



Doses and lung burdens of environmental tobacco smoke constituents in nonsmoking workplaces

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This paper models nicotine dose and ultraviolet-absorbing particulate matter (UVP) alveolar lung burden resulting from exposure to environmental tobacco smoke (ETS) for nonsmokers in workplaces where smoking was reported *not* to occur. Data were obtained from personal monitoring of ETS in 16 U.S. cities [Jenkins R.A., Guerin M.R., Palausky A., Counts R.W., Bayne C.K., and Dindal A.B. Determination of human exposure to environmental tobacco smoke (ETS): a study conducted in 16 U.S. cities. Draft final report by Oak Ridge National Laboratory for Center for Indoor Air Research, Linthicum, MD, 1996a; Jenkins R.A., Palausky A., Counts R.W., Bayne C.K., Dindal A.B., and Guerin M.R. Exposure to environmental tobacco smoke in sixteen cities in the United States as determined by personal breathing zone air sampling. *J. Expos. Anal. Environ. Epidemiol.* 1996b: 6(4): 473–502.]. This is a continuation of earlier analyses focusing on nonsmokers in smoking workplaces (SWs) [LaKind J.S., Graves C.G., Ginevan M.E., Jenkins R.A., Naiman D.Q., and Tardiff R.G. Exposure to environmental tobacco smoke in the workplace and the impact of away-from-work exposure. *Risk Anal.* 1999a: 19(3): 349–358; LaKind J.S., Jenkins R.A., Naiman D.Q., Ginevan M.E., Graves C.G., and Tardiff R.G. Use of environmental tobacco smoke constituents as markers for exposure. *Risk Anal.* 1999b: 19(3): 359–373; LaKind J.S., Ginevan M.E., Naiman D.Q., James A.C., Jenkins R.A., Dourson M.L., Felter S.P., Graves C.G., and Tardiff R.G. Distribution of exposure concentrations and doses for constituents of environmental tobacco smoke. *Risk Anal.* 1999c: 19(3): 375–390.]. Even though study participants characterized their workplaces as nonsmoking, some individuals reported observing cigarettes in the workplace. Individuals observing six or more cigarettes were excluded from the analysis on the grounds that they were in *de facto* SWs. Exposure to ETS was lower in nonsmoking than SWs, but even with this exclusion, exposure was not zero. Distributions were selected for each model input, and at least 2000 iterations of the model were made for each dose or lung burden characterization (e.g., for females, for males). In these nonsmoking workplaces (NSWs), neither nicotine nor UVP concentrations were lognormally distributed. Hence, observed concentrations were used directly via bootstrap sampling (nicotine) or a constant number of times (UVP) as input to the models. As in SWs, individuals from smoking homes (SHs) experienced greater exposure in NSWs to both nicotine and UVP than did individuals from nonsmoking homes (NSH; $P < 0.001$). The distributions of modeled nicotine dose and UVP lung burden were highly skewed, with most individuals receiving relatively low exposure to ETS in the workplace. Comparing doses from NSWs modeled here to doses from SWs modeled previously, less difference between smoking and NSWs was apparent in UVP levels than in nicotine levels. For average exposure, UVP alveolar lung burdens were approximately 10-fold higher in smoking than NSWs, while average nicotine doses were 20–25 times higher in smoking than NSWs. These findings are in the range observed by other investigators and are partly explained by very low denominators in the ratios (i.e., very low levels experienced in NSWs). For upper bound exposure, the nonsmoking-to-smoking ratios remained about the same for UVP. For nicotine, the upper bound ratios remained the same for people from NSHs but were halved for people from SHs. *Journal of Exposure Analysis and Environmental Epidemiology* (2000) 10, 365–377.

Keywords: 16-City Study, dose distributions, environmental tobacco smoke (ETS), nicotine, UVP, workplace exposure.

Introduction

This paper uses distributional analysis techniques to derive estimates of distributions of nicotine dose and ultraviolet-

absorbing particulate matter¹ (UVP) alveolar lung burden obtained in nonsmoking workplaces (NSWs). It is a continuation of the work discussed in three earlier reports on workplaces where smoking was reported to occur (LaKind et al., 1999a,b,c). The present paper, as well as the three previous reports, were based on a large personal monitoring study (the 16-City Study) that was designed to obtain realistic data on exposure to some constituents of environmental tobacco smoke (ETS) both at work and

1. Abbreviations: 3-EP, 3-ethenyl pyridine; EPA, U.S. Environmental Protection Agency; ETS, environmental tobacco smoke; FPM, fluorescing particulate matter; ICRP, International Commission on Radiological Protection; MMD, mass median diameter; NSH, nonsmoking home; NSW, nonsmoking workplace; RSP, respirable suspended particulate matter; SH, smoking home; SW, smoking workplace; UVP, ultraviolet-absorbing particulate matter.

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¹UVP is a measure of combustion-derived particulate matter and, as such, is a more specific indicator of particulate matter attributable to ETS than is respirable particulate matter (Ogden and Maiolo, 1989; Conner et al., 1990; Nelson et al., 1992).

away from work in 16 cities in the United States (Jenkins et al., 1996a,b).

The three earlier articles focused on the following:

- Patterns of exposure for various ETS constituents in workplaces where smoking occurred, and the impact on individual ETS exposure of away-from-work exposure and personal characteristics such as age, gender, race, income, education, and city of residence (LaKind et al., 1999a).
- The utility of various ETS constituent chemicals as markers for ETS workplace exposure. The ETS constituents included three gas phase ETS constituents — nicotine, 3-ethenyl pyridine (3-EP) and myosmine — and five particulate phase constituents — respirable suspended particulate matter (RSP), UVPM, fluorescing particulate matter (FPM), scopoletin, and solanesol (LaKind et al., 1999b).
- The distributions of individual exposure concentrations and doses for constituents of ETS encountered in workplaces where smoking occurred (LaKind et al., 1999c).

In the 16-City Study, participants were nonsmokers categorized in one of four cells according to whether they worked and/or lived in smoking environments. Cell definitions and sample sizes are shown in Table 1.² While cells were defined in this study according to the smoking/nonsmoking status within the workplace and home, exposure was measured at work and away from work. The away-from-work exposure included exposure at home, of course, but also included exposure encountered during other activities undertaken on the day of sampling (e.g., shopping, transportation, eating out, and other entertainment).

The earlier articles focused on subjects in cells 1 and 3 (i.e., smoking workplaces, SWs) because these cells included the work environments where the most smoking occurred. This focus was dictated by the expectation that environments with the most substantial exposure would yield the clearest picture of the effects of personal characteristics on exposure levels. Indeed, the highest workplace exposure concentrations resulted in the highest workplace dose levels and proved useful in assessing the utility of ETS constituent concentrations as indicators of ETS exposure (LaKind et al., 1999b,c).

The current paper extends the work reported in LaKind et al. (1999c) (i.e., the derivation and evaluation of distributions of workplace exposure and dose), but focuses on workplaces where smoking was reported *not* to occur

Table 1. Definition of cells in the 16-City Study.

Cell	Workplace	Home	Number in 16-City Study
1	Smoking	Smoking	175
2	Nonsmoking	Smoking	248
3	Smoking	Nonsmoking	298
4	Nonsmoking	Nonsmoking	843
All			1564

(i.e., subjects in cells 2 and 4). Study participants were categorized as members of these cells if they indicated on a screening questionnaire that either smoking was banned in their workplace or no co-workers, visitors, or clients smoked and, thus, smoking did not typically occur within 100 ft of their personal work space. Some of these same participants later reported on workplace diaries that they observed cigarettes in the workplace.

The rationale for the examination of these groups was that, although exposures to ETS were much lower in NSWs than SWs, exposures were not zero. Lower exposure levels should result in less “signal” from which to evaluate both the effect of personal characteristics on exposure and the utility of ETS constituents as exposure markers. Hence, the main focus of this work was to determine the distribution of ETS exposure in terms of nicotine dose and UVPM alveolar burden in workplaces perceived by study participants to be nonsmoking, and then to compare this result to the earlier evaluation of exposure in SWs. Such a comparison should yield a picture of the incremental exposure that results from a workplace where smoking occurs.

One of the findings from the first report (on the influence of personal characteristics on exposure) was that workers in cell 1 (SW and smoking home, SH) had significantly higher workplace exposure than workers from cell 3 (SW but nonsmoking home, NSH). The present paper also examined this phenomenon in the NSWs to determine if a similar relationship existed there.

Methods

The data considered here are the exposure results from the 16-City Study for the individuals in cells 2 and 4 (i.e., individuals from NSWs). In addition, some comparisons are drawn relative to the results for individuals in cells 1 and 3 (i.e., those from SWs). The 16-City Study is described in detail elsewhere (Jenkins et al., 1996a,b; LaKind et al., 1999a). The focus here is on two of the original eight ETS constituents measured in the study — nicotine and UVPM. This follows from the earlier evaluation of markers of ETS exposure (LaKind et al., 1999b), which found that in terms of the number of subjects who experienced quantifiable levels of ETS components and the availability of toxicological data, nicotine was the most useful marker for gas phase

²Jenkins et al. (1996a,b) omitted 66 cases because their salivary cotinine levels indicated that they were, at least, occasional smokers. The analysis presented here did not make this exclusion because the workplace levels of these occasional smokers were not significantly different from those of the remainder of the study population.

Table 2. Percentages of people in each cell observing a given number of cigarettes.

Number of cigarettes observed	Cell 1: SH, SW	Cell 2: SH, NSW	Cell 3: NSH, SW	Cell 4: NSH, NSW	All cells
0	12.6	78.2	31.3	86.0	66.1
1–5	34.9	18.5	36.7	11.6	20.1
6–10	21.1	2.1	17.3	1.8	7.0
11–15	15.4	1.2	5.4	0.5	3.2
16–20	5.7	0	2.4	0.1	1.2
21–25	3.4	0	2.4	0	0.8
26–30	1.7	0	2.0	0	0.6
>30	5.1	0	2.4	0	1.0

SH: Smoking home; SW: smoking workplace; NSW: nonsmoking workplace; NSH: nonsmoking home.

exposure and UVPM was the best marker for particle phase exposure in workplaces where smoking occurred.

An initial inspection of the data showed that 2–3% of individuals in cells 2 and 4 (eight and 20 individuals, respectively) observed six or more cigarettes during the course of their work day (Table 2). Since observation of this number of cigarettes was more typical of a SW than a NSW, these individuals were excluded from the analysis on the grounds that they were in *de facto* SWs. Including these individuals in the analysis would have understated differences between smoking and NSWs.

In addition, two individuals in cell 4 were excluded from the nicotine analysis because the apparatus used to collect gas phase constituents failed. Finally, some individuals were excluded from the analyses because their time either at work

or away from work was considered too short. Five individuals in cell 2 and eight in cell 4 were excluded because their reported work day was less than 1 h, and two individuals in cell 4 were eliminated because their time away from work was less than 2 h. After these adjustments were made, data from 235 individuals in cell 2 were available for both the nicotine and UVPM analyses. In cell 4, data from 811 and 813 individuals, respectively, were included in the nicotine and UVPM analyses.

The 16-City Study provided actual, personal breathing zone concentrations of ETS constituents to which each individual was exposed. Measured concentrations of ETS constituents in NSWs were generally low, many below the limit of detection (LOD). In fact, some of these concentration values were reported as negative values because they

Table 3. Number of observations and statistics by constituent and cell.

Constituent	Parameter	Cell 2: NSW, SH	Cell 4: NSW, NSH
Nicotine	Average 8-h LOD ^a	0.0405 $\mu\text{g}/\text{m}^3$	0.0405 $\mu\text{g}/\text{m}^3$
	Total number observations	235	813
	Number missing	0	2
	Number < 0	15	94
	0 ≤ Number ≤ LOD	75	437
	Number > LOD	145	280
	Median value	0.06 $\mu\text{g}/\text{m}^3$	0.02 $\mu\text{g}/\text{m}^3$
	Mean of values as observed	0.2438 $\mu\text{g}/\text{m}^3$	0.0780 $\mu\text{g}/\text{m}^3$
	Mean with negative values set to 0	0.2448 $\mu\text{g}/\text{m}^3$	0.0796 $\mu\text{g}/\text{m}^3$
UVPM	Mean with all values < LOD set to LOD/2	0.2458 $\mu\text{g}/\text{m}^3$	0.0841 $\mu\text{g}/\text{m}^3$
	Average 8-h LOD ^a	0.7185 $\mu\text{g}/\text{m}^3$	0.7185 $\mu\text{g}/\text{m}^3$
	Total number of observations	235	813
	Number < 0	1	29
	0 ≤ Number ≤ LOD	78	333
	Number > LOD	156	451
	Median value	1.07 $\mu\text{g}/\text{m}^3$	0.82 $\mu\text{g}/\text{m}^3$
	Mean of values as observed	3.2715 $\mu\text{g}/\text{m}^3$	1.5446 $\mu\text{g}/\text{m}^3$
	Mean with negative values set to 0	3.2718 $\mu\text{g}/\text{m}^3$	1.5504 $\mu\text{g}/\text{m}^3$
Mean with all values < LOD set to LOD/2	3.2602 $\mu\text{g}/\text{m}^3$	1.5554 $\mu\text{g}/\text{m}^3$	

NSW: Nonsmoking workplace; SH: smoking home; NSH: nonsmoking home.

^aLimit of detection (LOD).

were less than values observed for blank control samples. If these data were being used in a quantitative risk assessment, the authors might have substituted one-half the detection limit for observations below the LOD. The authors decided it was more valid for the dose and lung burden estimations described here to use the data as observed. However, all observations below zero were set to zero because actual concentrations must be positive and zero is the closest physically possible value to the measured value. The data, as observed (with negative observations set to zero), provided some distribution of values below the LOD rather than having all low values equal to one-half the LOD. As shown in Table 3, setting negative observations to zero made little difference in mean concentrations and, of course, no difference on the median value. An additional reason for using this convention was to estimate doses and lung burdens for NSWs in the same manner as those estimated for SWs in previous publications.

Because chemical concentrations in studies of this nature tend to be lognormally distributed (Ott, 1990), the Kolmogorov–Smirnov goodness-of-fit test (Lilliefors option) was applied to determine whether the concentration data from NSWs followed the lognormal distribution. In the earlier work on cells 1 and 3, UVPM was shown to be lognormally distributed, and nicotine was lognormal in cell 3 but not in cell 1 (LaKind et al., 1999c). However in cells 2 and 4, neither nicotine nor UVPM was considered to be lognormally distributed.

In spite of the lack of fit to the lognormal distribution, the data were transformed by taking base 10 logarithms for

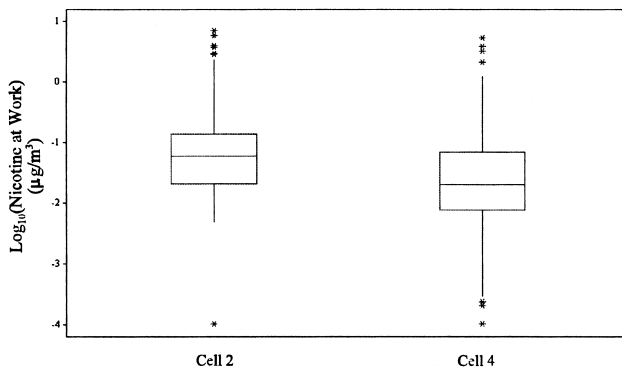


Figure 1. Box plots of nicotine concentrations (\log_{10} scale) observed in NSWs by cell. People observing more than five cigarettes in the workplace were excluded. Cell 2 is SH, NSW; cell 4 is NSH, NSW. Legend for box- and-whisker plots: the box illustrates the interquartile range (IQR) (i.e., the middle half of the observations from the 25th percentile [bottom of box] to the 75th percentile [top of box]). The line in the box is the median. The lines extending from the box (the whiskers) cover the observations within 1.5 times the IQR from the box. The * represents possible outliers and denotes observations from 1.5 to 3 IQR from the box. The O represents probable outliers and denotes observations more than three IQR from the box.

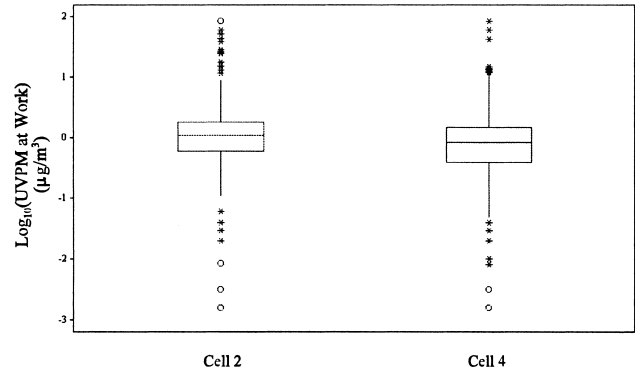


Figure 2. Box plots of UVPM concentrations (\log_{10} scale) observed in NSWs by cell. People observing more than five cigarettes in the workplace were excluded. Cell 2 is SH, NSW; cell 4 is NSH, NSW.

purposes of data display. Since some of the observed concentrations were zero and because the logarithm of zero was undefined, the log concentrations for those zero observations were set to the logarithm of one-half the lowest reported positive concentration. In this way, all values could be plotted and quantities such as the median could be calculated correctly. Figures 1 and 2 present box plots, by cell, of the distributions of the log-transformed nicotine and UVPM concentrations obtained in NSWs. These figures, together with Table 3, show that nicotine and UVPM are found in measurable quantities even in NSWs; however, the distributions are skewed. Comparison to data from the SWs considered earlier (LaKind et al., 1999c) show that distributions of concentrations from NSWs were more skewed than data from SWs (i.e., they have a greater proportion of values below the LOD). Consistent with the results observed in SWs, the observed concentrations of both nicotine and UVPM in NSWs are greater for individuals from SHs (cell 2) than from NSHs (cell 4).

As mentioned above, the primary purpose of this research was to use distributional analysis techniques to derive estimates of distributions of both nicotine dose and UVPM alveolar lung burden for individuals who work in NSWs. Toxicokinetic information exists for nicotine, so estimating systemic dose for this compound was reasonable. Lung burden, rather than dose, was estimated for UVPM for several reasons. UVPM is a complex mixture of many, varied compounds, each with unique physical and toxicological properties. Because of the complexity of UVPM, an absorbed dose cannot be definitively estimated. In addition, little is known about the toxicokinetics of many of the components of UVPM. Because neither nicotine nor UVPM was parametrically distributed, bootstrapping without *a priori* assigning a distribution was used. To accomplish this, the N observed data values were read into a data vector. A concentration to be used as the model input was produced by selecting a random number between 1 and N and using

the corresponding element of the data vector as the model input (i.e., the primary data themselves, rather than a distribution derived from the data, were the basis for dose and lung burden estimations using random selection of the observed values).

Different methods were used to derive gas (nicotine) and particulate phases (UVPM) estimates. The following sections include brief descriptions of the methods used to estimate workplace dose distributions of nicotine and lung burden distributions of UVPM. Further detail is provided in LaKind et al. (1999c). Two parameters used for both gas and particulate phases modeling are discussed first.

Parameters Used for Both Gas and Particulate Phases Estimations

The lognormal distributions from Brainard and Burmaster (1992), as given in the Exposure Factors Sourcebook (AIHC, 1994), were used for body weight distributions. For men, the geometric mean was 76.83 kg and the geometric standard deviation (SD) was 1.18. For women, the geometric mean was 64.82 kg and the geometric SD was 1.22. These distributions have been widely used and are generally accepted by the U.S. Environmental Protection Agency (EPA) (U.S. EPA, 1996b).

The probability distribution of breathing rates (minute volumes) for adult, indoor workers was developed from the statistical data published by Johnson et al. (1992) together with data for other demographic groups from the Cincinnati Activity Diary Study (Johnson, 1987). These rates were adopted by the EPA (U.S. EPA, 1996a). The analyses assumed a lognormal distribution of breathing rates with a geometric mean of 0.83 m³/h for men and 0.70 m³/h for women. For the nicotine dose modeling, a geometric SD of 1.34 was used. For the UVPM lung burden modeling, the geometric SD was reduced to 1.2 to reflect the long-term nature of the exposure.

Estimation of Gas Phase Nicotine Dose

The exposure analysis for gas phase nicotine was conducted as a Monte Carlo simulation where the observed data were sampled to provide the concentration term and probability distributions were specified for each of the other model inputs. The distributions for body weight and breathing rate have been described in the paragraphs above.

Daily exposure durations at work were derived from data provided by 16-City Study participants as part of their workplace diaries (Jenkins et al., 1996a,b). These values were used directly in the estimation of nicotine doses using bootstrap (i.e., random) sampling from the reported work durations. The mean work duration was 8.17 h and the SD was 1.61 h.

Two nicotine-specific parameters were required to model systemic dose of nicotine half-life in the body and fraction absorbed. Distributions for these parameters were determined based on a review of the literature. The half-life of nicotine in the body was assumed to be a triangular distribution with a minimum value of 1 h, a most likely value of 2 h, and a maximum value of 4 h (Benowitz et al., 1982; Feyerabend et al., 1985; Robinson et al., 1992; Zevin et al., 1997). The fraction of nicotine absorbed was assumed to be uniformly distributed between 0.6 and 0.8 (Armitage et al., 1975; Russell and Feyerabend, 1978; Benowitz and Jacob, 1987; Iwase et al., 1991; Molander et al., 1996).

Because the lack of fit to a lognormal distribution was pronounced in both cells 2 and 4, the observed nicotine concentrations were used directly via bootstrap sampling; i.e., when a nicotine exposure concentration was required as an input to the model, an actual nicotine measurement was selected at random from the 235 observed concentrations in cell 2 or from the 811 observed concentrations in cell 4.

The steps involved in modeling nicotine dose are summarized in Table 4, and were presented in detail in LaKind et al. (1999c). A separate model was specified for

Table 4. Steps used in estimating dose distributions of nicotine.

Sequence	Action
1	Select a gender (male or female) and cell (2 or 4)
2	For each of 2000 individuals, randomly select body weight, elimination half-life, and fraction absorbed
3	Based on the randomly selected half-life, calculate an adjustment factor for the 15-min exposure intake
4	Follow each individual for a calendar week using a 15-min time step (7 days/week × 24 h/day × 4 time steps/h = 672 time steps/week)
5	On each work day, select a random nicotine exposure level from observed concentrations in cell
6	On each work day, select a random length for the workday
7	For each hour (or fraction thereof) of the work day, select a random breathing rate
8	For each time step, calculate the decay-adjusted nicotine intake (zero for nonwork exposures), and calculate body burden
9	Calculate average body burden for the week
10	Calculate maximum hourly body burden for the week
11	Normalize average and maximum body burdens to micrograms per kilogram by dividing by the body weight selected in step 2
12	Output simulation result to a file

males and females within each cell, and the model was run 2000 times for each gender–cell combination. The model simulations covered 1 week of exposure. Due to the short half-life of nicotine, nicotine present in the body at the end of the prior work week (Friday) will have been virtually eliminated from the body by the start of the next work week (the following Monday). Because nicotine is not carried over in the body from the prior work week, modeling a 1-week period was sufficient to properly characterize the distribution of nicotine dose from workplace exposure.

As in the previous study, a sensitivity analysis of the model was performed to determine whether the variability in the modeled results might be understated because nicotine concentrations in some workplaces and thus worker exposures might be consistently higher than in other workplaces. The sensitivity analysis was performed in exactly the same manner as the modeling described above with the exception that individuals were randomly assigned to the top or bottom 50% of nicotine exposures (i.e., nicotine concentrations were manipulated to increase their variability).

Estimation of Particulate Phase UVPM Lung Burden

For UVPM exposure, the International Commission on Radiological Protection Publication 66 Respiratory Tract Model (ICRP66) was selected to estimate lung burdens in the alveolar region of the lung, a region that accounts for over 99% of the total lung burden (ICRP, 1994; James et al., 1996). ICRP66 was used to model the long-term lung burden of an exposure to a constant concentration for a period of 2 years, 5 days/week, 8 h/day. This model is, in effect, a statistical description of the results of a very complex model that incorporates factors such as lung geometry and differential clearance of particles of varying sizes and compositions. Thus, it does not lend itself to the probabilistic approach used to model nicotine dose.

The body weights and breathing rates necessary for the UVPM simulation were described above. For this particulate phase simulation, it was necessary to assume that, on

average, a work day was 8 h. This assumption of a constant length work day was required because of the inability of the model to incorporate variable exposure durations in estimating particle loading and clearance in the respiratory tract.

Because UVPM concentrations in cells 2 and 4 did not follow a lognormal distribution, an approach that paralleled the bootstrap methods used in the gas phase modeling of nicotine was used to model UVPM lung burden. For cell 2, there were 233 positive UVPM values, while for cell 4, there were 783 positive UVPM values. It seemed unreasonable to assume that long-term exposure would be zero even in nonsmoking offices; thus, the small percentage of zero measurements of UVPM (1% in cell 2 and 4% in cell 4) was excluded. Rather than randomly resample the UVPM measurements, each value was used *N* times in the calculations to attain at least 2000 simulations of lung burden; i.e., the 233 nonzero observations in cell 2 were each used nine times for a total of 2097 exposure estimates. Likewise, the 783 nonzero observations in cell 4 were each used three times for a total of 2349 exposure estimates in this cell. This approach is philosophically and mathematically similar to Latin hypercube sampling, wherein each probability distribution is divided into quantiles (e.g., quintiles, deciles, etc.), and an equal number of random measurements is drawn from each quantile. For the model developed here, each measurement was used an equal number of times, which —though not random— was representative. Separate calculations were performed for men and women within each cell and for UVPM particle mass median diameters (MMDs) of 0.2 and 0.4 μm . This range encompasses the likely range of ETS particle sizes (Black et al., 1987).

The estimates of long-term dose and lung burden are provided with the following caveat: the impact of individual variations in particulate levels, daily breathing rates, and the length of the work day were not considered as part of the modeled estimates presented in this paper. This is an artifact of the study design (Jenkins et al., 1996a,b), which

Table 5. Percentiles of simulated nicotine doses (ng/kg body weight) modeled for NSWs^a.

Gender, cell, and variable	Number of cases	Percentiles				
		5	25	50	75	95
Men, cell 2, average for week	2000	0.1693	0.3755	0.6654	1.528	6.585
Men, cell 2, hourly maximum	2000	1.373	3.201	6.391	17.30	96.00
Men, cell 4, average for week	2000	0.06013	0.1478	0.2702	0.5145	1.463
Men, cell 4, hourly maximum	2000	0.5878	1.475	2.616	5.734	19.40
Women, cell 2, average for week	2000	0.1697	0.3744	0.6653	1.535	6.569
Women, cell 2, hourly maximum	2000	1.360	3.176	6.430	17.40	95.30
Women, cell 4, average for week	2000	0.05849	0.1460	0.2666	0.5106	1.435
Women, cell 4, hourly maximum	2000	0.5692	1.464	2.625	5.767	19.60

^aParticipants who observed more than five cigarettes at work were excluded.

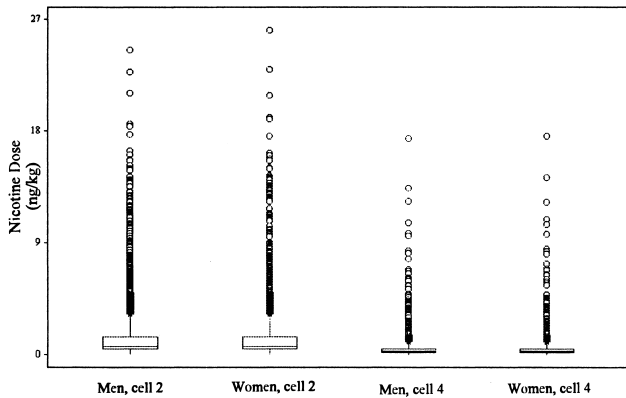


Figure 3. Box plots of average nicotine doses encountered in NSWs by gender and cell. Cell 2 is SH, NSW; cell 4 is NSH, NSW.

provided only single-day ETS measurement data for a large number of individuals, but no multiple exposure measurements for any individual. Thus, the data provide an estimate of variability across individuals, but not an estimate of variability in exposure for an individual. Instead, a conservative assumption was made that the observed variability was entirely due to variability across individuals (i.e., that the single measurement was representative of the long-term exposure of an individual).

In addition to deriving nicotine doses and UVPM lung burdens in NSWs, the earlier finding — that in SWs, individuals from SHs (cell 1) had higher exposures than individuals from NSHs (cell 3) — was investigated in NSWs; i.e., did individuals in cell 2 have higher exposures to nicotine and UVPM than individuals in cell 4? This hypothesis was examined graphically using box-and-whisker plots and then tested using the Mann-Whitney rank-sum test for differences in exposure level.

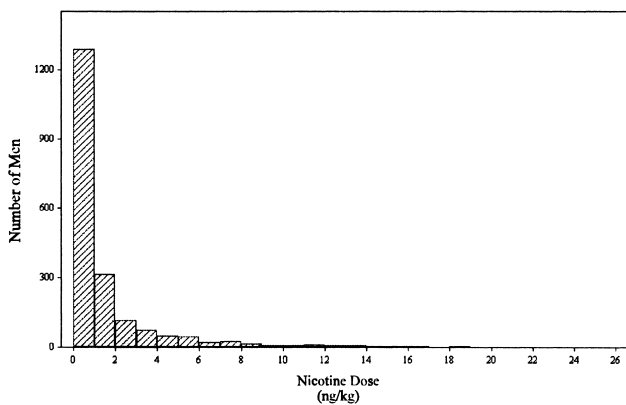


Figure 4. Representative histogram of average nicotine dose encountered in NSWs for men in cell 2 (SH, NSW).

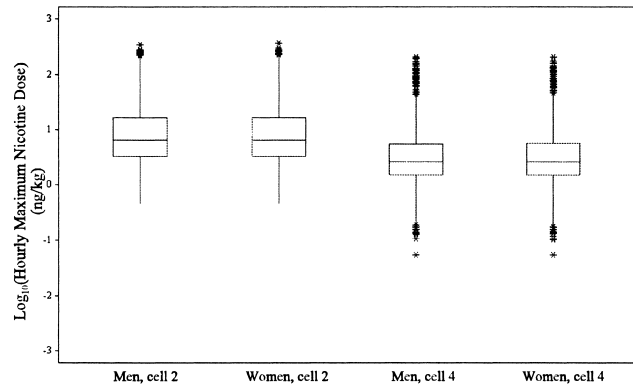


Figure 5. Box plots of hourly maximum nicotine doses encountered in NSWs (log₁₀ scale) by gender and cell. Cell 2 is SH, NSW; cell 4 is NSH, NSW.

Results

Inspection of Figures 1 and 2 suggests that individuals from self-reported SHs (cell 2) may have higher NSW exposures than individuals from self-reported NSHs (cell 4). Mann-Whitney rank-sum tests applied to the nicotine and UVPM exposure concentration data from cells 2 and 4 validated this impression. The difference was highly significant ($P < 0.001$) for both nicotine and UVPM, and the absolute difference was greater for nicotine than for UVPM.

Modeling Results

Results from the nicotine dose model are presented in Table 5 and in Figures 3–6. Several points are illustrated here. First, the distribution of modeled nicotine dose is highly skewed (Figure 3); i.e., a small number of individuals experience a relatively high dose while most individuals receive relatively low doses from exposure to

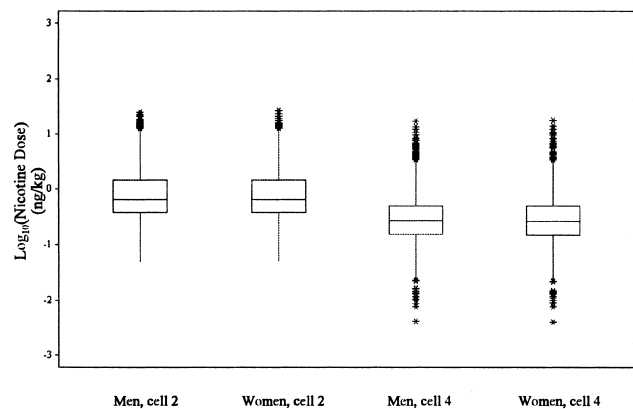


Figure 6. Box plots of average nicotine doses encountered in NSWs (log₁₀ scale) by gender and cell. Cell 2 is SH, NSW; cell 4 is NSH, NSW.

Table 6. Sensitivity analysis results showing percentiles of simulated nicotine doses (ng/kg body weight) modeled for men in NSWs^a.

Gender, cell, and variable	Number of cases	Percentiles				
		5	25	50	75	95
Men, cell 2, average for week	2000	0.07749	0.1613	0.4286	1.602	6.860
Men, cell 2, hourly maximum	2000	0.6920	1.177	2.418	13.60	98.50
Men, cell 4, average for week	2000	0.01836	0.04089	0.09945	0.6495	1.905
Men, cell 4, hourly maximum	2000	0.1795	0.3427	0.7166	5.202	20.00

^aParticipants who observed more than five cigarettes at work are excluded.

Table 7. Percentiles of simulated UVPM alveolar lung burdens (μg) derived from Monte Carlo error propagation for NSWs^a.

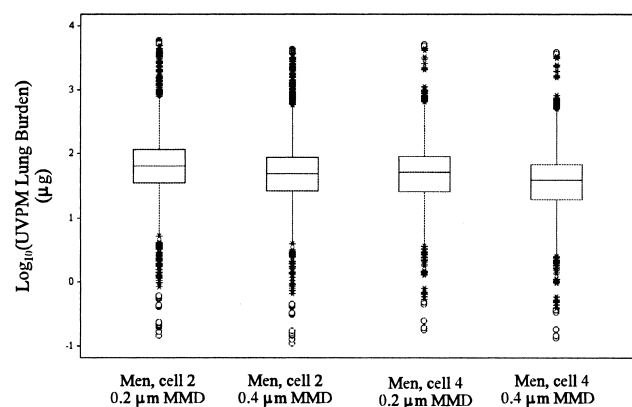
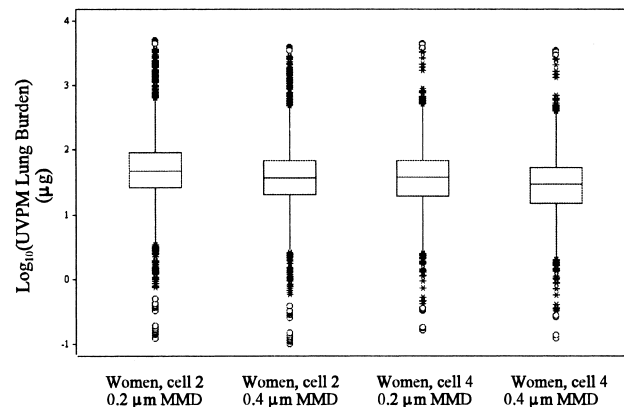
Gender, cell, and MMD	Number of cases	Percentiles				
		5	25	50	75	95
Men, cell 2, MMD=0.2 μm	2097	11.126	34.159	65.228	119.82	771.13
Men, cell 2, MMD=0.4 μm	2097	8.4554	25.771	49.038	89.946	579.66
Men, cell 4, MMD=0.2 μm	2349	8.3745	25.231	51.060	92.991	255.08
Men, cell 4, MMD=0.4 μm	2349	6.2720	18.979	38.520	70.253	193.73
Women, cell 2, MMD=0.2 μm	2097	7.8239	25.421	47.839	92.086	630.27
Women, cell 2, MMD=0.4 μm	2097	6.0347	19.668	37.023	70.885	485.31
Women, cell 4, MMD=0.2 μm	2349	5.9029	19.018	37.774	71.349	200.66
Women, cell 4, MMD=0.4 μm	2349	4.5817	14.738	29.251	55.085	155.54

^aParticipants who observed more than five cigarettes at work are excluded.

ETS at work. This is further illustrated in Figure 4 by the histogram of nicotine doses for men in cell 2. The histograms for women and for cell 4 are similar but are not shown.

Because of the skewness, it is informative to illustrate the model results using a log scale as in Figures 5 and 6. As expected, hourly maximum nicotine exposure (Figure 5) is 10 times higher than the time-weighted average exposure (Figure 6). Next, as the analysis of exposure levels in cell 2

vs. cell 4 suggests, dose levels from work exposure are higher for individuals from SHs (cell 2) than for individuals from NSHs (cell 4), even in NSWs. Finally, the sensitivity analysis shows that restricting individuals to the upper or lower 50% of the nicotine exposure distribution had greater impact on the lower percentiles. The 95th percentile values are essentially the same for the original dose estimates and for those calculated with the restriction on the nicotine concentration. Table 6 includes the

**Figure 7.** Box plots of UVPM alveolar lung burdens encountered in NSWs (\log_{10} scale) for males by cell and MMD of particles. Cell 2 is SH, NSW; cell 4 is NSH, NSW.**Figure 8.** Box plots of UVPM alveolar lung burdens encountered in NSWs (\log_{10} scale) for females by cell and MMD of particles. Cell 2 is SH, NSW; cell 4 is NSH, NSW.

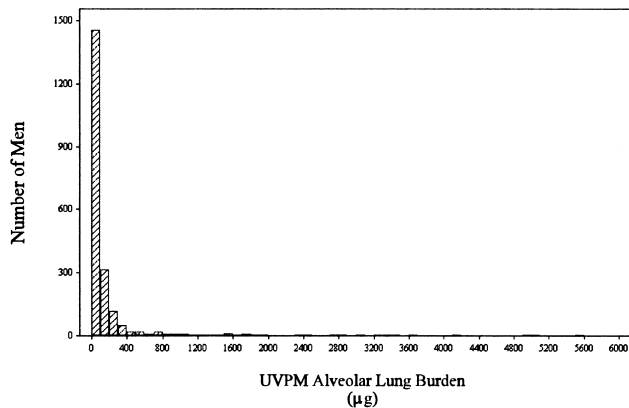


Figure 9. Representative histogram of UVPM alveolar lung burden encountered in NSWs for men in cell 2 (SH, NSW) from simulation with MMD of particles of 0.2 µm.

sensitivity analysis results for men; results for women are similar. These results parallel those found in the earlier study of exposure and dose in cells 1 and 3 (LaKind et al., 1999c).

Results from the UVPM alveolar lung burden model are presented in Table 7 and Figures 7–9. Like the nicotine doses, UVPM lung burdens are highly skewed. This skewness is evident in the histogram shown in Figure 9. In general, individuals in cell 2 (SHs) have higher predicted alveolar lung burdens of UVPM (as estimated from concentrations in NSWs) than individuals in cell 4 (NSHs). Assuming a smaller MMD (0.2 vs. 0.4 µm) results in a higher alveolar lung burden for individuals in both cells, but does not change the relationships between the cells. Estimated alveolar lung burdens of UVPM particles for males are 1.2–1.4 times the estimated lung burdens for

Table 8. 50th and 95th percentiles of predicted nicotine TWA and hourly maximum doses (ng/kg body weight) and UVPM alveolar lung burdens (µg) from exposure at work by cell.

	SW	NSW		SW	NSW
Nicotine TWA 50th percentile (ng/kg), males			Nicotine TWA 95th percentile (ng/kg), males		
SH	15.40	0.6654	SH	67.10	6.585
NSH	4.920	0.2702	NSH	29.50	1.463
Nicotine TWA 50th percentile (ng/kg), females			Nicotine TWA 95th percentile (ng/kg), females		
SH	15.40	0.6653	SH	68.00	6.569
NSH	4.851	0.2666	NSH	29.70	1.435
Nicotine hourly max 50th percentile (ng/kg), males			Nicotine hourly max 95th percentile (ng/kg), males		
SH	169.5	6.391	SH	825.4	96.00
NSH	64.50	2.616	NSH	446.8	19.40
Nicotine hourly max 50th percentile (ng/kg), females			Nicotine hourly max 95th percentile (ng/kg), females		
SH	168.6	6.430	SH	835.6	95.30
NSH	63.40	2.625	NSH	448.2	19.60
UVPM (MMD=0.2 µm) 50th percentile (µg), males			UVPM (MMD=0.2 µm) 95th percentile (µg), males		
SH	472.2	65.23	SH	7945	771.1
NSH	210.2	51.06	NSH	3231	255.1
UVPM (MMD=0.2 µm) 50th percentile (µg), females			UVPM (MMD=0.2 µm) 95th percentile (µg), females		
SH	368.6	47.84	SH	6972	630.3
NSH	135.5	37.77	NSH	2625	200.7
UVPM (MMD=0.4 µm) 50th percentile (µg), males			UVPM (MMD=0.4 µm) 95th percentile (µg), males		
SH	354.5	49.04	SH	7120	579.7
NSH	159.1	38.52	NSH	2455	193.7
UVPM (MMD=0.4 µm) 50th percentile (µg), females			UVPM (MMD=0.4 µm) 95th percentile (µg), females		
SH	296.8	37.02	SH	5368	485.3
NSH	117.2	29.25	NSH	2072	155.5

MMD: mass median diameter; SW: smoking workplace; NSW: nonsmoking workplace; SH: smoking home; NSH: nonsmoking home.

Table 9. ETS constituent doses and lung burdens encountered at work: ratios of SW to NSW given SH (column 4) or NSH (column 5).

ETS constituent	Measure	Gender	Cell 1 (SW, SH)	Cell 3 (SW, NSH)
			Cell 2 (NSW, SH)	Cell 4 (NSW, NSH)
Nicotine dose	TWA, 50th percentile	Men	23	18
		Women	23	18
	TWA, 95th percentile	Men	10	20
		Women	10	21
	Hourly maximum, 50th percentile	Men	27	25
		Women	26	24
	Hourly maximum, 95th percentile	Men	8.6	23
		Women	8.8	23
UVPM alveolar burden (MMD=0.2 μm)	50th percentile	Men	7.2	4.1
		Women	7.7	3.6
	95th percentile	Men	10	13
		Women	11	13
UVPM alveolar burden (MMD=0.4 μm)	50th percentile	Men	7.2	4.1
		Women	8.0	4.0
	95th percentile	Men	12	13
		Women	11	13

SW: Smoking workplace; SH: smoking home; NSW: nonsmoking workplace; NSH: nonsmoking home; MMD: mass median diameter.

women, reflecting the ratio of 1.2 for breathing rates. Again, these results agree with the earlier observations from SWs (LaKind et al., 1999c).

Comparison of ETS Exposure in SWs vs. NSWs

Table 8 presents the 50th and 95th percentiles of the modeled variables for cells 2 and 4 (the "NSW" columns) together with those of the earlier evaluation for cells 1 and 3 (the "SW" columns) (LaKind et al., 1999c). Tables 9 and

10 display ratios calculated from the values in Table 8. Table 9 provides comparisons of SWs and NSWs for SHs (cell 1 vs. cell 2) and for NSHs (cell 3 vs. cell 4). Table 10 provides similar comparisons, but of SHs and NSHs for SWs (cell 1 vs. cell 3) and for NSWs (cell 2 vs. cell 4).

A number of trends emerge from these ratios:

- In Table 9, for SWs vs. NSWs, less difference is evident in UVPM levels than in nicotine levels (i.e., the ratios are smaller for UVPM).

Table 10. ETS constituent doses and lung burdens encountered at work: ratios of SH to NSH given SW (column 4) or NSW (column 5).

ETS constituent	Measure	Gender	Cell 1 (SH, SW)	Cell 2 (SH, NSW)
			Cell 3 (NSH, SW)	Cell 4 (NSH, NSW)
Nicotine dose	TWA, 50th percentile	Men	3.1	2.5
		Women	3.2	2.5
	TWA, 95th percentile	Men	2.3	4.5
		Women	2.3	4.6
	Hourly maximum, 50th percentile	Men	2.6	2.4
		Women	2.7	2.4
	Hourly maximum, 95th percentile	Men	1.8	4.9
		Women	1.9	4.9
UVPM alveolar burden (MMD=0.2 μm)	50th percentile	Men	2.2	1.3
		Women	2.7	1.3
	95th percentile	Men	2.5	3.0
		Women	2.7	3.1
UVPM alveolar burden (MMD=0.4 μm)	50th percentile	Men	2.2	1.3
		Women	2.5	1.3
	95th percentile	Men	2.9	3.0
		Women	2.6	3.1

SH: Smoking home; SW: smoking workplace; NSH: nonsmoking home; NSW: nonsmoking workplace; MMD: mass median diameter.

- For nicotine, the lowest ratios were associated with upper percentiles on both average and hourly maximum exposure for cell 1 vs. cell 2. Other nicotine ratios are fairly consistent. In other words, for individuals from SHs, the difference between SWs and NSWs is lower at the extremes of exposure and dose (ranging from 8.6 to 10) than for average doses or for individuals from NSHs (ranging from 18 to 27).
- In general, the ratios in Table 9 suggest that 50th percentile nicotine doses (both the time-weighted average dose and the hourly maximum dose) are 20–25 times higher in SWs than in NSWs, regardless of the smoking status of in the home. The upper bound (i.e., 95th percentile) nicotine dose is 8–10 times higher for individuals from SHs but 20–25 times higher for individuals from NSHs.
- For UVPM alveolar lung burdens, MMD has little impact on the ratios. The lowest UVPM ratios are associated with median values in the cell 3 vs. cell 4 comparisons (SW vs. NSW for NSHs) and are approximately 4. Other UVPM ratios are higher and fairly consistent, ranging from 7 to 13.
- Average UVPM lung burden is about four times higher in SWs vs. NSWs for individuals from NSHs (cell 3 vs. cell 4) but is twice this (i.e., about eight times higher) for individuals from SHs. In other words, less relative difference exists between UVPM lung burdens between SWs and NSWs for individuals from NSHs than from SHs. The upper bound UVPM lung burden is 10–13 times higher in SWs than in NSWs regardless of the smoking status in the home.
- Table 10 compares SHs to NSHs. For SWs (cell 1 vs. cell 3), the ratios are fairly constant and are in the range of 2–3. For NSWs (cell 2 vs. cell 4), the ratios are in the same range with three exceptions: the upper bounds (95th percentiles) of both time-weighted average and hourly maximum nicotine doses have ratios approaching 5 and the ratio for 50th percentile UVPM alveolar lung burden only slightly exceeds unity (i.e., is 1.3). These ratios give an idea of the impact of SHs vs. NSHs even when the doses or lung burdens are estimated from ETS concentrations observed in NSWs.
- Overall, Table 10 shows that in SWs, individuals from SHs experience two to three times greater nicotine doses and UVPM lung burdens than individuals from NSHs. The ratios for individuals in NSWs have a wider spread ranging from just over 1 to 5.

Discussion

The data presented here are unique because they were obtained using personal monitors to measure workplace ETS exposure to nonsmokers in a putatively unexposed

population. These data show that, in general, individuals working in NSWs experience a 20- to 25-fold lower nicotine dose and a 10-fold lower UVPM alveolar lung burden than individuals in a workplace where smoking occurs.

Other researchers have compared concentrations (as opposed to dose or lung burden) in smoking vs. nonsmoking environments. Proctor (1989) observed lower ratios comparing nicotine concentrations in smokers' offices (median $3.1 \mu\text{g}/\text{m}^3$; mean $6.0 \mu\text{g}/\text{m}^3$) to concentrations in nonsmokers' offices' (both median and mean, $0.6 \mu\text{g}/\text{m}^3$). Proctor's smoking–nonsmoking ratio of medians was 5.2, while the ratio of means was 10. Holcomb (1993), in a compilation of studies measuring ETS constituents, found the mean nicotine concentration in smoking offices and public places to be $6.2 \mu\text{g}/\text{m}^3$ compared to $0.3 \mu\text{g}/\text{m}^3$ in nonsmoking offices and public places. This smoking-to-nonsmoking ratio of 21 was similar to the ratio observed in the 16-City Study. Hammond et al. (1995) observed median work site nicotine concentrations of $8.6 \mu\text{g}/\text{m}^3$ (smoking allowed), $1.3 \mu\text{g}/\text{m}^3$ (smoking restricted), and $0.3 \mu\text{g}/\text{m}^3$ (smoking banned). The ratio of concentrations comparing workplaces where smoking was allowed to those where it was banned was 29, which is slightly higher than the ratios observed in the 16-City data.

Heavner et al. (1996) reported UVPM ratios that were comparable to those observed in the 16-City data. These authors observed a median smoking–workplace UVPM concentration of $21.9 \mu\text{g}/\text{m}^3$ (mean $29.8 \mu\text{g}/\text{m}^3$) and a median NSW UVPM concentration of $2.4 \mu\text{g}/\text{m}^3$ (mean $3.7 \mu\text{g}/\text{m}^3$). Their results yield smoking–nonsmoking ratios of 9.1 (median) and 8.1 (mean). The UVPM concentration ratios of Proctor (1989) were somewhat lower. This author observed median UVPM concentrations of $24 \mu\text{g}/\text{m}^3$ in smokers' offices (mean $23 \mu\text{g}/\text{m}^3$) and $8.8 \mu\text{g}/\text{m}^3$ in nonsmokers' offices (mean $8 \mu\text{g}/\text{m}^3$) for smoking–nonsmoking ratios of 2.7 (median) and 2.9 (mean).

Table 9 indicates that UVPM ratios are smaller than nicotine ratios when comparing SWs to NSWs, regardless of whether the individuals come from SHs or NSHs. This observation is not surprising. Airborne nicotine is derived almost exclusively from tobacco smoke while UVPM results from a variety of sources of combustion. Therefore, a larger differential in nicotine levels would be expected when comparing workplaces where the nominal difference is the presence or absence of smoking. Considering the ratios in Table 9, while the nicotine ratios between SWs and NSWs appear large, it is noted that the average nicotine doses encountered in NSWs shown in Table 8 are in fractions of nanograms (i.e., in fractions of billionths of a gram). As the denominator of a ratio becomes smaller, the ratio itself becomes larger, so a very small denominator (as would be expected when

monitoring nicotine in a nonsmoking environment) can generate a large ratio.

In Table 10, the average UVPM lung burdens suggest that there is little difference between cells 2 and 4, which is exactly what is expected if there are no ETS sources in the workplace. The nicotine data, though, disagree with this expectation, so speculation is offered concerning the low-level nicotine source. It is unlikely that ETS is the source because this is inconsistent with the UVPM data and the subjects' own observations of no or very few cigarettes in the workplace. One speculation is that the nicotine derives from off-gassing from the clothing of individuals exposed at home. The unusual decay of nicotine could explain the detectable presence of nicotine while UVPM is not detectable. It is also possible that not all NSWs are created equal, with those more recently converted to nonsmoking having more backsliding and therefore more true ETS. It is also possible that individuals from a SH may voice fewer complaints about observed smoking in a NSW and therefore higher (though still very low) levels of nicotine and UVPM in the air. Finally, the NSWs with higher nicotine levels also may also be those with smoking lounges, with the concomitant spillover of UVPM and nicotine into regular work areas.

Other researchers have also reported differences in workplace exposure depending on the smoking status of the home. Hammond et al. (1995) measured concentrations of ETS constituents and found ratios similar to those observed here (i.e., nonsmokers married to smokers were exposed to three to four times the nicotine concentration as nonsmokers married to nonsmokers). In a study of nonsmoking British women, Proctor et al. (1991) observed a mean nicotine exposure of $1.6 \mu\text{g}/\text{m}^3$ for working women married to smokers and half this level ($0.8 \mu\text{g}/\text{m}^3$) for working women married to nonsmokers. If home smoking status is not considered when assessing workplace ETS exposure, significant confounding will be added and will, in turn, make the search for other patterns more difficult.

Finally, data from the 16-City Study suggest that once a workplace becomes nonsmoking, the great majority of individual exposures to ETS are eliminated. Thus, if the goal of a nonsmoking policy is reduction in ETS exposure, it is likely to be quite effective.

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Carol G. Graves, The Sapphire Group, 3 Bethesda Metro Center, Suite 830, Bethesda, Maryland 20814. Please include a check for US\$10 to cover costs.

References

- AIHC (American Industrial Health Council). *Exposure Factors Sourcebook*. Washington, DC, 1994.
- Armitage A.K., Dollery C.T., George C.F., Houseman T.H., Lewis P.J., and Turner D.M. Absorption and metabolism of nicotine from cigarettes. *Br. Med. J.* 1975; 4: 313–316.
- Benowitz N.L., and Jacob P. III Metabolism, pharmacokinetics, and pharmacodynamics of nicotine in man. In: Martin W.R., van Loon G.R., Iwamoto E.T., and Davis D.L. (Eds.). *Advances in Behavioral Biology — Tobacco Smoking and Nicotine: A Neurobiological Approach*. Plenum Press, New York, NY, 1987, pp. 357–373.
- Benowitz N.L., Jacob P. III, Jones R.T., and Rosenberg J. Interindividual variability in the metabolism and cardiovascular effects of nicotine in man. *J. Pharmacol. Exp. Ther.* 1982; 221 (2): 368–372.
- Black A., Pritchard J.N., and Walsh M. An exposure system to assess the human uptake of airborne pollutants by radiotracer techniques, with particular reference to sidestream cigarette smoke. *J. Aerosol Sci.* 1987; 18 (6): 757–760.
- Brainard J., and Burmaster D.E. Bivariate distributions for height and weight of men and women in the United States. *Risk Anal.* 1992; 12 (2): 267–275.
- Conner J.M., Oldaker G.B. III, and Murphy J.J. Method for assessing the contribution of environmental tobacco smoke to respirable suspended particles in indoor environments. *Environ. Toxicol.* 1990; 11: 189–196.
- Feyerabend C., Ings R.M.J., and Russell M.A.H. Nicotine pharmacokinetics and its application to intake from smoking. *Br. J. Clin. Pharmacol.* 1985; 19: 239–247.
- Hammond S.K., Sorensen G., Youngstrom R., and Ockene J.K. Occupational exposure to environmental tobacco smoke. *JAMA* 1995; 274 (12): 956–960.
- Heavner D.L., Morgan W.T., and Ogden M.W. Determination of volatile organic compounds and respirable suspended particulate matter in New Jersey and Pennsylvania homes and workplaces. *Environ. Int.* 1996; 22 (2): 159–183.
- Holcomb L.C. Indoor air quality and environmental tobacco smoke: concentration and exposure. *Environ. Int.* 1993; 19: 9–10.
- ICRP (International Commission on Radiological Protection). Human respiratory tract model for radiological protection. ICRP Publication 66. *Ann. ICRP* 1994; 24 (1–4): 1–482.
- Iwase A., Aiba M., and Kira S. Respiratory nicotine absorption in nonsmoking females during passive smoking. *Int. Arch. Occup. Environ. Health* 1991; 63: 139–143.
- James A.C., Jarabek A.M., Morrow P.E., Schlesinger R.B., Snipes M.B., and Yu C.P. Dosimetry of inhaled particles in the respiratory tract. In: *Air Quality Criteria for Particulate Matter*, Vol. II. U.S. Environmental Protection Agency, Office of Research and Development, Washington, DC, 1996, EPA/600/P-95/001bF.
- Jenkins R.A., Guerin M.R., Palausky A., Counts R.W., Bayne C.K., and Dindal A.B. Determination of human exposure to environmental tobacco smoke (ETS): a study conducted in 16 U.S. cities. Draft final report by Oak Ridge National Laboratory for Center for Indoor Air Research, Linthicum, MD, 1996a.
- Jenkins R.A., Palausky A., Counts R.W., Bayne C.K., Dindal A.B., and Guerin M.R. Exposure to environmental tobacco smoke in sixteen cities in the United States as determined by personal breathing zone air sampling. *J. Expos. Anal. Environ. Epidemiol.* 1996b; 6 (4): 473–502.

- Johnson T.R. A study of human activity patterns in Cincinnati, Ohio. Report by PEI Associates, Inc., for Electric Power Research Institute. Available from Ted R. Johnson, IT Corporation, 3710 University Drive, Durham, NC 27707, 1987.
- Johnson T.R., Capel J.E., Olaguer E., and Wijnberg L. Estimation of carbon monoxide exposures by urban residents using a probabilistic version of NEM. Report by IT Air Quality Services for the U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC, 1992.
- LaKind J.S., Graves C.G., Ginevan M.E., Jenkins R.A., Naiman D.Q., and Tardiff R.G. Exposure to environmental tobacco smoke in the workplace and the impact of away-from-work exposure. *Risk Anal.* 1999a: 19 (3): 349–358.
- LaKind J.S., Jenkins R.A., Naiman D.Q., Ginevan M.E., Graves C.G., and Tardiff R.G. Use of environmental tobacco smoke constituents as markers for exposure. *Risk Anal.* 1999b: 19 (3): 359–373.
- LaKind J.S., Ginevan M.E., Naiman D.Q., James A.C., Jenkins R.A., Dourson M.L., Felter S.P., Graves C.G., and Tardiff R.G. Distribution of exposure concentrations and doses for constituents of environmental tobacco smoke. *Risk Anal.* 1999c: 19(3): 375–390.
- Molander L., Lunell E., Andersson S.B., and Kuylentierna F. Dose released and absolute bioavailability of nicotine from a nicotine vapor inhaler. *Clin. Pharmacol. Ther.* 1996: 59 (4): 394–400.
- Nelson P.R., Heavner D.L., Collie B.B., Maiolo K.C., and Ogden M.W. Effect of ventilation and sampling time on environmental tobacco smoke component ratios. *Environ. Sci. Technol.* 1992: 26 (10): 1909–1915.
- Ogden M.W., and Maiolo K.C. Collection and determination of solanesol as a tracer of environmental tobacco smoke in indoor air. *Environ. Sci. Technol.* 1989: 23 (9): 1148–1154.
- Ott W.R. A physical explanation of the lognormality of pollutant concentrations. *J. Air Waste Manage. Assoc.* 1990: 40: 1378–1383.
- Proctor C.J. A comparison of the volatile organic compounds present in the air of real world environments with and without environmental tobacco smoke. Presented at the 82nd Annual Meeting of the Air and Waster Management Association, Anaheim, CA, 1989.
- Proctor C.J., Warren N.D., Bevan M.A.J., and Baker-Rogers J. A comparison of methods of assessing exposure to environmental tobacco smoke in nonsmoking British women. *Environ. Int.* 1991: 17: 287–297.
- Robinson D.E., Balter N.J., and Schwartz S.L. A physiologically based pharmacokinetic model for nicotine and cotinine in man. *J. Pharmacokinet. Biopharm.* 1992: 20 (6): 591–609.
- Russell M.A.H., and Feyerabend C. Cigarette smoking: a dependence on high-nicotine boli. *Drug Metab. Rev.* 1978: 8 (1): 29–57.
- U.S. EPA (U.S. Environmental Protection Agency). Air Quality Criteria for Particulate Matter, Vols. I, II, and III. Office of Research and Development, Washington, DC, 1996a, EPA/600/P-95/001aF.
- U.S. EPA (U.S. Environmental Protection Agency). Exposure Factors Handbook. Exposure Assessment Group, Office of Research and Development, Washington, DC, 1996b, EPA/600/P-95/002Ba.
- Zevin S., Jacob P. III, and Benowitz N. Cotinine effects on nicotine metabolism. *Clin. Pharmacol. Ther.* 1997: 61: 649–654.