Cotinine in Children Admitted for Asthma and Readmission

AUTHORS: Judie A. Howrylak, MD, PhD,[a] Adam J. Spanier, MD, PhD, MPH,[b] Bin Huang, PhD,[c] Roy W. A. Peake, PhD,[d] Mark D. Kellogg, PhD,[d] Hadley Sauers, MPH,[c] and Robert S. Kahn, MD, MPH[c]

[a]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, and [b]Department of Pediatrics, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania; [c]Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; and [d]Clinical Epidemiologic Research Laboratory, Boston Children's Hospital, Boston, Massachusetts

KEY WORDS
tobacco smoke exposure, parental smoking, pediatrics, secondhand smoke, asthma, hospital readmission

ABBREVIATIONS
CCHMC—Cincinnati Children's Hospital Medical Center
CI—confidence interval
LOD—limit of detection

Drs Howrylak and Spanier conceived and designed the research, performed the data analysis, and drafted the initial manuscript; Dr Huang performed the data analysis and provided critical feedback; Drs Peake and Kellogg developed and performed the laboratory assays and contributed critical feedback; Mr Sauers recruited study participants and obtained consent and drafted the initial manuscript; Dr Kahn conceived and designed the study, edited all manuscript drafts, and provided critical feedback; and all authors approved the final manuscript as submitted.

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Address correspondence to Robert S. Kahn, MD, MPH, Division of General and Community Pediatrics, Department of Pediatrics, Cincinnati Children's Hospital, 3333 Burnet Ave, Cincinnati, OH 45229. E-mail: robert.kahn@cchmc.org

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WHAT'S KNOWN ON THIS SUBJECT: Serum and salivary cotinine have previously been identified as reliable biomarkers for exposure to tobacco smoke.

WHAT THIS STUDY ADDS: We found that detectable serum and salivary cotinine is common among children admitted for asthma and is associated with readmission. This finding may inform clinical care for children at increased risk of asthma morbidity.

abstract

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OBJECTIVE: To explore the relationship between tobacco smoke exposure (reported versus biomarker) and rates of readmission for children hospitalized for asthma.

METHODS: We enrolled a prospective cohort of 774 children aged 1 to 16 years admitted for asthma or bronchodilator-responsive wheezing. The primary outcome was at least 1 asthma- or wheeze-related readmission within 1 year. Caregivers reported any tobacco exposure at home, in a secondary residence, or in the car. We measured serum and saliva cotinine levels with mass spectrometry. We used logistic regression to evaluate associations between tobacco exposure and readmissions.

RESULTS: A total of 619 children had complete tobacco exposure data; 57% were African American and 76% had Medicaid. Seventeen percent of children were readmitted within 1 year. Tobacco exposure rates were 35.1%, 56.1%, and 79.6% by report, serum, and saliva measures, respectively. Caregiver report of any tobacco exposure was not associated with readmission (adjusted odds ratio: 1.18; 95% confidence interval: 0.79–1.89), but having detectable serum or salivary cotinine was associated with increased odds of readmission (adjusted odds ratio [95% confidence interval]: 1.59 [1.02–2.48] and 2.35 [1.22–4.55], respectively). Among children whose caregivers reported no tobacco exposure, 39.1% had detectable serum cotinine and 69.9% had detectable salivary cotinine. Of the children with reported exposure, 87.6% had detectable serum cotinine and 97.7% had detectable salivary cotinine.

CONCLUSIONS: Detectable serum and salivary cotinine levels were common among children admitted for asthma and were associated with readmission, whereas caregiver report of tobacco exposure was not. *Pediatrics* 2014;133:e355–e362

In children, asthma represents a significant burden, both in terms of increased rates of health care spending as well as the economic impact of days of missed school and work. There is evidence that tobacco exposure has a detrimental effect on airflow and airway responsiveness in children[1–7] and leads to poor asthma control.[8–12] For this reason, obtaining information about tobacco exposure could allow clinicians to distinguish which children might be at increased risk of future asthma exacerbations and to define a group who would benefit from interventions to decrease tobacco exposure.

The best method to assess secondhand smoke exposure is unclear. Obtaining a detailed history from the primary caregiver regarding levels of tobacco exposure is a straightforward approach and has shown a modest association with asthma control.[12] However, when compared with objective measures of exposure, the reliance on report of exposure may misclassify child exposure in outpatient settings.[13,14] Although the relationship between self-reported and cotinine-assessed smoking status has been studied,[15] to our knowledge no studies have explored this relationship in a pediatric inpatient setting, where the bias to underreport secondhand smoke exposure could be particularly strong.

Our objectives were to assess the prevalence of tobacco smoke exposure in a cohort of children admitted for wheezing or asthma and to explore the relationship between tobacco smoke exposure (reported versus biomarker) and readmission rates.

METHODS

Study Design and Population

We evaluated a prospective observational cohort, the Greater Cincinnati Asthma Risk Study, which has been described previously.[16] Briefly, this study enrolled 774 children, aged 1 to 16 years, admitted between August 2010 and October 2011 to Cincinnati Children's Hospital Medical Center (CCHMC), an urban, tertiary care, pediatric stand-alone hospital. Patients were identified by use of the evidence-based clinical pathway for acute asthma or bronchodilator-responsive wheezing (used in children for whom the diagnosis of asthma has not yet been made). The CCHMC Institutional Review Board approved this study.

A random 25% subsample of the 774 enrolled children were contacted by telephone ~12 months after the index admission to assess rates of potential loss to follow-up and admission to sites other than CCHMC. If staff were unable to complete the call, the participant's current home address was identified by using the electronic medical record and public records. A total of 95.9% of the random subsample were confirmed as having maintained residence in CCHMC's primary service area. Of those reached by telephone (84%), none reported an admission for asthma to a hospital other than CCHMC during the follow-up period. Data indicate that CCHMC receives >85% of admissions in our 8-county service area, making the chances of rehospitalization at an alternate hospital unlikely.

Primary Outcome

Our primary outcome, readmission to the hospital within 12 months of enrollment, was captured by using the International Classification of Diseases, Ninth Revision, Clinical Modification, classification codes of primary or secondary discharge diagnoses (493.XX or 786.07 for asthma or wheeze, respectively) recorded in hospital billing data. Outcome accuracy was verified by review of the electronic medical record to ensure that each readmission event met the same inclusion and exclusion criteria as the index admission.

Exposure Assessment

At the time of enrollment, we assessed reported tobacco exposure through interviews conducted with the primary caregiver in which we asked "Does anyone smoke inside your home?" We also asked the caregiver whether the child slept away from the home, and if so, "Does anyone smoke inside that home?" To assess smoking in the car, we asked the parent/guardian to describe the situation regarding smoking in the car with 4 response options: (1) there is no smoking inside the car, (2) smoking only occurs in the car when the child is not inside, (3) smoking is allowed in the car, or (4) do not have a car. An answer of "yes" to the statement "Smoking is allowed in the car" was considered as evidence of exposure in the car. We also ran a sensitivity analysis including smoking only when the child was not inside.

Trained nurses collected serum and saliva specimens from patients during the index admission. We collected serum either through venipuncture or through an existing intravenous line. We processed, froze, and shipped in batches the serum to an offsite laboratory. We collected saliva on a cotton swab (Salimetrics, State College, PA), and the saliva was then centrifuged, frozen, and batch shipped to the same location. We collected samples as soon as possible after admission (median of 22.8 hours; interquartile range: 16.8–33.12 hours). We measured cotinine, a metabolite of nicotine, in these specimens. Analysis of serum and salivary cotinine levels was performed at Boston Children's Hospital by liquid chromatography tandem mass spectrometry by using an Acquity Ultraperformance LC system coupled to a Quattro Premier triple quadropole tandem mass spectrometer (Waters Corporation, Milford, MA). This method was validated in accordance with US Food and Drug Administration guidance on bioanalytic assay validation.[17] The serum and salivary cotinine assays achieved sensitivities of 100 and 50 pg/mL, respectively. These values served as the lowest detectable cotinine concentrations where the respective assays performed with

acceptable reproducibility (<20% total precision).[17] We evaluated these measurements as dichotomous (detectable/not detectable) variables with values either above or below the limit of detection (LOD) to make them comparable to the reported exposure variable.

Covariates

Trained research assistants administered surveys at the time of enrollment. Surveys assessed demographic characteristics, such as age, gender, and race (categorized as white, African American, multiracial, or other). We also collected information on the education of the primary caregiver and annual household income. To characterize children with more persistent asthma, we also considered reported use of an asthma controller medication before admission. Our questionnaire did not specify the type of controller medication (eg, inhaled corticosteroid or leukotriene inhibitor or other).

Statistical Analysis

Subjects with complete exposure data (n = 619) comprised the analytic sample. We used t tests and χ^2 tests to make comparisons between children with and without complete exposure data. We calculated counts and percentages or arithmetic means and SDs for all variables measured.

We compared percentages of subjects with detectable levels of serum and salivary cotinine across several demographic characteristics by using the χ^2 test. Due to potential correlation with the outcome of interest, we also examined the relationship between selected covariates and hospital readmission in bivariate analyses. To evaluate the agreement between caregiver reports of secondhand smoke exposure and measured cotinine levels, we performed bivariate analyses.

We first conducted unadjusted logistic regression analysis to evaluate the association of secondhand smoke exposure measures and potential covariates with hospital readmissions. We then conducted a multivariable analysis considering potential covariates. In the initial multivariable model, we included covariates that had a P value <.05 in univariable analysis. We used backward elimination techniques for variable reduction. Covariates were retained in the analysis when they were significant or when removal caused a >10% change in the estimate for secondhand smoke exposure. In all analyses, we included a variable for the timing of sample collection to account for the metabolism of nicotine byproducts. Finally, we conducted a post hoc analysis focused on children with detectable saliva cotinine to look for evidence of a dose-response relationship between saliva cotinine and readmission. We also assessed for potential effect modification by age (≤6 or >6 years), given that the definition of asthma becomes clearer as children age. We used R version 2.15.2 (www.r-project.org) for all data analyses.

RESULTS

Characteristics of Study Subjects

Complete data were available for 619 of the 774 (80%) study participants. Participants with complete exposure data were somewhat older than those with incomplete data (Table 1). Of those with complete data, a majority of the participants were African American (57.4%), had an annual income <$60 000 (81.6%), and had less than a 4-year college degree (86.2%) (Table 1). A minority of caregivers reported the use of any type of asthma controller medication in these children before admission. There was an increased rate of readmission among participants with incomplete data compared with those with complete data (Table 1).

Thirty-five percent of caregivers reported that their children had any reported tobacco exposure, with 23.7% of caregivers reporting exposure in the primary residence, 12.0% reporting exposure in the secondary residence, and 12.3% reporting exposure in the car. Conversely, a majority of children had serum and salivary cotinine levels above the LOD (56.1% and 79.6%, respectively).

Demographic Characteristics and Serum and Salivary Cotinine Levels

The percentage of children with detectable cotinine varied significantly by sociodemographic status. African American children had the highest rates of detectable serum (61.1%) and salivary (86.8%) cotinine (Table 2). There was also a significant inverse relationship between annual household income and detectable cotinine; 71.9% of children in households reporting an annual income of <$15 000 had detectable serum cotinine compared with 11.4% of children with household incomes >$90 000. A similar inverse relationship was observed between caregiver education and cotinine levels. Rates of detectable cotinine did not differ by gender or reported asthma controller medication use.

Reported Versus Measured Tobacco Exposure

There was a discrepancy between reports of tobacco exposure and biomarker measurements of tobacco exposure. Of the children with any reported exposure to secondhand smoke, 87.6% had detectable serum cotinine levels and 97.7% had detectable salivary cotinine levels (Table 2). However, among children whose caregivers reported no exposure to secondhand smoke, 39.1% had detectable serum cotinine levels and 69.9% had detectable salivary cotinine levels. A sensitivity analysis that broadened the definition of car exposure did not change these results.

Relationship Between Tobacco Exposure and Hospital Readmissions

Readmission rates were not significantly different between children with

TABLE 1 Participant Demographic Characteristics and Exposures

Variable	Included	Excluded	*P*
Total, *n*	619	155	
Race, *n* (%)			.29
White	198 (32.0)	56 (36.1)	
African American	355 (57.4)	86 (55.5)	
Multiracial	60 (9.69)	8 (5.16)	
Other	6 (0.97)	2 (1.29)	
Missing	0 (0.00)	3 (1.94)	
Gender, *n* (%)			.82
Male	404 (65.3)	99 (63.9)	
Female	215 (34.7)	56 (36.1)	
Age, mean (SD), y	6.43 (4.02)	5.08 (3.58)	<.0001
Type of insurance, *n* (%)			.99
Private	138 (22.3)	33 (5.3)	
Public	451 (72.9)	111 (17.9)	
Self-pay	22 (3.6)	5 (0.8)	
Other	7 (1.1)	2 (0.3)	
Don't know	1 (0.20)	0 (0.0)	
Income, *n* (%)			.31
<$15 000	221 (35.7)	40 (25.8)	
$15 000–$29 000	165 (26.7)	47 (30.3)	
$30 000–$44 999	83 (13.4)	25 (16.1)	
$45 000–$59 999	36 (5.82)	10 (6.45)	
$60 000–$89 999	64 (10.3)	14 (9.03)	
>$90 000	44 (7.11)	11 (7.10)	
Missing	6 (0.97)	8 (5.16)	
Caregiver education, *n* (%)			.02
Eighth grade or less	3 (4.85)	3 (1.94)	
More than eighth grade, not high school	90 (14.5)	25 (16.1)	
High school graduate	163 (26.3)	41 (26.5)	
Some college	176 (28.4)	44 (28.4)	
2-year college	75 (12.1)	8 (5.16)	
4-year college or above	88 (14.2)	29 (18.7)	
Missing	24 (3.88)	5 (3.22)	
Use of daily asthma controller medication, *n* (%)			.21
Yes	249 (40.2)	70 (45.2)	
No	369 (59.6)	81 (52.2)	
Missing	1 (1.6)	4 (2.6)	
Serum cotinine[a]			.59
Above LOD	347 (56.1)	34 (21.9)	
Below LOD	272 (43.9)	22 (14.2)	
Missing	—	99 (63.9)	
Salivary cotinine[a]			.06
Above LOD	493 (79.6)	79 (51.0)	
Below LOD	126 (24.4)	10 (6.45)	
Missing	—	66 (42.6)	
Any reported tobacco exposure			.38
Yes	217 (35.1)	44 (28.4)	
No	402 (64.9)	99 (63.9)	
Missing	—	12 (7.74)	
Readmission within 12 months of enrollment			.007
Yes	103 (16.6)	41 (26.5)	
No	516 (83.4)	114 (73.5)	

—, no data available.

[a] Refers to cotinine level as measured by liquid chromatography tandem mass spectrometry.

reported secondhand smoke exposure and those without (19.4% vs 15.2%; P = .21) (Table 3). However, readmission rates for children with detectable cotinine compared with those without detectable cotinine were 19.6% versus 12.9% (P = .03) and 18.7% versus 8.7% (P = .007) for serum and salivary cotinine, respectively.

In adjusted analyses, caregiver reports of any secondhand smoke exposure were not significant predictors of hospital readmissions (adjusted odds ratio: 1.23; 95% confidence interval [CI]: 0.79–1.89) (Table 4). Smoking in the primary residence was also not associated with the outcome. Both detectable serum cotinine and salivary cotinine were significantly associated with hospital readmission (adjusted odds ratio [95% CI]: 1.59 [1.02–2.48] and 2.35 [1.22–4.55], respectively). In a post hoc analysis of children with detectable saliva cotinine, we found no evidence of either a dose-response relationship or a threshold effect between cotinine and readmission rate. Results were unchanged when we adjusted for time between admission and specimen collection.

We performed a stratified analysis on the basis of child age (>6 and ≤6 years). For children in both strata, the direction of the association between cotinine and readmission remained the same as in the full sample. For the ≤6-year subgroup (n = 328), salivary cotinine remained a significant predictor of readmission, but the other comparisons were no longer significant due to an increase in the SEs.

DISCUSSION

Secondhand tobacco exposure was common among children admitted to the hospital for asthma or bronchodilator-responsive wheezing. In addition, tobacco exposure, as measured by detectable levels of serum and saliva cotinine, was associated with repeat hospitalization for asthma or wheezing within 1 year. Conversely, caregiver reports of children's secondhand smoke exposure were not predictive of hospital readmission and did not correlate well with secondhand smoke exposure as measured by serum and salivary cotinine levels.

We found a strong, independent association between cotinine, an established biomarker for tobacco exposure, and asthma- and wheezing-related readmission within 12 months. The point

TABLE 2 Secondhand Smoke Exposure Rates by Demographic Characteristics

Variable	*n* (%)	Detectable Serum Cotinine[a]		Detectable Salivary Cotinine[a]		Any Reported Tobacco Exposure	
		n (%)	*P*	*n* (%)	*P*	*n* (%)	*P*
Race (*N* = 619)			.001		<.0001		.02
White	198 (32.0)	99 (50.0)		136 (68.7)		57 (28.8)	
African American	355 (57.4)	217 (61.1)		308 (86.8)		141 (39.7)	
Multiracial	60 (9.7)	31 (51.7)		48 (80.0)		19 (31.7)	
Other	6 (1.0)	0 (0)		1 (16.7)		0 (0.0)	
Income (*N* = 613)			<.0001		<.0001		<.0001
<$15 000	221 (36.1)	159 (71.9)		209 (94.6)		101 (45.7)	
$15 000–$29 000	165 (26.9)	106 (64.2)		143 (86.7)		69 (41.8)	
$30 000–$44 999	83 (13.5)	40 (48.2)		63 (75.9)		24 (28.9)	
$45 000–$59 999	36 (5.9)	19 (52.8)		25 (69.4)		9 (25.0)	
$60 000–$89 999	64 (10.4)	14 (21.9)		32 (50.0)		7 (10.9)	
>$90 000	44 (7.2)	5 (11.4)		15 (34.1)		4 (9.1)	
Caregiver education (*N* =595)			<.0001		<.0001		<.0001
Eighth grade or less	3 (1)	3 (100)		3 (100)		1 (33.3)	
More than eighth grade, not high school	90 (15.1)	75 (83.3)		85 (94.4)		43 (47.8)	
High school graduate	163 (27.4)	95 (58.3)		138 (84.7)		102 (62.6)	
Some college	176 (29.6)	106 (60.2)		144 (81.9)		112 (63.6)	
2-year college	75 (12.6)	38 (50.7)		62 (82.7)		51 (68.0)	
4-year college and above	88 (14.8)	16 (18.2)		40 (45.5)		79 (89.8)	
Gender (*N* = 619)			.61		.75		.09
Male	404 (65.3)	223 (44.8)		320 (80.4)		130 (67.3)	
Female	215 (34.7)	124 (42.3)		173 (79.2)		272 (60.5)	
Use of controller medication for asthma (*N* = 618)			.98		.76		.98
Yes	249 (40.3)	139 (55.8)		200 (80.3)		162 (65.0)	
No	369 (59.7)	207 (56.1)		292 (79.1)		240 (65.0)	
Any reported tobacco exposure (*N* = 619)			<.0001		<.0001		
Yes	217 (35.1)	157 (87.6)		281 (97.7)			
No	402 (64.9)	190 (39.1)		212 (69.9)			

[a] Dichotomized on the basis of values being either above or below the LOD.

estimate for detectable saliva cotinine was somewhat higher at an ∼2.4-fold increased risk of readmission compared with serum cotinine. However, we found no evidence for a dose-response relationship. This finding may be due to the patient-to-patient variability in nicotine metabolism. Studies have used cotinine levels obtained from meconium, umbilical cord blood, and maternal hair, urine, or serum to assess prenatal tobacco exposure and have associated increased levels with increased respiratory symptoms and asthma in children.[14,18–21] One study performed in adults explored the relationship between cotinine levels and asthma-related hospital admissions; however, this study found that higher hair concentrations of nicotine, but not cotinine, were associated with increased rates of hospitalization.[22] Another study linked urine cotinine levels to hospitalizations for bronchiolitis in infants.[23] The current study lends additional support to an emerging role for cotinine measurements as a biomarker and potential clinical measure for predicting future hospitalizations in children, especially those with respiratory conditions.

An additional finding of the current analysis was the discrepancy between caregiver reports of children's exposure to secondhand smoke and measurements of secondhand smoke exposures as reflected by serum and salivary cotinine levels. This finding runs counter to several recent studies that showed agreement between parental reports of secondhand smoke exposure and cotinine measurement, and may reflect a bias toward underreporting in the acute-care inpatient setting. A similar discrepancy has been noted in situations in which social desirability to underreport tobacco exposure might be heightened, such as in evaluating prenatal secondhand smoke exposure and maternal smoking.[14,24–27] Our findings could reflect a similar bias toward underreporting or could indicate significant hidden secondhand smoke exposure from factors unique to a low-income population, such as multiunit housing.[28,29] Alternatively, our findings could reflect a lack of specificity in our questions regarding secondhand smoke exposure. For example, caregivers may not respond affirmatively to the question, "Does anyone smoke inside your home?" even if a smoker lived in the home but smoked outside or on the porch.

We also found a significant difference in tobacco smoke exposure between different demographic subgroups. The current results echo those of recent studies, including 1 study by Dempsey et al[30] that evaluated serum cotinine levels in an urban outpatient pediatric

TABLE 3 Hospital Readmission Rate as a Function of Demographic Characteristics and Exposures

Variable	*n* (%)	Hospital Readmission, *n* (%)	*P*
Race (*N* = 619)			<.001
White	198 (32.0)	14 (7.1)	
African American	355 (57.4)	77 (21.7)	
Multiracial	60 (9.7)	11 (18.3)	
Other	6 (1.0)	1 (16.7)	
Income (*N* = 613)			.009
<$15 000	221 (36.1)	44 (19.9)	
$15 000–$29 000	165 (26.9)	29 (17.6)	
$30 000–$44 999	83 (13.5)	18 (21.7)	
$45 000–$59 999	36 (5.9)	6 (16.7)	
$60 000–$89 999	64 (10.4)	4 (6.2)	
>$90 000	44 (7.2)	0 (0)	
Caregiver education (*N* = 595)			.002
Eighth grade or less	3 (1)	2 (66.7)	
More than eighth grade, no high school	90 (15.1)	21 (23.3)	
High school graduate	163 (27.4)	27 (16.6)	
Some college	176 (29.6)	27 (15.3)	
2-year college	75 (12.6)	15 (20.0)	
4-year college and above	88 (14.8)	3 (11.5)	
Gender (*N* = 619)			.73
Male	404 (65.3)	69 (17.1)	
Female	215 (34.7)	34 (15.8)	
Use of controller medication for asthma (*N* = 618)			<.001
Yes	249 (40.3)	57 (22.9)	
No	369 (59.7)	45 (12.2)	
Any reported tobacco exposure (*N* = 619)			.21
Yes	217 (35.1)	42 (19.4)	
No	402 (64.9)	61 (15.2)	
Serum cotinine above LOD[a] (*N* = 619)			.03
Yes	347 (56.1)	68 (19.6)	
No	272 (43.9)	35 (12.9)	
Salivary cotinine above LOD[a] (*N* = 619)			.007
Yes	493 (79.6)	92 (18.7)	
No	126 (20.4)	11 (8.7)	

[a] Dichotomized on the basis of values being either above or below the LOD.

TABLE 4 Unadjusted and Adjusted Association of Tobacco Exposure With Hospital Readmission

	Unadjusted Model		Adjusted Model[a]	
	OR	95% CI	OR	95% CI
Serum cotinine[b]	1.65	1.06–2.57	1.59	1.02–2.48
Salivary cotinine[b]	2.40	1.24–4.63	2.35	1.22–4.55
Tobacco exposure in the primary residence[c]	0.97	0.58–1.60	0.89	0.54–1.47
Any reported tobacco exposure	1.34	0.86–2.07	1.23	0.79–1.89

Each row represents a separate model. OR, odds ratio.

[a] Adjusted for race, caregiver education, history of use of at least 1 asthma controller medication, and the elapsed time between admission and sample collection.

[b] Dichotomized on the basis of values being either above or below the LOD.

[c] Dichotomized on the basis of yes or no answers to history of tobacco exposure.

clinic. They found that, although there were no significant gender or age differences in cotinine levels, African American children had consistently higher cotinine levels than did children of other racial backgrounds.[31] The reasons for this particular finding are potentially multifactorial and include different exposure risks as well as potential racial differences in nicotine metabolism.[32]

For all study participants, the LOD was lower for salivary than for serum cotinine, consistent with the previously noted increased sensitivity of salivary cotinine levels.[33,34] This difference may be explained by the fact that saliva is a "cleaner matrix," with fewer metabolites to detect. This difference results in a slightly better signal:noise ratio for salivary cotinine. Salivary cotinine is an attractive option for a pediatric biomarker due to the minimal effort and invasiveness needed to obtain specimens.

The ability to measure serum and salivary cotinine levels presents the possibility of an objective measure that can be obtained when a child is seen in the emergency department or in the hospital and may be used to predict future hospitalizations. Such a measure for exposure to tobacco smoke could be used to target specific interventions at caregivers of those children before discharge from the hospital. Several interventions, including parental counseling and contact of the primary care physician, have already been described for use in the inpatient setting and could be adopted in clinical practice.[35,36]

There were limitations to this study. First, asthma admission data were only available for children hospitalized at CCHMC facilities; children may have been admitted elsewhere. When a random sample of children enrolled in the cohort was reached 1 year after recruitment, no parent or guardian reported the child being admitted elsewhere for asthma or wheezing. However, we cannot rule out the possibility that they were admitted elsewhere with other potentially related diagnoses (eg, bronchiolitis). In addition, our outcome did not include visits to emergency departments or acute-care centers and so we may have missed a less severe but important component of asthma morbidity. Second, our sample was composed primarily of African American and white children, limiting the generalizability of our findings. Third, there were significant differences between children included and those not included in the analysis, specifically more hospital readmissions among children who were not included; however, this situation

would most likely have created a bias toward the null in our results. Fourth, we could have used a more detailed set of questions to obtain additional information regarding tobacco exposure, which might have improved the sensitivity of the caregiver report compared with biomarkers. However, we sought to replicate what might be reasonably asked during typical care in the inpatient setting. Fifth, we cannot rule out that children with tobacco exposure were readmitted at a lower threshold of severity because tobacco exposure may be associated with other unmeasured variables, such as family disruption. However, we did adjust for potentially correlated variables, such as low caregiver education. A final limitation was our lack of detailed information regarding asthma controller medication use in our cohort on index admission and readmission. We did not have specific information about inhaled corticosteroid use and adherence rates, which could have an impact on the number of exacerbations children experienced.

CONCLUSIONS

We found that secondhand smoke exposure was common among children admitted for wheezing or asthma and that, when assessed with biomarkers, the exposure was independently associated with readmission. Serum and salivary cotinine levels may allow for more effective risk stratification of these children and lead to the development of targeted interventions. Such interventions, if effective, could serve to decrease the occurrence of readmission.

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