for blood lead screening of young children enrolled in Medicaid: targeting a group at high risk. *MMWR Recomm Rep.* 2000;49(RR-14):1–13.

12. Wengrovitz AM, Brown MJ. Recommendations for blood lead screening of Medicaid-eligible children aged 1–5 years: an updated approach to targeting a group at high risk. *MMWR Recomm Rep.* 2009;58(RR-9):1–11.

13. Centers for Disease Control and Prevention. CDC response to Advisory Committee on Childhood Lead Poisoning Prevention recommendations in "Low level lead exposure harms children: a renewed call of primary prevention." Available at: http://www.cdc.gov/nceh/lead/acclpp/cdc_response_lead_exposure_recs.pdf. Accessed July 27, 2013.

14. Murphy SE, Wickham KM, Lindgren BR, Spector LG, Joseph AM. Cotinine and trans 3'-hydroxycotinine in dried blood spots as biomarkers of tobacco exposure and nicotine metabolism. *J Expo Sci Environ Epidemiol.* 2013;23(5):513–518.

15. National Oceanic and Atmospheric Administration. Average mean temperature index by month. Available at: http://www.esrl.noaa.gov/psd/data/usclimate/tmp.state.19712000.climo. Accessed July 27, 2013.

16. Centers for Disease Control and Prevention. State-specific prevalence of cigarette smoking and smokeless tobacco use among adults—United States, 2009. *MMWR Morb Mortal Wkly Rep.* 2010;59(43):1400–1406.

17. Tobin J. Estimation of relationships for limited dependent variables. *Econometrica.* 1958;26(1):24–36.

18. Apostolou A, Garcia-Esquinas E, Fadrowski JJ, McLain P, Weaver VM, Navas-Acien A. Secondhand tobacco smoke: a source of lead exposure in US children and adolescents. *Am J Public Health.* 2012;102(4):714–722.

19. Environmental Protection Agency. Report on the environment: blood cotinine level. Available at: http://cfpub.epa.gov/eroe/index.cfm?fuseaction=detail.viewInd&lv=list.listByAlpha&r=223968&subtop=208. Accessed July 27, 2013.

20. Dempsey DA, Meyers MJ, Oh SS, et al. Determination of tobacco smoke exposure by plasma cotinine levels in infants and children attending urban public hospital clinics. *Arch Pediatr Adolesc Med.* 2012;166(9):851–856.

21. Marano C, Schober SE, Brody DJ, Zhang C. Secondhand tobacco smoke exposure among children and adolescents: United States, 2003–2006. *Pediatrics.* 2009;124(5):1299–1305.

22. Mannino DM, Homa DM, Matte T, Hernandez-Avila M. Active and passive smoking and blood lead levels in U. S. adults: data from the Third National Health and Nutrition Examination Survey. *Nicotine Tob Res.* 2005;7(4):557–564.

23. Mannino DM, Albalak R, Grosse S, Repace J. Second-hand smoke exposure and blood lead levels in U. S. children. *Epidemiology.* 2003;14(6):719–727.

24. Lee MG, Chun OK, Song WO. Determinants of the blood lead level of US women of reproductive age. *J Am Coll Nutr.* 2005;24(1):1–9.

25. Menezes-Filho JA, Viana GF, Paes CR. Determinants of lead exposure in children on the outskirts of Salvador, Brazil. *Environ Monit Assess.* 2012;184(4):2593–2603.

26. Yoshinaga J, Takagi M, Yamasaki K, Tamiya S, Watanabe C, Kaji M. Blood lead levels of contemporary Japanese children. *Environ Health Prev Med.* 2012;17(1):27–33.

27. Yolton K, Dietrich K, Auinger P, Lanphear BP, Hornung R. Exposure to environmental tobacco smoke and cognitive abilities among U.S. children and adolescents. *Environ Health Perspect.* 2005;113(1):98–103.

28. Tanski SE, Klein JD, Winickoff JP, Auinger P, Weitzman M. Tobacco counseling at well-child and tobacco-influenced illness visits: opportunities for improvement. *Pediatrics.* 2003;111(2):E162–E167.

29. Winickoff JP, Tanski SE, McMillen RC, et al. Acceptability of testing children for tobacco-smoke exposure: a national parent survey. *Pediatrics.* 2011;127(4):628–634.