Journal of Occupational and Environmental Hygiene, 6: 698–704
ISSN: 1545-9624 print / 1545-9632 online
DOI: 10.1080/15459620903249893

Assessment of Exposure to Secondhand Smoke at Outdoor Bars and Family Restaurants in Athens, Georgia, Using Salivary Cotinine

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Exposure to secondhand smoke (SHS) in outdoor settings is a growing public health concern due to recent indoor smoking bans. The objective of this study was to measure salivary cotinine, a metabolite of nicotine, in subjects aged 21–30 exposed to SHS outside bars and restaurants in Athens, Georgia. Nonsmokers participated during 6-hr periods in outdoor standing or seating areas of bars and restaurants where indoor smoking was banned, as well as a control outdoor location with no smokers over six weekends during the summer and early fall of 2007. Pre- and post-exposure saliva samples ($N = 25$ person-days at the bar site, $N = 28$ person-days at the restaurant site, and $N = 11$ person-days at the control) were collected and analyzed for cotinine. The mean change in the response, (ln(post) - ln(pre)) salivary cotinine levels, was significantly impacted by the type of site (bar, restaurant, control) ($F = 5.09$; d.f. $= 2, 6.7$; $p = 0.0455$). The median percent increase in salivary cotinine from pre-test to post-test was estimated to be 162%, 102%, and 16% at the bar, restaurant, and control sites, respectively, values that were significant increases at bars ($t = 4.63$; d.f. $= 9.24$; $p = 0.0011$) and restaurants ($t = 4.33$; d.f. $= 4.47$; $p = 0.0097$) but not at the control sites. On average, these pre-test to post-test increases in salivary cotinine were significantly higher at bar sites than control sites ($t = 3.05$; d.f. $= 9.85$; $p = 0.0176$) and at restaurant sites compared with control sites ($t = 2.35$; d.f. $= 5.09$; $p = 0.0461$). Nonsmokers outside restaurants and bars in Athens, Georgia, have significantly elevated salivary cotinine levels indicative of secondhand smoke exposure.

Keywords biomarker, outdoors, salivary cotinine, secondhand smoke

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

INTRODUCTION

Secondhand smoke (SHS), also referred to as environmental tobacco smoke (ETS), is a mixture of almost 5000 chemical compounds, of which 43 are known human and animal carcinogens.[1,2] SHS consists primarily of the smoke emitted from the smoldering tip of a cigarette and smoke that the smoker exhales.[3] In addition to the known carcinogens, other compounds present in SHS include carbon monoxide (CO), ammonia, nicotine, hydrogen cyanide, and sulfur dioxide.[4–7] Because of the harmful components and adverse health effects associated with exposure, SHS is considered the most significant contaminant of indoor air.[8]

Secondhand smoke places children at increased risk for acute respiratory infections, exacerbation of asthma, and sudden infant death syndrome, and exposure of adults causes coronary heart disease and lung cancer.[9] Serious impacts of SHS on children include both the induction and exacerbation of asthma, bronchitis and pneumonia, middle ear infection, chronic respiratory symptoms, and low birth weight.[5,10] In 2006, the *United States Surgeon General's Report* stated that SHS contains many chemicals that can quickly irritate and damage the lining of the airways. Even brief exposure can result in upper airway changes in healthy persons and can lead to additional and more frequent asthma attacks in children who already have asthma. The Surgeon General also reported that increasing scientific evidence shows there is no level of exposure to SHS that is considered safe.[9]

Because of increasing scientific evidence associating adverse health effects with exposure to SHS, indoor smoking bans at establishments open to the general public have been introduced in many countries. Ireland, Italy, Norway, Scotland,

TABLE I. Descriptions of All Sites

Site ID	Site Type	Week Sampled	No. of Tables	Roof at Site	Outdoor Patio Area (m^2)
A	Bar with outdoor patio	1 to 6	6	None	176
B	Family restaurant outdoor patio	1 to 5	8	None	605
C	Bar with outdoor patio	4	12	None	273
D	Family restaurant with outdoor patio	5 to 6	17	None	549
E	Bar with outdoor patio	6	10	None	208
G	Open air area on north campus of University of Georgia	1 to 6	0	None	1124

Finland, Australia, New Zealand, and the United States have all passed laws banning indoor smoking either on a local or national level.[11]

Studies have been conducted in these countries prior to and following imposition of smoking bans to monitor select indoor air pollutants associated with SHS, most notably $PM_{2.5}$ and CO, with the results showing a significant decrease in indoor levels of these pollutants.[12,13] Bar workers in San Francisco and Ireland reported significantly decreased respiratory illnesses after implementation of indoor smoking bans, and a decrease in the rate of hospital admissions for acute myocardial infarction was observed in New York state and Italy after implementation of smoking bans.[13–16] These studies provide evidence that SHS is harmful and that decreased exposure can result in positive health outcomes.

To determine personal SHS exposure, air contaminants associated with SHS such as $PM_{2.5}$ and CO can be measured, but use of a biological marker of exposure may provide a stronger representation of the actual internal SHS dose. Cotinine, the proximate metabolite of nicotine, is considered the best biomarker of exposure to tobacco smoke in both active smokers and nonsmokers due to its high specificity for tobacco.[17,18] Cotinine has a relatively long half-life of 17 hr and can be measured by sampling serum, saliva, urine, or hair.[19]

Due to the noninvasive method of saliva collection, many studies conducted in field settings have used salivary cotinine as an SHS exposure assessment tool.[20] Studies that include both children and adults have reported decreased salivary cotinine levels after exposure to SHS has been either lowered or eliminated.[12,21,22]

Current recommendations emphasize avoiding exposure to SHS in enclosed spaces, indoors, or in automobiles. An implied assumption is that smoking in outdoor settings is not a significant source of exposure of nonsmokers to SHS but that has not been established. The objective of this study was to further evaluate this issue by monitoring the exposure to SHS of a group of nonsmokers, aged 21–30, in outdoor seating and standing areas of bars and family restaurants in Athens, Georgia, using salivary cotinine as a biological marker.

METHODS

Study Locations

This study was conducted in the summer and fall of 2007 in outdoor standing and seating areas of bars and family restaurants where indoor smoking was banned in Athens, Georgia, a city with a population of approximately 102,000. Verbal approval to conduct the study was obtained from individual restaurant and bar managers and owners prior to the first day of sampling.

Descriptions of the study sites and the dates they were sampled are shown in Table I. During the summer, two bars (Site A and Site C) and one family restaurant (Site B) were chosen as study sites. All locations were sampled for 6 hr each on four weekend nights (Weeks 1–4) in June, with the exceptions of Site A, which was sampled only during Weeks 1–3, and Site C, which was sampled only during Week 4. Each subject was present for the entire 6-hr sampling period at the study sites on the day of their participation except for brief restroom breaks inside the locations.

During the fall, two family restaurants and three bars were chosen as study sites. In Week 5, two family restaurants (Site B and Site D) and one bar (Site A) were sampled. On Week 6, three bars (Site A, Site E, and Site F) and one family restaurant (Site D) were sampled. Sites A, B, and D were sampled on October 6, 2007, from 2–8 p.m.; Site D on November 2, 2007, from 4 p.m.–10 p.m.; Sites A, E, and F on November 3, 2007, from 7 p.m.– 1 a.m. The two fall study dates were chosen in anticipation of large crowds, and related high outdoor SHS exposures, at the study sites due to popular athletic events in Athens, Georgia.

For both summer and fall sessions, a control site (Site G) was located on the north campus of the University of Georgia (UGA). This area was located outdoors with no walls or roof and had very little pedestrian traffic or secondhand tobacco smoke (SHS) exposure.

Subject Selection

Volunteers in this study were all nonsmoking college students between the ages of 21 and 30. An initial 10 subjects participated during the first 3 weeks in the summer, but one subject was replaced during Week 4 after salivary cotinine levels characteristic of occasional smokers were reported for that subject. Subjects contributed between 1 and 4 person-days during the summer (N = 35 person-days total, n = 11 person-days at bar, n = 16 person-days at restaurant, and n = 8 person-days at the control sites). Twenty subjects participated in the fall contributing between 1 and 2 person-days (N = 29 person-days total, n = 14 person-days at bar, n = 12 person-days at restaurant, and n = 3 person-days at control sites). Five subjects participated in both the summer and fall study periods. Subjects participated only on Friday or Saturday of each study week to avoid potential carryover effect from SHS exposure on the previous day.

Oral questionnaires were administered to potential study participants to determine each person's eligibility for the study and included questions on current and past smoking status and current SHS exposure. If the individual did not smoke, did not live with a smoker, and did not use nicotine in any other form (i.e., smokeless tobacco, nicotine replacement therapy), they were considered eligible to participate. Study protocol was reviewed and approved by Institutional Review Boards at the University of Georgia and the Centers for Disease Control and Prevention. The sample population was not randomly selected, rather, subjects were chosen on availability and were all students at UGA.

Exposure Assessment

Human subjects provided saliva samples, both pre- and post-exposure to SHS, using Salivettes (Sarstedt, Newton, N.C.). The samples were collected at UGA's Environmental Health Science (EHS) building within 30 min before and after a 6-hr "hang out" period at the study sites where they were potentially exposed to SHS. Smokers at the bar and restaurant sites were between half a meter and 7 meters from where the subjects were seating or standing. The EHS laboratory is located approximately one mile from the study sites, and subjects were transported in vehicles to ensure no additional contact with SHS after the 6-hr study period at the sites.

Subjects fully saturated the cotton swab portion of the Salivette with saliva; usually taking about 2 min. The subjects were instructed to avoid SHS exposure as much as possible 48 hr prior to providing the saliva sample to minimize the pre-exposure salivary cotinine concentration. Questionnaires were administered pre-exposure to monitor any SHS exposure within 48 hr of the study, and pre-exposure saliva samples were obtained from each subject to establish his or her baseline concentration.

The salivette cases were labeled with: the week number of the study, the subject ID number, and either PRE or POST (to distinguish pre- or post-SHS exposure). The samples were collected by the investigators and immediately placed in plastic storage bags and then in a freezer (−20°C) to preserve the saliva until analysis at the Centers for Disease Control and Prevention (CDC) in Atlanta. The samples were shipped on dry ice overnight to CDC each week of the study.

Salivary Cotinine Analysis

Salivary cotinine analysis was performed by a method described elsewhere in detail.[23] Briefly, samples were spiked with a trideuterated cotinine internal standard, extracted with methylene chloride, dried, and reconstituted in water, and analyzed by liquid chromatography atmospheric-pressure chemical ionization tandem mass spectrometry. Cotinine concentrations were quantified by comparison with standards using weighted least squares linear regression. All analytical runs included a blank and two QC pools, and all results were from runs confirmed to be in statistical control by use of a complex, multi-rule algorithm implemented within SAS-QC that has been described elsewhere in detail.[24]

Statistical Analysis

The geometric means of the pre- and post-exposure salivary cotinine concentrations were calculated, respectively, and the difference between the post- and pre-exposure geometric means were computed for all three site types (bar, restaurant, and control). Data from the subject with the suspected occasional smoking status were omitted from all statistical analyses. To determine whether salivary cotinine levels were greater in subjects exposed to SHS outside restaurants and bars compared with subjects at the control location, a linear mixed effects model was fit to the data. More formally, the model can be written as:

$$y_{ijk} = \mu_k + s_i + d_{j(k)} + e_{ijk}, \quad \textbf{(1)}$$

where, y_{ijk} is the response ln(post-exposure cotinine) - ln(pre-exposure cotinine) in the ith subject at the kth site on the jth day; μ_k represents the mean change in salivary cotinine at the kth site; s_i represents the subject effect; $d_{j(k)}$ represents the day effect; and e_{ijk} is the error term.

Site type is nested in day since restaurants and bars were not sampled on the same day. Subjects and days of monitoring were introduced as random variables in the model, and type of site was introduced as a fixed effect, since we were interested in comparing SHS exposure across site types. Estimates for the mean response at each study site were calculated along with statistics to test if the mean response was zero. Exponential transformations of these estimated means provide estimates of the median percent change in cotinine from pre-test to post-test.

Estimates of the differences between the mean response at the control site and each of the other site types were calculated, and t-tests conducted to determine if the difference is significantly different from zero. Due to the use of multiple comparisons with the control site, adjusted p-values were calculated to determine the significance of the results using Dunnett's method. All statistical tests were considered significant at $\alpha = 0.05$.

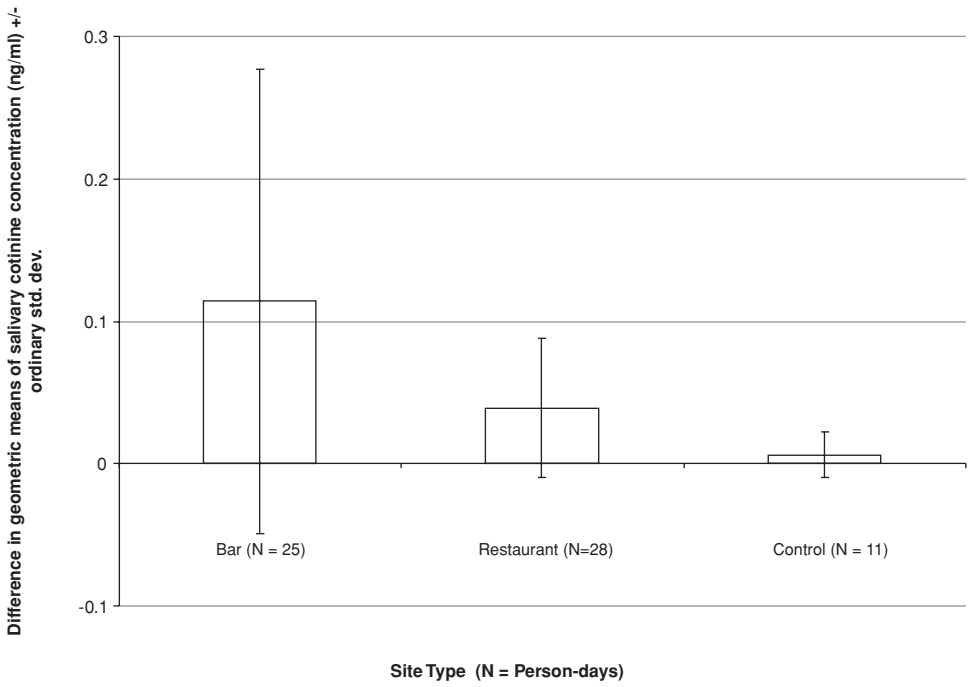

FIGURE 1. Difference between geometric means of post-secondhand smoke (SHS) exposure and pre-SHS exposure from subjects in seating and standing areas outside restaurants and bars and a control location with no observable SHS. Participants remained outside the locations for 6 hr. N represents person-days.

RESULTS

Subjects were studied at seven locations over the duration of the study period. Table I shows descriptions of the study sites and the dates each site was sampled over the 6-week study period. During the summer, Site A was canceled after the third sampling period for logistical reasons and replaced with Site C. Site A was used again for the fifth and sixth sampling days. Site G (control) was the same location for all six sampling periods.

Calculated by post- minus pre-SHS exposure salivary cotinine levels, the subjects at the bar sites had the largest increase in salivary cotinine after the exposure period, followed by subjects at the restaurant sites, and lastly by subjects at the control sites (Figure 1 and Table II). The differences between geometric means for all subjects located at the bar, restaurant, and control site were 0.114 ng/mL, 0.039 ng/mL, and 0.006 ng/mL, respectively.

Using the linear fixed-effects model (Eq. 1), it was determined that the mean response was not the same for all site types ($F = 5.09$, d.f. $= 2, 6.7$, p-value $= 0.045$). The p-values demonstrate there was a significant increase in ln(cotinine) from pre-exposure to post-exposure in subjects outside both the bar and restaurant but not the control site. The p-values for the bar, restaurant, and control were 0.0011, 0.0097, and 0.4397, respectively (Table III).

Table IV shows the estimates of the difference between the bar and the control groups' mean response and the difference between the restaurant and the control groups' mean response. This is mathematically represented as (bar mean–control mean) and (restaurant mean–control mean). Adjusted p-values demonstrated that the estimated differences between the bar and control and restaurant and control were significantly different from zero ($p = 0.0176$ and $p = 0.0461$, respectively).

DISCUSSION

Many studies have shown an association between indoor exposure to SHS and an increase in salivary cotinine concentration.[12,23] However, we are not aware of any prior studies that have documented exposure to SHS in outdoor settings using salivary cotinine measurements. This exposure warrants attention because the many indoor smoking bans established across the world have encouraged the movement of previous indoor smoking outdoors, and thus, estimating the extent of outdoor SHS exposure of nonsmokers is a potentially significant public health issue. Many previous studies have utilized questionnaires to determine the amount of SHS exposure, but objective and quantitative methods such as biomarker measurements can be particularly beneficial in this area.

Salivary cotinine was chosen as the biological marker for this study because of the noninvasive saliva collection and ease of collection in the field setting. Cotinine is the major metabolic product of nicotine with a half-life of about 17 hr, so it was appropriate for this study design.[12,21,22] The most recent National Health and Nutrition Examination Survey

TABLE II. Salivary Cotinine Data

Site	Statistics	Pre-Exposure Cotinine Level (ng/mL)	Post-Exposure Cotinine Level (ng/mL)	Change in Salivary Cotinine (ng/mL)
Bar (N = 25)	Geo. Mean	0.069	0.182	0.114
	Minimum	0.011	0.040	−0.275
	Maximum	0.959	1.056	0.559
	Median	0.048	0.128	0.070
	Std. Dev.	0.268	0.296	0.163
Restaurant (N = 28)	Geo. Mean	0.036	0.075	0.039
	Minimum	0.011	0.025	−0.010
	Maximum	0.218	0.404	0.186
	Median	0.036	0.072	0.037
	Std. Dev.	0.048	0.078	0.049
Control (N = 11)	Geo. Mean	0.043	0.049	0.006
	Minimum	0.030	0.027	−0.006
	Maximum	0.081	0.094	0.039
	Median	0.041	0.051	0.001
	Std. Dev.	0.015	0.023	0.016

Notes: N = person-days.

(NHANES) indicates a national average for serum cotinine among nonsmokers of 0.034 ng/mL,[17] salivary cotinine levels are typically about 15–30% higher.[25] Previous studies have shown that serum and salivary levels of cotinine are highly correlated with a 1.1–1.4 saliva to blood ratio.[26,27]

The increase in salivary cotinine in subjects outside the bars and restaurants was significantly different from zero, while the change in cotinine in the control subjects was not significant (Table III). This was expected due to the absence of SHS exposure at the control site. Subjects located outside the bar and restaurant sites had a greater increase in salivary cotinine compared with subjects at the control sites, as presented in Table IV. The changes in subjects outside the bars were also higher than what was observed in subjects outside the restaurants. This may be due to the higher number of smokers that is typically seen at bars compared with restaurants. While we observed higher numbers of smokers at the bar sites, an accurate number was not obtained. These results demonstrate exposure to SHS outside restaurants and bars where indoor smoking is banned.

TABLE III. Test of Whether Differences in Mean Log-Transformed Salivary Cotinine Levels from Subjects at Each Site Type are Different from Zero

Site	Parameter Estimate (ln(ng/mL))	t-value	p-value
Bar	0.9645	4.63	0.0011
Restaurant	0.7042	4.33	0.0097
Control	0.1478	0.86	0.4397

Note: Tests are significant at $\alpha = 0.05$.

To compare the pre-exposure cotinine concentrations observed in this study with NHANES 2001–2002 background serum cotinine levels, we applied the regression model (Eq. 2) to predict salivary cotinine using the reported 0.034 ng/mL NHANES 2001–2002 serum cotinine background levels of nonsmokers, age >20.[25]

$$\log_{10}(\text{salivary cotinine}) = 0.962817 * \log_{10}(\text{serum cotinine}) + 0.127478 \quad \textbf{(2)}$$

After applying this equation, the 0.034 ng/mL serum cotinine NHANES background mean would be approximately equivalent to 0.052 ng/mL for saliva cotinine. The pre-exposure bar, restaurant, and control means were 0.069, 0.036, and 0.043 ng/mL, respectively. Thus, the pre-exposure salivary cotinine levels from this study, after adjustment, are consistent with the NHANES background levels.

TABLE IV. Pairwise Comparisons Between Log-Transformed Differences in Mean Salivary Cotinine Levels from Subjects Outside the Bar and Restaurant Sites and the Mean Changes in Salivary Cotinine Levels in Subjects at the Control Location with No Observable Secondhand Smoke Exposure

Site	Parameter Estimate (ln(ng/mL))	t-value	p-value	Adjusted p-value
Bar vs. control site	0.8167	3.05	0.0062	0.0176
Restaurant vs. control site	0.5564	2.35	0.0321	0.0461

The relatively large variation in pre-exposure cotinine levels for subjects at the bar sites can be attributed to subjects who had pre-exposure salivary cotinine levels much higher than the majority of participating subjects. An example is subject 009, who participated only during Weeks 1–4, with a geometric mean pre-exposure cotinine value of 0.604 ng/mL (N = 4). The geometric mean pre-exposure cotinine values for all subjects during the first 4 weeks, excluding subject 009, was 0.0483 ng/mL (N = 31person-days).

Subject 009 reported that his roommate smokes cigarettes but not inside the home, so he did not believe that he was directly exposed to any SHS. This demonstrates the sensitivity of using salivary cotinine as a biological marker of SHS exposure. Etter et al.[27] found that nonsmokers who lived with smokers or had friends who smoke had salivary cotinine levels 1.5 times higher than nonsmokers who do not live with smokers or do not have friends who smoke.[28] Subject 009 was retained in the study because the observed background levels could be accommodated, since only concentration differences (post-exposure – pre-exposure) were used in each case.

Nonsmoking hotel workers in Ireland who were exposed to SHS during their 8-hr work shift had a mean post-work salivary cotinine level of 2.86 ng/mL. This level decreased to 1.29 ng/mL after a smoking ban was put into effect in Ireland.[12] A study of nonsmoking hospitality workers in New Zealand found a mean salivary cotinine difference (post – pre) of 1.11 ng/mL in workers of smoking-allowed workplaces and 0.02 ng/mL in workers of nonsmoking workplaces.[29] This difference in cotinine concentrations observed in workers not exposed to SHS in the workplace is below the mean difference for both the bar and restaurant type sites in our study (0.116 ng/mL and 0.05 ng/mL, respectively) but similar to what we found at the control site

Repace and colleagues[30] determined that an average salivary cotinine level of 0.40 ng/mL corresponds to an increased lifetime mortality risk of 1/1000 for lung cancer and 1/100 for heart disease. The average salivary cotinine levels for all six study dates in our study did not reach this level, although the average post-exposure salivary cotinine level for the bar site participants in the summer was 0.30 ng/mL, which is close in magnitude to the levels reported by Repace and colleagues. Additional studies are needed to determine if workers repeatedly exposed to SHS at outdoor bars have sustained salivary cotinine levels in the range of 0.30 ng/mL to 0.40 ng/mL, which would indicate an increased risk for lung cancer and heart disease.

This study had several limitations. An accurate count of the total number of cigarettes lit during each sampling period might have provided an independent estimate of the amount of smoke the subjects were exposed to while at the sites. In addition, the concentration of components of SHS in an outdoor location is heavily influenced by meteorological factors, such as wind speed, temperature, and humidity. These variables were not measured and taken into account and, therefore, pose a problem when comparing SHS concentration over multiple sites, days, and seasons.

However, we attempted to control for this potential heterogeneity between the different days of sampling by introducing "day of sampling" as a random effect in the linear mixed-effects model. Further, this study would have been strengthened if we had measures of air nicotine for the sites of interest. This could have been used as a direct estimate of the concentration of ambient SHS and, thus, the level of smoking at the sites. The study population consisted of healthy college students between the ages of 21 and 30. Different age groups such as those of children and the elderly could have different nicotine metabolism rates that would result in either decreased or increased mean salivary cotinine changes.[31] To obtain a more diverse study population, race should also be taken into consideration in future studies. This study included 15 Caucasians, 5 African Americans, 1 Hispanic, and 2 students from India.

CONCLUSIONS

Subjects who spend several hours in areas outside bars and restaurants where indoor smoking is banned but outdoor smoking is allowed have higher concentrations of the nicotine metabolite, cotinine, in their saliva compared with subjects congregating where people do not smoke, indicating higher SHS exposure in the former group. Although the increment in cotinine concentrations and, thus, the SHS exposure levels were relatively low at the sites of interest, the current view is that there is no level of personal exposure to SHS that can be regarded as safe.[9] This study demonstrates the ongoing exposure of nonsmokers to SHS outside restaurants and bars, and the limitations of indoor smoking bans alone in protecting the public from exposure to SHS outside these establishments.

ACKNOWLEDGMENTS

The authors wish to thank all the participating establishments and study participants. The contributions of Connie Sosnoff, Rick Alexander, and LaQuasha Gaddis to the cotinine analyses are also gratefully acknowledged. This work was funded in part by the Northeast Health District, Athens Community Wellness Council, and the Athens Tobacco Prevention Coalition.

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