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Exposure to second-hand smoke air pollution assessed from bar patrons' urinary cotinine

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We used physical and pharmacokinetic modeling to estimate personal exposures to respirable particle (RSP) and carcinogenic particulate polycyclic aromatic hydrocarbon (PPAH) air pollution from second-hand smoke (SHS) from the increase in urinary cotinine of eight patrons of three bars in Bismarck, North Dakota. We compared SHS-RSP levels to the U.S. Air Quality Index (AQI), used to forecast outdoor air pollution conditions. We measured smoker density and air exchange rates to generalize our results. Urinary cotinine increased by an average of 4.28 ng/ml to 6.88 ng/ml to 9.55 ng/ml above preexposure background from 6-hr exposures in the three bars. Corresponding estimated SHS-RSP levels were, respectively, 246 μg/m^3, 396 μg/m^3, and 549 μg/m^3, comparable to those measured in 6 Wilmington, Delaware, bars and in 14 western New York bars. Estimated personal SHS-RSP air pollution exposures for the eight subjects, when converted to the 24-hr averaging time of the AQI, were "code red" (unhealthy). Measured outdoor air quality RSP levels for the same period were 1%–3% of the indoor RSP levels in the three bars, and were AQI "code green" (healthy). Estimated SHS-PPAH levels were comparable to peak 3-hr PPAH levels reported at a highway tollbooth. Bismarck cotinine-estimated SHS-RSP varied with smoker density, as did measured SHS-RSP levels in smoking bars in Delaware and New York. Our results show that smoking in bars produces levels of personal air pollution for bar patrons that merit air pollution alerts when sustained in the outdoor air.

Introduction

Indoor air pollution from second-hand smoke (SHS) in bars and taverns has historically been investigated using air quality monitors (Ott, Switzer, & Robinson, 1996, Repace, 2004; Repace & Lowrey, 1980; Travers et al., 2004). Recent air monitoring studies of SHS in 6 bars in Wilmington, Delaware, and in 14 bars in three counties in western New York, before and after statewide clean indoor air laws went into effect, found that SHS contributes about 90% of the respirable particle (RSP) and particulate polycyclic aromatic hydrocarbon (PPAH) air pollution in bars (Repace, 2004). Measured levels greatly exceeded levels of these contaminants encountered on major truck highways and polluted city streets. The RSP levels from SHS in these venues *de facto* violated the U.S. Annual National Ambient Air Quality Standard (NAAQS) for fine particulate matter, generating significant health risks for bar staff (Repace, 2004; Travers et al., 2004). However, air quality monitors do not measure inhaled personal exposure, which can be assessed only with dosimetry. Moreover, air quality monitoring often may not be feasible because of external deadlines, lack of trained personnel, remote locations, or budgetary, temporal, or security reasons.

A recent investigation showed that serum cotinine could be estimated accurately from measured SHS nicotine exposures for 40 adults exposed to SHS in an environmental chamber using default respiration rates for sedentary persons (Repace, Al-Delaimy, & Bernert, 2006). Earlier studies showed that SHS-RSP may be estimated from airborne nicotine by the ratio of 10:1 in places where smoking occurs regularly (Repace & Lowrey, 1993). We therefore decided to use pharmacokinetic modeling to assess short-term personal air pollution exposures to SHS using

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cotinine dosimetry, and to compare these estimated levels to U.S. federal air quality alerts. These data were used to train graduate student volunteers from a university health promotion program to use available resources to present—at a public hearing on a proposed city-wide smoking ban—locally gathered scientific data on air quality in bars with smoking.

We investigated the intensity of SHS exposure at three bars frequented by college students in Bismarck, North Dakota. The Bismarck metropolitan area has a population of 72,250 and three colleges. Although the city of Bismarck monitors its outdoor air quality, it has no ordinance regulating air quality inside stand–alone bars. The primary objectives of the present study were (a) to determine whether a 6-hr stay by nonsmokers in three bars in Bismarck would result in measurably increased levels of urinary cotinine, a marker for nicotine exposure, (b) to estimate the inhaled RSP air pollution concentration from exposure to the smoky bars from the change in urinary cotinine levels after SHS exposure, and (c) to compare the results with contemporaneous outdoor air quality measurements from the state air monitoring network and to the U.S. Air Quality Index (AQI) (U.S. Environmental Protection Agency [USEPA], 2005).

We estimated SHS air pollution levels from urinary cotinine doses using published physical-pharmacokinetic models. We computed the volunteers' personal RSP air pollution exposure related to SHS (SHS-RSP), and compared these levels to state health advisory indices based on the color-coded federal outdoor AQI. RSP is taken to be the same as $PM_{2.5}$, which generally consists of combustion-generated airborne particles with a mass-median diameter of 2.5 μm or less, the size range that can penetrate deep into the lung to the level of the terminal bronchioles and has prolonged residence times (USEPA, 1999). These particles are so small that they can be detected only with an electron microscope. Sources of fine particles outdoors include all types of combustion, including from motor vehicles, power plants, residential wood burning, forest fires, agricultural burning, and some industrial processes. Indoors, sources of fine particles include smoking, cooking, and fireplaces.

Air quality forecasts are provided by state and local agencies, using the AQI, a uniform index that provides general information to the public about air quality and associated health effects. Table 1 summarizes these index descriptors. Health advisories and warnings are based on the current AQI as well as the forecasted AQI. Air quality authorities maintain running averages for each pollutant, and an appropriate AQI is reported that generally corresponds to the current average. For most major cities, air quality forecasts, based on predicted meteorological conditions and monitored air quality, also are released to the public usually during the afternoon hours of the day preceding the forecast period. These forecasts are for particulate matter and ozone, because these are the pollutants that generally contribute to unhealthy air quality. If pollutant levels are expected to be unhealthy, the state and local agencies will release a color-coded health warning or advisory to the local media and post these advisories on their web sites (T. Ellsworth, USEPA Air Protection Division, personal communication, January 24, 2005). The color codes and corresponding normalized AQIs are based on breakpoints or ranges of minimum-to-maximum particulate levels corresponding to increasing severity of expected health effects. The AQI is not linearly related to $PM_{2.5}$. In many U.S. communities, AQI values are usually below 100, with values greater than 100 occurring at most several times a year. Typically, larger cities have more severe air pollution problems, and the AQI may exceed 100 more often in these areas than in smaller cities. AQI values higher than 200 are infrequent, and AQI values above 300 are extremely rare (Ott, Klepeis, & Switzer, 2003).

Table 1. Levels of fine particulate ($PM_{2.5}$) air pollution and corresponding U.S. health advisory descriptors with accompanying simplified color code (USEPA, 1999).

$PM_{2.5}$ (μg/m^3) breakpoints	Air Quality Index (AQI)	Category	Color code
0.0–15.4	0–50	Good	Green
15.5–40.4	51–100	Moderate	Yellow
40.5–65.4	101–150	Unhealthy SG	Orange
65.5–150.4	151–200	Unhealthy	Red
150.5–250.4	201–300	Very unhealthy	Violet
250.5–350.4	301–400	Hazardous	Maroon
350.5–500.4	401–500	Very hazardous	Maroon
>505	500	(Significant harm)[a]	—

Note. SG=sensitive groups.
[a]This category exists but is not a part of the AQI (T. Ellsworth, USEPA Air Protection Division, personal communication, January 24, 2005).

Method

Subjects

Eight healthy nonsmokers (five female, three male), aged 21–32 years (M=24, SD=4), who were students at the University of Mary/St. Alexius Medical Center respiratory therapy program in Bismarck, North Dakota, volunteered for this study. As part of their health promotion course, they decided to investigate the intensity of SHS exposure at three local bars frequented by college students. Inclusion criteria were (a) age 21 years or older, (b) non–tobacco user using no nicotine replacement therapy, (c) living with a nonsmoker, (d) working in a nonsmoking

environment or in an environment with limited exposure to SHS. All subjects were told that a baseline urinary cotinine analysis would be used to validate self-reported smoking status. The University of Mary Institutional Review Committee approved the study protocol, and written consent was obtained from all study participants.

Procedures

Subjects were told to avoid SHS for at least 5 days prior to the study, documenting any inadvertent exposure in a diary. Subjects provided a baseline urine sample (250 ml) 1 hr prior to participation in the study. All participants in the study spent 6 hr in one of the three randomly selected bars, Wednesday or Friday night, October 13, 15, and 22, 2004. Study participants were divided into three groups. Each group spent 6 hr in one of three Bismarck bars selected by a random sample of 11 bars frequented by college students. The 6-hr duration was predicated on what a regular bar patron's or staff person's major SHS exposure period might be. Wednesday, Friday, and Saturday nights were considered to be the most popular nights for college students to frequent bars. Three visits were conducted as follows: Venue 1 (group 1), October 13 (Wednesday); venue 2 (group 2), October 15 (Friday); and venue 3 (group 3), October 22 (Friday). Three volunteers visited the first two venues, and two visited the third venue. Throughout the visits, participants counted the number of patrons and the number of actively smoking patrons every 15 min. Dimensions of the three venues were measured using an electronic ruler. Following their 6-hr exposure, subjects were asked to contribute two additional 250 ml urine samples at 2 hr and 12 hr after departing the venues. All urine samples were labeled and frozen within 1 hr of sampling, at -22°C and were kept frozen until analysis.

Sample analysis

Urinary concentrations of the nicotine metabolite cotinine were measured using high-performance liquid chromatography and atmospheric pressure chemical ionization tandem mass spectrometry (Bernert, Turner, Pirkle, & Sosnoff, 1997; Hukkanen, Jacob, & Benowitz, 2005).

Results

Outdoor air pollution levels

Table 2 gives the outdoor air pollution levels for $PM_{2.5}$ for Bismarck for the period October 3–November 29, 2004. The following data were reported by the North Dakota Department of Health for $PM_{2.5}$ concentrations in Bismarck, surrounding and during the October 13–22, 2004, bar visits: October 12, 7.8 $\mu g/m^3$; October 15, 3.5 $\mu g/m^3$; October 18, 5.9 $\mu g/m^3$; October 21, 9.7 $\mu g/m^3$; and October 24, 12.4 $\mu g/m^3$. Thus the outdoor air quality for October 13, 15, and 22, 2004, was in the "good" range, between 0 and 15.4 $\mu g/m^3$, as shown by the breakpoints in Table 1. Venue 1 is 2.8 miles from the state air quality monitoring site. Venue 2 is 1 mile and venue 3 is 2 miles from this site.

Table 2. Bismarck, North Dakota, daily outdoor air quality summary, October 1–November 30, 2004. Network: North Dakota Department of Health.

Date	$PM_{2.5}$ ($\mu g/m^3$)
10/03/04	3.3
10/06/04	6.3
10/09/04	4.8
10/12/04	7.8
10/15/04	3.5
10/18/04	5.9
10/21/04	9.7
10/24/04	12.4
10/27/04	17.9
10/30/04	11.2
11/02/04	2.9
11/05/04	3.8
11/08/04	5.7
11/11/04	5.6
11/14/04	7.0
11/17/04	8.4
11/20/04	5.2
11/23/04	3.5
11/26/04	8.0
11/29/04	4.6

$PM_{2.5}$ outdoor air pollution is well known to penetrate indoors with 100% efficiency because of the fine particle size. Thus for the three dates of the study the indoor non-SHS background $PM_{2.5}$ levels were taken to be identical to the outdoor values: 6 $\mu g/m^3$ for October 13, 4 $\mu g/m^3$ for October 15, and 11 $\mu g/m^3$ for October 22.

Urinary cotinine levels

Table 3 shows the urinary cotinine levels for the eight volunteers, before, and 2 hr and 12 hr after, visiting the three venues. Three volunteers visited the first two venues, and two visited the third venue. The net change in cotinine represents an average of the two background-subtracted 2-hr and 12-hr cotinine samples. Because nicotine has a 2-hr half-life, at 2-hr postexposure, the measured cotinine level may underestimate nicotine exposure. However, all of the nicotine would be converted to cotinine by 12-hr postexposure. Because of the variability of the cotinine levels, we averaged the 2-hr and 12-hr doses and used the average cotinine concentration to estimate the respired nicotine doses for all subjects for each venue (average net cotinine, each venue, in Table 3), to minimize potential error.

Table 3. Preexposure cotinine (A), 2-h postexposure (B), and 12-h postexposure (C) for eight subjects. Net change in cotinine=([B+C]/2–A): 2- and 12-h average minus preexposure cotinine.

Venue number, subject number	Date	Time	Cotinine (ng/ml)	Net change in cotinine, each subject (ng/ml)	Average net cotinine, each venue (ng/ml)
1, 1A	10/13/04	1630	2.88		
1, 1B	10/14/04	0210	6.08	3.55	
1, 1C	10/14/04	1225	6.77		
1, 2A	10/13/04	1720	0.07		
1, 2B	10/14/04	0210	3.04	5.67	} 4.28
1, 2C	10/14/04	1225	8.43		
1, 3A	10/13/04	1710	0.11		
1, 3B	10/14/04	0215	4.71	3.52	
1 3C	10/14/04	1225	2.54		
2, 4A	10/15/04	1820	1.57		
2, 4B	10/16/04	0245	6.58	4.21	
2, 4C	10/16/04	1304	4.97		
2, 5A	10/15/04	1810	0.05		
2, 5B	10/16/04	0240	10.47	12.9	} 9.55
2, 5C	10/16/04	1250	15.42		
2, 6A	10/15/04	1810	0.09		
2, 6B	10/16/04	0240	15.34	11.46	
2, 6C	10/16/04	1330	7.75		
3, 7A	10/22/04	1845	1.00		
3, 7B	10/23/04	0302	8.44	5.94	
3, 7C	10/23/04	1315	5.43		} 6.88
3, 8A	10/22/04	1835	0.28		
3, 8B	10/23/04	0302	5.52	7.82	
3, 8C	10/23/04	1320	10.67		

Figure 1 shows the urinary cotinine values for the eight subjects in the three venues, preexposure (P) and 2-hr and 12-hr postexposure. The measured space volume, and the counted average numbers of active smokers and of patrons are given for each venue. The 12-hr cotinine levels are higher than the 2-hr cotinine levels in half the cases; in the other cases, the 12-hr levels are lower. However, for the eight volunteers, 2-hr cotinine values showed an overall average increase of 6.8 ng/ml (SD=4.2; Mdn=5.2), whereas 12-hr cotinine values increased by an average of 7.0 ng/ml (SD=4.4; Mdn=6.0). Thus, there was little difference on average between the 2-hr and 12-hr measurement periods. The creatinine-adjusted net cotinine increase differed little (Mdn=5.0 ng/mgCr) from unadjusted values (Mdn=5.2 ng/ml); however, the variance in the creatinine-adjusted cotinine values was approximately 14 times greater than in the unadjusted cotinine values (280 vs. 20.7). Thus, creatinine adjustment would have increased experimental error considerably and was not performed.

Cotinine-to-SHS-RSP conversion

The relationship between urinary cotinine (U) and airborne nicotine (N) from SHS (see Appendix) can be derived from the pharmacokinetic models (Repace et al., 2006; Repace, Jinot, Bayard, Emmons, & Hammond, 1998; Repace & Lowrey, 1993):

$$U = \kappa\phi\alpha\rho\delta_r HN/\delta_t V_u \quad (1)$$

where κ=1,000 is the number of nanograms per microgram, and for the other parameters, the following default values are assumed: ϕ=0.78 is the nicotine-to-cotinine conversion efficiency by liver enzymes, α=0.71 is the nicotine absorption efficiency through the lung, ρ=0.75 m^3/hr is a typical adult respiration rate (USEPA, 1997) for activity ranging between sedentary and alternate sitting and light work, δ_r=5.9 ml/min is the renal cotinine clearance rate; δ_t=64 ml/min is the total cotinine clearance rate, H=6 is the number of hours of exposure, N=SHS personal air nicotine exposure concentration (μg/m^3), and V_u=1,300 ml is the adult daily urinary output. $D_c=\kappa\phi\alpha\rho HN$ represents the cotinine dose derived from the total nicotine dose. Rearranging, U=(1,000)(0.78)(0.71)(0.75)(5.9)HN/([64][1,300])= 0.029HN, where the values used for the parameters are shown in the brackets in the order in which they appear in the equation. Solving this for N yields: $N=U/([0.029][H])=34.5U/H$, and for an H=6-hr exposure, N (μg/m^3)=34.5U/6=5.75U (ng/ml).

In addition, the SHS-respirable particulate concentration (SHS-RSP) R can be estimated from the nicotine concentration as R=10 N (Repace et al., 1998; Repace & Lowrey, 1993), yielding the following relationship between urinary cotinine and

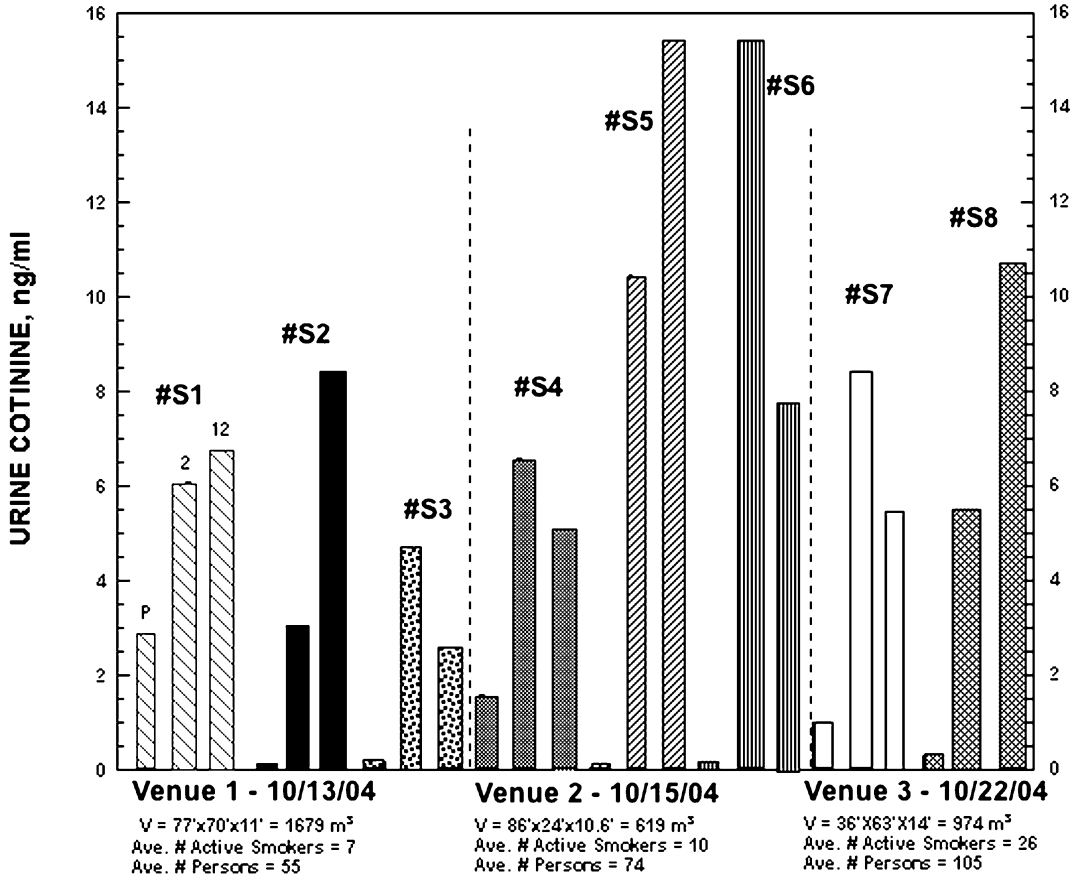

Figure 1. Urinary cotinine concentrations in eight bar patrons measured pre- (P) and 2-hr and 12-hr postexposure to second-hand smoke in three Bismarck bar venues. Patrons were exposed for 6 hr. Also shown are measured space volumes, *V*, time-averaged numbers of active smokers, and total number of persons in each bar.

the 6-hr average SHS-RSP:

$$R_{6-\mathrm{hr}-\mathrm{avg.}}\left(\mu g/m^3\right) = (10)(5.75)\ U = 57.5\ U(\mathrm{ng/ml}) \quad (2)$$

Thus, the 6-hr average increase in RSP exposure for the eight subjects related to their visits to the three bars is based as follows on the average cotinine increase over preexposure baseline from Table 3. The entries in Table 4 are calculated as illustrated: Venue 1, $R_6 = 57.5U = (57.5)(4.28\ \mathrm{ng/ml}) = 246\ \mu g/m^3$. Converting this to a 24-hr average by dividing $R_{6\text{-hr-avg}}$. by 4, to compare to the averaging time of the AQI, yields for venue 1: $R_{24} = (246/4) = 62\ \mu g/m^3$. The total personal air pollution burden for the eight subjects in the three venues is then calculated by adding in, as a non-SHS-RSP background, the outdoor RSP levels estimated above: $6\ \mu g/m^3$ for venue 1 on October 13, yielding a total estimated $PM_{2.5}$ burden of $62+6 = 68\ \mu g/m^3$. The RSP values are calculated similarly for venues 2 and 3, with non-SHS-RSP background levels of $4\ \mu g/m^3$ for October 15 and $11\ \mu g/m^3$ for October 22. The estimated average outdoor background, estimated SHS-RSP levels, and estimated total 6-hr and 24-hr air pollution levels derived from the sum of SHS-RSP plus outdoor background, for all three venues are summarized in Table 4. For comparison, results from the Wilmington, Delaware, air quality study of 6 bars and the 14 bars from the western New York study are included at the bottom of the table.

PPAH fraction of SHS-RSP

In a study of a casino, six bars, and a pool hall in Wilmington, Delaware, and in a controlled experiment, the ratio of RSP to PPAH in SHS was about 2:1 when RSP was expressed in units of micrograms per cubic meter and PPAH in units of nanograms per cubic meter (Repace, 2004). Thus:

$$SHS_{\mathrm{PPAH}}\left(\mathrm{ng/m^3}\right) = 0.5\ SHS_{\mathrm{RSP}}\left(\mu g/m^3\right) \quad (3)$$

Substituting this into Equation 2 yields:

$$PPAH_{6-\mathrm{hr}-\mathrm{avg.}}\left(\mathrm{ng/m^3}\right) = (0.5)(57.5)\ U = 28.8\ U(\mathrm{ng/ml}) \quad (4)$$

Again, for venue 1, the estimated concentration of $PPAH_{6\text{-hr-avg.}} = (28.8)(4.28\ \mathrm{ng/ml}) = 123\ \mathrm{ng/m^3}$, and the estimated PPAH values for the three venues are summarized in Table 4.

Table 4. SHS-RSP & SHS-PPAH estimated from cotinine for three Bismarck bars versus values measured in 6 Wilmington, Delaware (Repace, 2004), and 14 western New York State bars (Travers et al., 2004).

1. Bar venue number, date in 2004	2. Average outdoor background RSP ($\mu g/m^3$)	3. Estimated 6-h average SHS-RSP ($\mu g/m^3$)	4. Estimated 6-h average SHS-PPAH ($\mu g/m^3$)	5. Measured active smoker density, D_s	6. Estimated 24-h average SHS-RSP ($\mu g/m^3$)	7. Estimated 24-h average total RSP ($\mu g/m^3$)
1, Oct. 13	6	246	123	0.41	62	68
2, Oct. 15	4	549	275	2.66	137	141
3, Oct. 22	11	396	198	1.62	99	110
All three venues	7	397 (*SD*=152)	198 (*SD*=176)	1.56 (*SD*=1.1)	—	—

Air quality studies	Average outdoor background RSP ($\mu g/m^3$)	Measured average SHS-RSP ($\mu g/m^3$)	Measured average SHS-PPAH ($\mu g/m^3$)	Measured active smoker density, D_s	Estimated[a] 24-h average SHS-RSP ($\mu g/m^3$)	Estimated[a] 24-h average total RSP ($\mu g/m^3$)
6 Delaware bars	10	149 (*SD*=110)[b]	83 (*SD*=83)[b]	0.47 (*SD*=0.56)[b]	37	47
14 Western New York bars	27	385 (*SD*=328)[c]	—	1.36 (*SD*=0.90)[c]	96	123

Note. Estimated indoor RSP levels from SHS plus outdoor background averaged 57 times higher than outdoor air RSP levels in Bismarck. SHS-RSP levels estimated from urinary cotinine differed by 3% from average levels measured in 14 western New York State bars, and averaged 2.7 times higher than 6 Wilmington, Delaware, bars. [a]Assuming 6-h daily exposure. [b]~30-min averages. [c]~38-min averages.

Discussion

Postexposure cotinine levels

Our finding that the average urinary cotinine concentration was similar at 2 hr and 12 hr after exposure to SHS is in agreement with the results of Willers, Skarping, Dalen, and Skerfving (1995), who performed a semiexperimental exposure study on 21 nonsmokers (aged 37–42 years, M=40) exposed to SHS on a Swedish tour bus for 2 hr. Urinary cotinine concentrations rose until 3-hr postexposure, reached a plateau for 8 hr (range=1–22 hr), and then declined log linearly. This log-linear decrease in concentration had a half-life of 19 hr (95% *CI*=17–20), similar to the 17-hr half-life of cotinine in blood serum reported by Benowitz (1996). This prolonged plateau of urinary cotinine most likely represents a pseudo-equilibrium between cotinine being generated from nicotine as nicotine is being released from body tissues, and the rate of elimination of cotinine. These results indicate that urinary measurements in general are stable for some time after exposure to SHS.

The range of variation in the pharmacokinetic parameters and other uncertainties are discussed in the Appendix. Although individual variations in the pharmacokinetic parameters lend uncertainty to these calculations, a Monte Carlo analysis of the errors involved in predicting air nicotine and salivary cotinine in office workers incorporating 12 different physical and pharmacokinetic parameters with all their known ranges found that the measures of central tendency (means and medians) could be predicted to within 10%, whereas any significant deviations occurred at or above the 90th percentile or below the 40th percentile. In the present study, averaging over several individuals in each bar tends to average out deviations in individual pharmacokinetic parameters. We considered the possibility that drinking in a bar might increase urinary flow rate, resulting in a more dilute urine and lower urinary cotinine concentrations. To the best of our knowledge, the effect of increased urinary flow rate on cotinine renal clearance has not been studied. However, if anything, the result of increased urinary flow would be that we have underestimated the blood cotinine level and therefore underestimated the subjects' exposure to nicotine and tobacco smoke toxins, which does not vitiate our conclusions.

Air exchange rate estimation

Our findings also can be used to examine ventilation practices of these venues using a version of the mass-balance equation called the habitual smoker model (HSM) for the prediction of respirable particulate matter (RSP, 3.5 microns or less, called $PM_{3.5}$) from SHS (SHS-RSP), in units of micrograms per cubic

meter (Repace, 2004; Repace, in press; Repace & Lowrey, 1980):

$$SHS_{RSP} = 650\frac{D_s}{C_v}\left(\mu g/m^3\right) \qquad (5)$$

where D_s is the active smoker (AS) density during the observation time (in units of average number of burning cigarettes [n_s] per hundred cubic meters of space volume), and C_v is the air exchange rate related to ventilation in units of air changes per hour (hr^{-1}). This model assumes a 14 mg RSP per cigarette emission, and the constant incorporates a default 30% decay rate of RSP related to removal by surface deposition (Repace, in press). The HSM assumes that the typical habitual smoker smokes at the national average rate of 2 cigarettes/hr and takes 10 min to smoke a cigarette; a single habitual smoker spends one-third of the hour smoking; therefore, three habitual smokers will consume 6 cigarettes/hr. Thus the average active smoker count n_s, measured over an interval comparable to the cigarette smoking time, multiplied by 3, yields the estimated number of habitual smokers n_{hs} ($n_{hs}=3n_s$). From the venue parameter values shown in Figure 1 for venue 1, $D_s=100\,n_s/V=(100)(7 \text{ AS}/1{,}679\,m^3)=0.42$ active smokers per 100 m^3, and $SHS_{RSP}=246\,\mu g/m^3$ from Table 4, the air exchange rate may be estimated using Equation 5: $C_v=650(D_s)/SHS_{RSP}=(650)(0.42)/246=1.1\,hr^{-1}$. Similarly, for venue 2: $C_v=(650)(10/6.19)/548=1.9\,hr^{-1}$, and for venue 3: $C_v=(650)(26/9.74)/395=4.4\,hr^{-1}$, yielding a three-venue average of $2.5\,hr^{-1}$ ($SD=1.7$) and a range of 1.1–4.4 hr^{-1}.

Smoking prevalence

The venues' smoking prevalence may be estimated from the ratio n_{hs}/P, where P is the average patron count from Figure 1. Using this method, we estimated the smoking prevalence n_{hs}/P for the three venues as follows: Venue 1, $n_{hs}/P=3n_s/P=(3)(7)/55=38\%$; venue 2, (3)(10)/74=41%; and venue 3, (3)(26)/105=74%. By comparison, in 2004 the North Dakota statewide smoking prevalence was 21.5%; for those with 12 or more years of schooling, the prevalence was 18.1%, and in the 18- to 29-year-old age group, it was 25.7%, suggesting that for this college crowd, the nonsmokers are avoiding these smoky venues. This supposition agrees with the results of Biener and Fitzgerald (1999), who found that in 1996 there were more nonsmokers in Massachusetts who avoided patronizing smoky restaurants and bars than there were smokers in the state.

SHS-RSP levels

Our model predictions for 6-hr SHS-RSP exposures for venues 1, 2, and 3 ranged from 246 $\mu g/m^3$ to 396 $\mu g/m^3$ to 549 $\mu g/m^3$ ($M=397$, $SD=152$) for observed active smoker densities ranging from $D_s=0.41$ to 1.62 to 2.66 AS/100 m^3 ($M=1.56$, $SD=1.1$; Table 4). Figure 2 plots the Bismarck, Wilmington, and western New York bar SHS-RSP versus active smoker density D_s. A regression fit is made separately to each of the three sets of data, with the fits forced through zero, to conform to Equation 5. The scatter in the data is interpreted using the HSM as being because of variations in the air exchange rates of each venue. The HSM of Equation 5 also allows us to interpret the reciprocal slope of the regression lines as proportional to the least-squares air exchange rate C'_v for all data in each study, showing the variation of SHS-RSP with D_s for each dataset. The regressions are expressed in the form of $y=kx$, where $k=650/C'_v$. Thus $C'_v=650/k=650/223=2.9\,hr^{-1}$ for Bismarck, and similarly, $C'_v=2.6\,hr^{-1}$ for Wilmington, and $C'_v=2.8\,hr^{-1}$ for western New York. Figure 2 shows that the Bismarck SHS-RSP data estimated from cotinine vary in much the same way with D_s, as do the Wilmington and western New York measured atmospheric SHS-RSP data (Repace, 2004; Travers et al., 2004), further generalizing our results. Non-SHS-RSP background is subtracted from all measured SHS-RSP levels, and preexposure cotinine has been subtracted from postexposure cotinine, justifying a regression forced through zero for comparative slope determination purposes among the three studies; forcing the fit through zero makes goodness-of-fit statistics (e.g., r^2) meaningless.

Figure 3 shows the estimated 24-hr total RSP for the three Bismarck venues from column 7 of Table 4 plotted against the federal AQI. Comparing these results with the breakpoints for the AQI (Table 1), we see that all three bars are "code red," or unhealthy for everyone, with members of sensitive groups at risk for more serious health effects. This finding places the air pollution generated by smoking into a new perspective: Air pollution levels of this magnitude in the outdoor air are regarded by the federal government as unacceptable, and states that fail to control emission sources are penalized. However, in North Dakota, as well as in 41 other states, air pollution in bars goes unregulated. By comparison, by dividing column 2 by the sum of columns 2 and 3 in Table 4, we find that the outdoor RSP air pollution levels in Bismarck were, respectively, (6/252)=2.4%, (4/553)=0.72%, and (11/407)=2.7% of those inside the three bar venues, which were polluted by SHS. Thus, if smoking had been prohibited in these bars, RSP air pollution levels would have dropped by an estimated ~97% to 99%. At this writing, the U.S. states of California, Connecticut, Delaware, Maine, Massachusetts, Montana, New York, Rhode Island, and Vermont

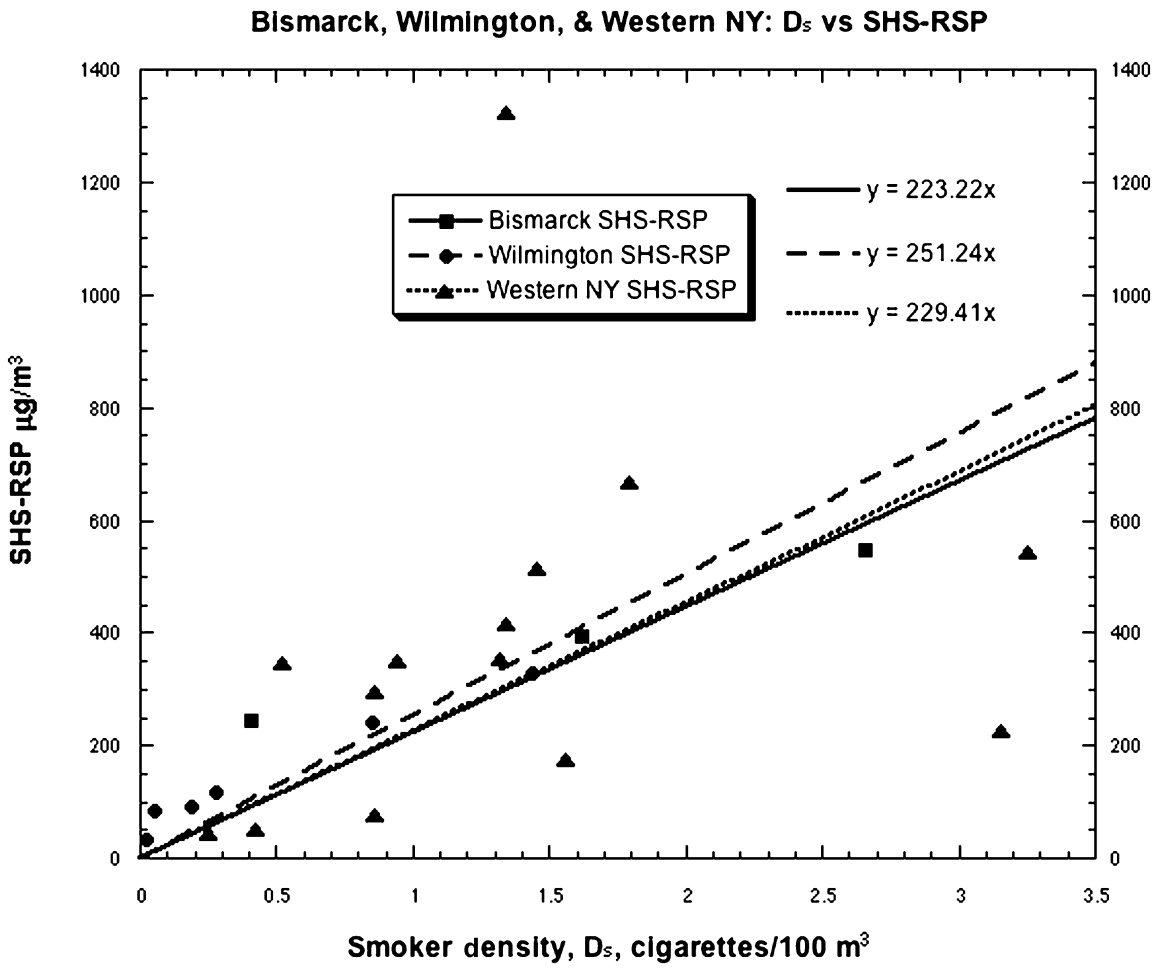

Figure 2. Variation of Bismarck cotinine-estimated SHS-RSP for three bars (squares, 6-hr averages) with measured active smoker density D_s is similar to air-quality-monitor-measured SHS-RSP for 6 bars in Wilmington (circles, ~30-min averages; Repace, 2004) and for 14 bars in western New York (diamonds, ~38-min averages; Travers et al., 2004). Regression lines are force-fit through zero, as per Equation 5. The ratio $k=y/x$ gives the slope of the lines for the three sets of data.

have smoke-free bar laws, and abroad, Bhutan, Ireland, Italy, Malta, New Zealand, Norway, and Sweden have such laws in place as well (Americans for Nonsmokers' Rights, 2006).

PPAH exposures

The estimated average PPAH levels during exposure in the three Bismarck bar venues ranged from 123 ng/m^3 to 275 ng/m^3, and averaged 198 ng/m^3 (SD=176). By comparison, the measured PPAH levels for the six bars in the Wilmington study ranged from 44 ng/m^3 to 249 ng/m^3 and averaged 83 ng/m^3 (SD=83; Repace, 2004). Although outdoor PPAH levels are not measured by the state monitoring system, it is highly likely that these were quite low, because they are particle bound and the outdoor particulate levels shown in Table 2 were very low. As a basis for comparison, in the Wilmington study the outdoor PPAH levels averaged 27 ng/m^3 (SD=28) on the first visit, when the outdoor RSP levels averaged 11 µg/m^3 (SD=3.2), and 3 ng/m^3 (SD=1.9) on the second visit, when outdoor particle levels averaged 2.0 µg/m^3 (SD=1.9). By way of further comparison, the peak 3-hr median PPAH at a Baltimore, Maryland, Harbor Tunnel tollbooth was 199 ng/m^3 (early morning rush hour; Sapkota & Buckley, 2003). Mean estimated PPAH levels in the present study were nearly identical to this other value.

Finally, data from this study were presented to North Dakota state and local lawmakers as supportive evidence of the need for 100% clean indoor air legislation. Study findings also were featured in a number of local media stories examining the effects of SHS. The study looked at the fall of 2004, when the Bismarck Tobacco Free Coalition was in the midst of broad community education efforts. The state of North Dakota ultimately passed clean indoor air legislation that went into effect August 1, 2005, and Bismarck, the capitol city, passed strengthened local legislation that went into effect October 11, 2005. Neither of these laws provide 100% protection

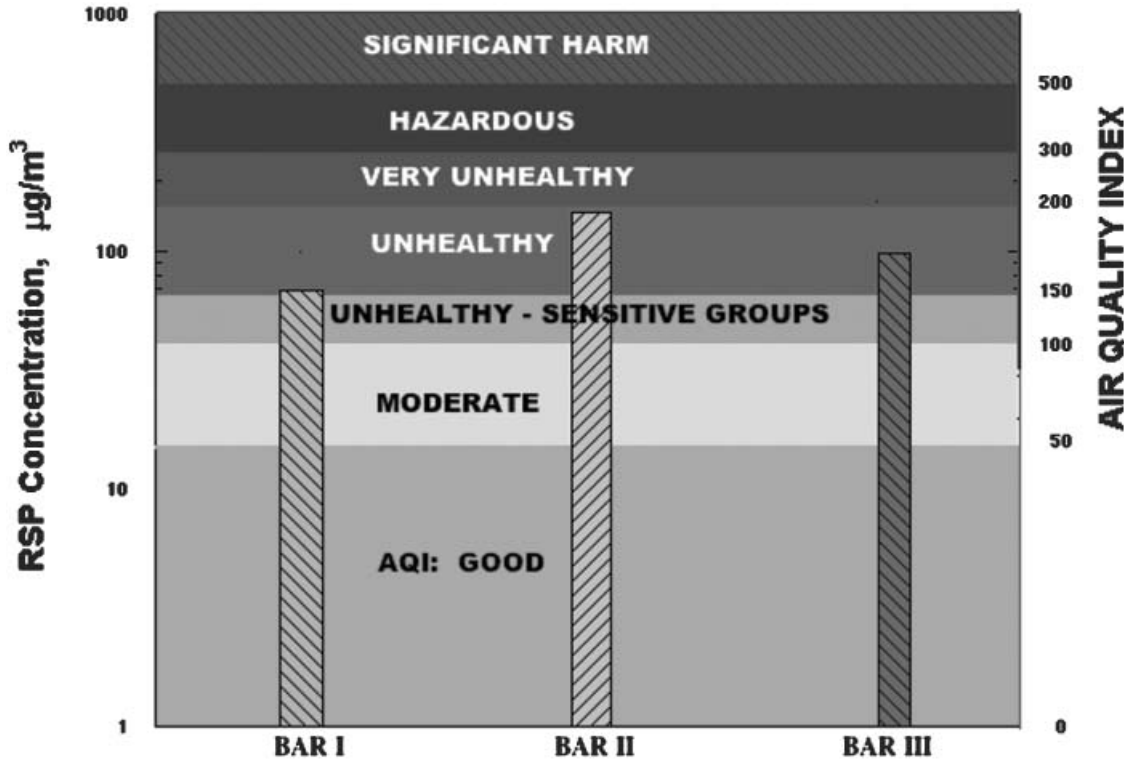

Figure 3. The 24-hr average SHS-RSP plus outdoor background estimated from volunteer patrons' urinary cotinine for three Bismarck bar venues plotted against the health-based federal outdoor Air Quality Index (AQI). All three bars are in the "code red," or unhealthy, range. Contemporaneous outdoor air levels were 1%–3% of indoor levels, and in the "code green," or good, range. The AQI is nonlinearly related to $PM_{2.5}$. See online for colour figure.

for everyone (standalone bars are exempt under both laws), but the Bismarck ordinance, by prohibiting enclosed smoking sections to be built in bars or restaurants, stands as the strongest clean indoor air legislation to date in North Dakota. The results of this study contributed to the successes in Bismarck and in North Dakota by providing strong locally obtained evidence—and publicity for the notion—that unhealthy levels of air pollution related to SHS exist in indoor air in our communities.

Urinary cotinine measured in bar patrons was used to estimate for the first time, using pharmacokinetic and physical modeling, the concentration of inhaled SHS respirable particulate air pollution (SHS-RSP) and SHS smoke carcinogenic particulate polycyclic aromatic hydrocarbons (SHS-PPAH) in three bars. Despite the uncertainties introduced by the method (see Appendix), our estimates compared well with physical air quality measurements made in similar microenvironments, and our method is likely to be particularly useful for situations where air quality monitoring is often impossible, such as in casinos, in prisons, or in workplace disputes over passive smoking. On a 24-hr average basis, using the federal outdoor API for fine particulate matter ($PM_{2.5}$) as a guideline, we found that the estimated RSP air quality in three Bismarck bars was "code red," or unhealthy, because of SHS. Estimated PPAH carcinogen exposure levels were higher than those measured in bars in an air quality study in Wilmington, Delaware, and were identical to the peak 3-hr measurements reported in a study of PPAH at the Baltimore Harbor Tunnel tollbooth, representing a considerable carcinogenic exposure. Although estimated mean air exchange rates for Bismarck were similar, the cotinine-estimated SHS-PPAH and SHS-RSP levels in the three Bismarck bars averaged more than double that measured in six Wilmington, Delaware, bars, probably related to a higher mean smoker density in the Bismarck bars. This work demonstrates the viability of using biomarkers to estimate inhaled short-duration exposure levels to SHS.

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Appendix A: Discussion of uncertainty in the cotinine-to-SHS-RSP conversion

The following relationship can be derived from the pharmacokinetic model of Repace and colleagues (Repace et al., 1998; Repace & Lowrey, 1993):

$$U = \kappa\phi\alpha\rho\delta_r HN/\delta_t V_u \qquad \text{(A1)}$$

where U is the urine cotinine concentration in units of ng/ml, ϕ is the nicotine-to-cotinine conversion efficiency by the liver (#),~ α is the nicotine absorption efficiency through the lung (#), ρ is the subject's estimated respiration rate, δ_r is the renal cotinine clearance rate (ml/min), δ_t is the total cotinine clearance rate, H is number of daily hours of exposure, N=SHS personal air nicotine exposure concentration ($\mu g/m^3$), and V_u=is the daily urinary output in milliliters.

It is of interest to compare Equation A1 with the model of Benowitz and Jacob (1994), who gave an equation for estimating the daily average intake of nicotine D_{sm} (μg/day) in smokers from their steady-state cotinine levels P_{ss} (ng/ml): $D_{sm}=80\ P_{ss}$. Repace and Lowrey (1993) derived, for nonsmokers, the following time-averaged model:

$$P = \kappa\phi\alpha\rho HN/\delta_t T \text{ ng/ml} \qquad \text{(A2)}$$

where T is the averaging time. Taking κ=1,000 ng/mg, the nonsmokers' (ns) daily nicotine dose from SHS is $D_{ns}=\alpha\rho HN$/T (μg/day), and the ratio $D_{ns}/\kappa P=(\alpha\rho HN/T)/([1{,}000][\phi\alpha\rho HN/\delta_t T])=\delta_t/1{,}000\phi=(64$ ml/min)(1,440 min/day)/(780)=118 ml/day. However, Benowitz and Jacob report ϕ=0.72 and δ_t=40.6 ml/min for smokers (sm). Substituting the values for smokers, we find: $D_{sm}/\kappa P=\delta_t/1{,}000\phi=(40.6$ ml/min)(1,440 min/day)/(720)=81 ml/day. Thus Equation A2 is consistent with the results of Benowitz and Jacob (1994). For the time-averaged case, the ratio of Equation A1 to Equation A2 is:

$$U/P=(\kappa\phi\alpha\rho\delta_r HN/\delta_t V_u)/(\kappa\phi\alpha\rho HN/\delta_t T)=\delta_r T/V_u \qquad \text{(A3)}$$

However, we do not have a daily average urinary dose, but a peak urinary dose, from which we wish to estimate the air nicotine concentration, and thence the air SHS-RSP concentration. It can be shown that the difference between a time-averaged model and a peak concentration model involves the substitution of the averaging time T with the residence time for cotinine in serum, τ_c, where τ_c=24.5 h=1,470 min is the cotinine mean life (1.44 times the half-life of 17 hr; Ott et al., 2003; Repace, in press). Thus, for a short-term exposure,

$$U/P=(\kappa\phi\alpha\rho\delta_r HN/\delta_t V_u)/(\kappa\phi\alpha\rho HN/\delta_t T)=\delta_r\tau_c/V_u \qquad \text{(A4)}$$

The relationship between P and N for short-term exposures is:

$$P' = \phi\alpha\rho HN/\delta_r\tau_c \text{ ng/ml} \qquad \text{(A5)}$$

Ott et al. (2003) have shown that equations with the structure of Equation A5 approximate a maximum concentration provided that the exposure time is small compared with the mean life, and that if the mean life is equal to the averaging time, such equations will approximate the average concentration. Thus, because $\tau_c \approx T_d$, Equation A5 will approximate the daily average concentration or represent the peak concentration, since the mean life for cotinine (24.5 hr) is nearly identical to the length of a day.

A final issue is that of the error introduced by this approximation: cotinine dose will increase in blood as $P(t) = P_o\left(1 - e^{-\lambda_n t}\right)$, where $P_o = \phi\alpha\rho N/\delta_t$, and $\lambda_c = 1/\tau_c = 0.0408\,\text{hr}^{-1}$ and t is elapsed time. If the exponential term is expanded in a MacLaurin infinite series and the nonlinear terms are neglected, $P(t) = P_o H/\tau_c$, as in Equation A5. At 2-hr postexposure, or at $t = 8$ hr, 8/24.5 = 0.327. If the full expression is used, the result is $P(8)/P_o = \left(1 - e^{-8\lambda_c}\right) = 0.278$, 15% lower.

Nicotine also will follow the first-order kinetics, with $\lambda_n = 1/\tau_n = 0.347\,\text{hr}^{-1}$, and at 8 hr, $t = 8$, nicotine will have increased to $N(8)/N_o = \left(1 - e^{-8\lambda_n}\right) = 94\%$ of its equilibrium dose. Thus the result of combined overestimation of cotinine and nicotine is (0.94)(0.327) = 0.307, which is a 10.6% overestimate. However, we average the 2-hr and 12-hr cotinines. Willers et al. (1995) found that urinary cotinine had begun to decline after 8 hr in adults. If we allow for a 4-hr decline in cotinine, this is $e^{-4\lambda_c} = 85\%$, yielding a 12-hr postexposure cotinine that is 15% lower than at peak. Thus Equation A5 produces an 11% overestimate, but by averaging in the cotinine at 12 hr, which has declined by an estimated 15%, we use a cotinine value that averages (1–0.85)/2 = 7.5% low. Thus 10.6%–7.5% = ~3% overestimate. This is well within the experimental fluctuations of cotinine and can be neglected.

Repace and colleagues discuss the variation in measured pharmacokinetic parameters in nonsmokers (Repace et al., 2006; Repace et al., 1998; Repace & Lowrey, 1993). In general, δ_r, renal cotinine clearance rates in nonsmokers average 5.9 ml/min ($SD = 1.7$) (based on the three cited studies); δ_t, total cotinine clearance rates average 64 ml/min ($SD = 9$) (based on the three studies); total urine output averages 1,300 ml/day and ranges from 1000 to 1600 ml/day (Bakerman, 1984); and adult respiration rates range from 0.5 m^3/hr for sedentary adults to 1 m^3/hr for light activity (Repace et al., 2006).