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Journal

Environmental Science & Technology Letters, 11(4)

ISSN

2328-8930

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Publication Date

2024-04-09

DOI

10.1021/acs.estlett.4c00116

Inhalation of trace metals in secondhand and thirdhand tobacco smoke can result in increased health risks

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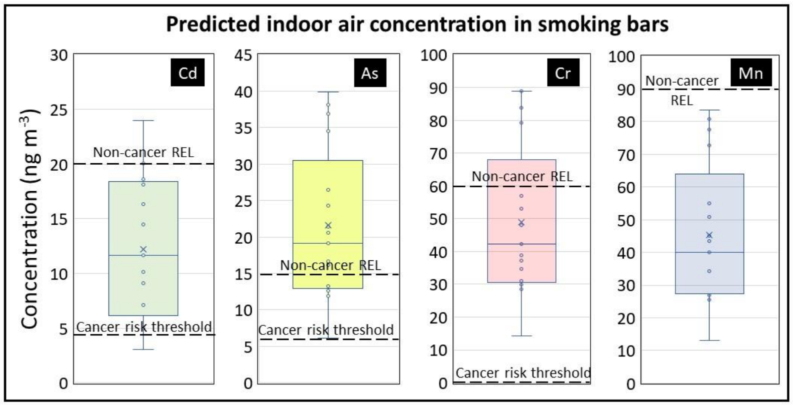
Abstract

The presence of toxic metals in tobacco smoke is well documented. However, few studies have quantified trace metals in secondhand smoke (SHS) and thirdhand tobacco smoke (THS). Their presence in indoor air can contribute to non-smokers' exposures and health effects. Emission and deposition rates of toxic trace metals were determined, and their airborne concentration in typical indoor scenarios was predicted. $PM_{2.5}$ was collected on Teflon-coated filters at various times following a smoking event in a room-sized chamber, over a 43-h period. The concentration of 28 trace metals was determined by extraction and analysis using inductively coupled plasma-triple quadrupole-mass spectrometry (ICP-QQQ-MS). Emission and indoor deposition rates of cadmium, arsenic, chromium, manganese, beryllium and selenium were determined, and used to predict concentrations expected in a smokers' home and a smoking bar. In most of the considered scenarios, samples collected more than three hours after smoking ended presented average indoor concentrations of Cd, As and Cr that exceeded their corresponding cancer risk thresholds and, in some cases, also non-cancer reference exposure levels. The fraction of cadmium that remained airborne was significantly higher than those of other metal traces and that of $PM_{2.5}$, suggesting an association of Cd traces with small particles.

Keywords: Cadmium, Arsenic, Chromium, Manganese, Beryllium, Selenium, ICP-MS, cancer risk.

Synopsis: Cadmium, arsenic and chromium traces were found in secondhand and thirdhand tobacco smoke at levels that may result in negative health impacts.

TOC Art


Predicted indoor air concentration in smoking bars
Concentration (ng m-3)
Cd
As
Cr
Mn
Non-cancer REL
Cancer risk threshold
0
5
10
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Introduction

Mainstream and sidestream tobacco smoke contain several harmful trace metal constituents, including carcinogens listed by the World Health Organization's International Agency for Research on Cancer(IARC) in Group 1 (Cd, As, Be, Cr, Po-210) and Groups 2a/2b (Pb and Ni) [1]. Cadmium and Arsenic are listed as harmful and potentially harmful tobacco constituents by the US Food and Drug Administration (FDA).[2] The California Environmental Protection Agency has established No Significant Risk Levels (NSRLs) for chemicals known to cause cancer, including Cd, As, Cr (VI), Pb and Be.[3] Similarly, the State listed non-cancer reference exposure levels (RELs) for acute and chronic exposures to Cd, As, Cr (III), Mn and Ni.[4] Trace elements are primarily released in particulate matter, and are likely to be present in indoor air, subsequently settling on surfaces and contributing to secondhand smoke (SHS) and long-term thirdhand smoke (THS) exposures. They have been measured in indoor air, on surfaces and in settled dust, but little information exists on the contribution of smoking to the total burden to which non-smoking occupants are exposed. A recent study showed a correlation of lead and cadmium levels with nicotine –a specific tobacco tracer– in settled dust from smokers' homes, indicating that THS can be a significant Pb and Cd source, and contribute to the overall exposure.[5] Other studies found a correlation of levels of cotinine (a nicotine metabolite) with concentrations of Pb and other metals in children's saliva,[6] and increased levels of Cd and Pb in the blood of nonsmokers with residential and occupational exposures to tobacco smoke.[7]

In a study of 41 smokers' homes and 32 control homes (occupied by children with and without respiratory ailments), $PM_{2.5}$, Ce, La, Cd, and Tl had higher indoor air concentrations in dwellings where smoking took place, and these compounds were associated with more likely presence of respiratory symptoms.[8] Cadmium is of particular concern because it has been associated with different forms of cancer,[9, 10] and tobacco smoke was identified as a major source, with higher levels found in smokers' biofluids than in non-smokers.[11] Cadmium has been measured in smoker's homes air at levels significantly higher than those in non-smokers' households, with median levels of 0.8 and 0.1 ng m^{-3} respectively, and even higher Cd levels (2.6 – 9.7 ng m^{-3}) were measured in restaurants, pubs and discotheques.[12] The same study found similar trends for the rare earth metals cerium and lanthanum, with Ce median levels of 9.6 ng m^{-3} (smokers) vs. 0.4 ng m^{-3} (control), and La concentrations of 5.9 ng m^{-3} (smokers) vs. 0.2 ng m^{-3} (control), while the hospitality venues had between 18.5 and 50 ng m^{-3} Ce and between 10.6 and 23 ng m^{-3} La.[12] In a recent study, higher levels of La, Ce and other rare earth elements were found in the hair of nonsmokers living in a smoking household, compared with a control group in non-smoking households.[13]

Cadmium was found to be associated to smaller-size particles, compared with other trace metals. In one study, 80% of Cd measured in indoor air impacted by tobacco smoke was found in particles with aerodynamic diameters below 1.8 µm.[14] Piadé *et al.* reported that 40-55% of the cadmium present in cigarettes is exhausted via sidestream smoke, and postulated its release as organocadmium species, such as $Cd(CH_3)_2$, to explain its higher volatility compared to other trace elements.[15] However, other studies could not verify the presence of organocadmium in smoke, possibly due to reactivity under smoldering and sampling conditions.[16] Similarly, Taebunpakul et al.[17] reported that, in unburned cut tobacco, 89% of the total water-soluble arsenic is primarily inorganic As(V) species, and a small amount of the organoarsenic species dimethylarsinic acid (DMA) and monomethylarsonic acid (MMA). In water-soluble extracts of mainstream smoke condensate, both arsenate (As(V)) and arsenite (As(III)) were found, suggesting the presence of a reduction process during combustion.

Here, we determined trace metal concentrations in THS aerosols as a function of the aerosol aging time indoors, and used this information to predict the associated exposure doses expected in commonly found scenarios. We identified trace metals that can be present in THS at high enough levels to amount to a health hazard, and described the significance of inhalation as an exposure route for nonsmokers.

Methods and Materials

Environmental chamber. The concentration of toxic trace metals in tobacco smoke was determined in experiments using LBNL's 18-m^3 room-size chamber. The experimental protocol and aerosol sampling approach was described in a previous study, in which VOCs and SVOCs concentrations were determined in the same samples.[18] Briefly, six tobacco cigarettes (three Marlboro Special Blend and three Camel 99s Turkish Domestic Blend) were consumed simultaneously at time $t = 0$, followed by sampling of aerosol particles using Teflon-coated fiberglass filters over a 43-h period. Four different samples were collected at different times to determine contaminant concentration changes as the emitted aerosol aged in the chamber. Samples were taken immediately after smoking to characterize SHS at times $6 < t$ (m) < 24, the SHS/THS transition period at times $72 < t$ (m) < 204, and two consecutive THS periods identified as THS1 ($246 < t$ (m) < 1086) and THS2 ($1140 < t$ (m) < 2580). The timeframe to differentiate SHS from THS is somehow arbitrary, as there is no sharp cutoff between those two different but related exposures.[19] During the SHS/THS transition period, there is coexistence of both direct inhalation and indirect exposures to contaminants that remain airborne, are reemitted or resuspended. Two different THS samples were collected to evaluate long-term deposition and resuspension, corresponding roughly to an overnight sample (THS1) and a subsequent 24-h long sample (THS2). More details on the environmental chamber operation are provided in the Supporting Information.

Sample handling and analysis. A half of each filter was used for the VOC/SVOC analysis reported in our previous study,[18] and the other half was used for the trace metal analysis reported here. Aerosol-loaded filters were stored in the freezer at -20°C immediately after sampling, until they were processed for trace metal analysis by digestion with a 9 mL/3 mL ultrapure HNO_3/HCl (aq) mixture in a microwave oven (Multiwave 3000, Anton Paar) following the EPA 3051A standard procedure.[20] Samples and acids were placed in a sealed fluoropolymer vessel, and the temperature was increased to 175 °C in 5.5 min, remaining at the same temperature during a 10-min digestion period. After cooling, the extracts were filtered with 0.45 µm PVDF membranes (Acrodisc LC 13-mm, Pall Life Science), diluted and analyzed by an advanced Agilent 8900 triple quadrupole inductively coupled plasma mass spectrometry system (Agilent 8900 QQQ ICP-MS, Agilent Technologies). The concentration of trace metals in the extract was determined as the average of five replicates using calibration curves for each analyte, and correcting by the corresponding dilution factor. The relative experimental error in analyte concentrations, derived from the standard deviation/average ratio of five replicates, was in most cases between 1 and 5%, except for analytes determined at very low concentrations, which had relative experimental errors up to 15%. Details on the analytical methods, QA/QC, data processing and reporting are provided in Section S1, Tables S1 and S2 (Supporting Information).

Chamber air concentration and THS airborne fraction. For each sampling period, we determined the concentration of each trace metal in air (expressed in ng m^{-3}) by normalizing the corresponding blank-subtracted extract concentration by the liquid extract volume and the corresponding sample air volume. The fraction of the *i*-th trace metal remaining airborne during the THS/SHS transition period (θ_i^{THS}) with respect to fresh smoke determined in the SHS sample was calculated as:

$$\theta_i^{THS} = \frac{C_i^{SHS/THS}}{C_i^{SHS}} \times 100 \qquad (1)$$

where $C_i^{SHS/THS}$ and C_i^{SHS} are its concentration in the SHS/THS period and SHS period, respectively.

***Prediction of trace metal concentration in residential indoor air*.** We estimated the contribution of smoking to daily average indoor trace metal levels in homes using a simple box model. The time-resolved airborne concentrations of trace metals were calculated from the combination of their emission rate, the number of cigarettes consumed per day, and the metal removal rate due to a combination of ventilation and particle deposition. Model simulations comprised space volumes of 20 m^3< V < 100 m^3, and three different air exchange values in the range 0.1 h^{-1} < λ < 0.5 h^{-1}. The emission rate of health-relevant trace metals, e_i, was determined as the product of their concentration in SHS (C_i^{SHS}) and the chamber volume ($V_{chamber}$), normalized by the number of cigarettes smoked simultaneously in the experiment (n):

$$e_i = \frac{C_i^{SHS} \times V_{chamber}}{n} \qquad (2)$$

This calculation assumes minimal losses due to chamber ventilation and particle deposition in the SHS period. The deposition rate of element i (d_i) in our experimental chamber was calculated by subtracting the air exchange rate ($\lambda_{chamber}$ = 0.3 h^{-1}) from the total decay rate for the same element (D_i) determined by fitting a single exponential curve to the first two or three experimental results, corresponding to either the 3.4 h or 18.1 h following the smoking event, during which air concentrations dropped due to the added effect of ventilation and deposition:

$$d_i = D_i - \lambda_{chamber} \qquad (3)$$

Prediction of trace metal concentration in public smoking venues. For this analysis, we used data from a survey of seventeen smoking bars in Austin, TX, carried out by Waring and Siegel.[21] The contribution of smoking to average concentration of element i in room air corresponding to the x-th bar was calculated by assuming steady-state conditions, as

$$\overline{C_{i,x}} = \frac{E_i \times N_x}{(\lambda_x + d_i) \times V_x} \qquad (4)$$

in which E_i is the emission rate of ten cigarettes smoked over the course of one hour. The parameters N_x, λ_x and V_x correspond the reported hourly average number of lit cigarettes, the air exchange rate and the space volume of the x-th venue, respectively. The corresponding values for each bar are presented in Table S3 (Supporting information).

Results and Discussion

Chamber concentration and airborne fraction during the SHS/THS transition. A total of 38 elements were detected with concentrations above the analytical limit of detection and the reactant blank. From those, ten elements (which included Pb) had high chamber blank and/or filter blank levels, and could not be quantified. Table 1 summarizes results obtained for the remaining 28 elements for which significant concentrations were detected in chamber air during the post-smoking period. At its peak, during the SHS period, trace metal concentrations spanned six orders of magnitude, with highest levels (in the range 10^4-10^6 ng m^{-3}) corresponding to the crust minerals Mg, Al, Ca, Ti and Fe. Several toxic metals were detected in SHS, including Cd, As, Cr, Be and Mn (in the range 1-10^3 ng m^{-3}). The limit of quantification (LOQ) was calculated as the reactant and filter blank values expressed in concentration units, and it was in most cases 0.5 ng m^{-3}.

Table 1. Chamber air concentration determined for each trace metal at four different times during indoor aerosol aging.

	Chamber blank	**SHS**	**SHS/THS transition**	**THS #1**	**THS #2**
time elapsed post smoking (m)		6 – 24	72 – 204	246 – 1086	1140 – 2580
sample volume (m^3)	108	2.4	12.6	84	144
PM$_{2.5}$ concentration (µg m^{-3})	1.4	1441	482	22.6	1.2
Element (atomic number)	**Chamber air concentration (ng m^{-3})**				
Li (3)	8.6	651	79	15	2.7
Be (4)	< LOQ	3.8	0.4	< LOQ	< LOQ
Mg (12)	1.4×10^3	1.8×10^5	1.4×10^4	4.3×10^3	1.4×10^3
Al (13)	6.6×10^3	6.0×10^5	5.0×10^4	1.6×10^4	5.5×10^3
Ca (20)	1.1×10^4	1.4×10^6	1.0×10^5	4.0×10^4	1.2×10^4
Ti (22)	50	3.6×10^4	4.8×10^3	880	160
V (23)	3.1	765	67	17	1.9
Cr (24)	3.1	432	23	11	3.9
Mn (25)	3.7	361	30	11	4.6
Fe (26)	170	2.8×10^4	1.6×10^3	690	200
Co (27)	0.5	20	1.3	0.5	< LOQ
As (33)	1.2	167	16	4.3	1.0
Se (34)	< LOQ	1.9	0.32	< LOQ	< LOQ
Sr (38)	130	1.5×10^4	1.4×10^3	480	140
Y (39)	4.5	75	33	2.3	0.75
Zr (40)	3.0	440	67	13	3.5
Mo (42)	< LOQ	68	7.6	1.5	< LOQ
Ag (47)	< LOQ	47	0.6	< LOQ	< LOQ
Cd (48)	< LOQ	60	25	1.7	< LOQ
Sn (50)	6.6	164	41	4.0	1.5
Sb (51)	< LOQ	924	3.2	23.9	< LOQ
Cs (55)	< LOQ	51.3	3.5	1.3	< LOQ
La (57)	2.0	35	16	1.4	0.8
Ce (58)	3.9	62	32	2.8	1.7
Nd (60)	1.9	30	15	1.3	0.9
Yb (70)	< LOQ	5.5	3.0	< LOQ	< LOQ
Th (90)	< LOQ	33	2.3	0.9	< LOQ
U (92)	< LOQ	18	1.1	0.5	< LOQ

LOQ = limit of quantification

The airborne fraction θ_i^{THS} was calculated for the identified metal traces, and the results are presented in Figure 1 as a function of the concentration of each element in chamber air during the SHS/THS transition period. In the same period, the $PM_{2.5}$ concentration was 482 µg m^{-3}, which represented a 33% of the SHS sample. The airborne fraction θ_i^{THS} determined for most elements was between 5% and 15%, which suggests that those metal traces were associated with large particles that settled faster than $PM_{2.5}$. However, a few elements showed a significantly larger airborne fraction, including Sn (θ_{Sn}^{THS} = 25%), Cd (θ_{Cd}^{THS} = 42%), La (θ_{La}^{THS} = 42%) and Ce (θ_{Ce}^{THS} = 48%). These relatively more volatile elements may be associated with smaller (fine and ultrafine) particles, which remain airborne for longer periods than $PM_{2.5}$. Figure 1 shows also the remaining gas phase fraction of a non-sorptive trace (e.g., CO_2) released simultaneously with smoke, which represented 56% during the same period. This quantity was higher than those determined for all the trace metals, including the most volatile ones, and provides an upper limit for the anticipated range of θ_i^{THS} values.

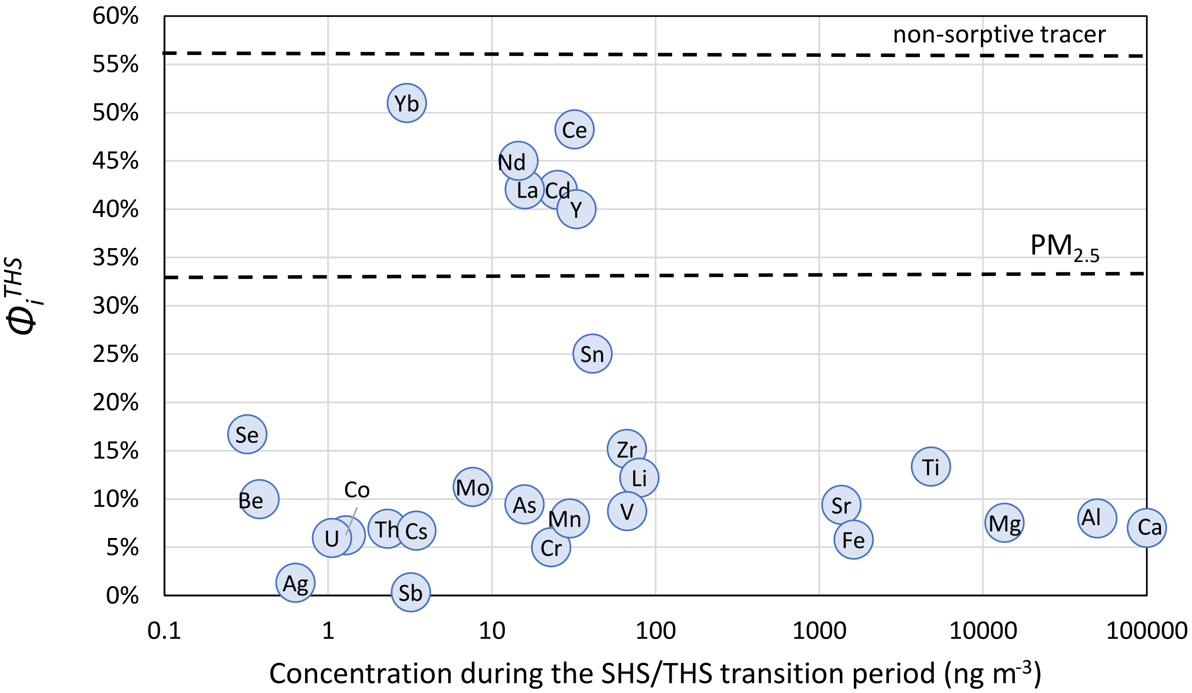

Figure 1. Airborne fraction θ_i^{THS} of metals traces during the SHS/THS transition period (1.2 to 3.4 h post-smoking) with respect to fresh smoke (SHS period, 0.1 to 0.4 h post-smoking), as a function of their average concentration in chamber air during the same period. The dotted lines correspond to the airborne fraction of $PM_{2.5}$ determined experimentally, and the predicted gas phase fraction of a non-sorptive tracer released during smoking. The relative experimental error in θ_i^{THS} values was, in most cases, between 2 and 10%.

Our observation of the relative "volatility" of cadmium is consistent with reported differences in how this metal transfers from a cigarette to smoke, with respect to other trace metals. A higher Cd concentration was observed in smaller particles when it was released during combustion [15, 22]. Similarly, other elements showing high θ_i^{THS} values may also be associated with small aerosol particles.

Predicted trace metal concentration in residential indoor air. The experimental results from the environmental chamber were used to predict the concentration of trace metal contaminants expected to be found in a smoker's home. The emission rate, e_i, and deposition rate, d_i, were calculated using values from our chamber results in equations 2 and 3, for six toxic tobacco-related trace metals listed by the California OEHHA (Cd, As, Cr, Be, Mn and Se). These values, along with the corresponding cancer risk threshold and non-cancer RELs, are listed in Table 2. The cancer risk threshold (C_{CRT}), expressed in ng m^{-3}, was derived from the corresponding NSRL for inhalation (expressed in ng day^{-1}), as follows:

$$C_{CRT} = \frac{\text{NSRL}}{V_b \times \alpha_{inhal}} \qquad (5)$$

where V_b = 15 m^3 day^{-1} is the adult daily breathing volume,[23] and α_{inhal} is the fraction of aerosol particles retained in the respiratory system during normal respiration (unitless). A comprehensive review on retention of tobacco smoke constituents in the respiratory tract found that, on average, 60 to 80% of smoke particulate matter is retained after inhalation.[24] For that reason, we use here the mid-range value α_{inhal} = 0.7 for the calculation of C_{CRT}.

Table 2. Cancer risk threshold concentration, chronic non-cancer Reference Exposure Level (REL), calculated emission rate and deposition rate for selected trace metals

Element	**Cancer risk threshold for inhalation C_{CRT} (ng m^{-3})**	**Non-cancer REL for inhalation (ng m^{-3})**	**Emission rate e_i (ng/cig)**	**Deposition rate d_i (h^{-1})**
Cd	4.8	20	180	0.022
As	5.7	15	501	0.91
Cr	0.1 (Cr VI)	60 (Cr III) 200 (Cr VI)	1,296	1.3
Be	9.5	7	11.4	0.88
Mn	N.A.	90	1,083	0.98
Se	N.A.	20,000	5.8	0.62

The emission rates reported in Table 2, corresponding to the transfer of each element from one cigarette to indoor air upon smoking, can be compared with mainstream emission values reported in the literature, even if those are determined differently. In the case of cadmium, our determination of e_{Cd} = 180 ng cig^{-1} is higher than the median mainstream smoke yields determined for a worldwide survey of 568 cigarettes, of 18.2 ng cig^{-1} and 75.1 ng cig^{-1} when determined with the ISO and Health Canada Intense (HCI) smoking regime, respectively.[15] Our emission rate for arsenic, e_{As} = 501 ng cig^{-1}, is significantly higher than the values reported in the same study (<3.75 and < 8.71 ng cig^{-1} with the ISO and HCI method). A different study[16] reported 76 ng Cd released in mainstream emissions of the experimental 3R4F cigarette under ISO smoking conditions. The observed differences between emissions from smoldering (primarily composed of sidestream smoke) and those reported for mainstream smoke suggest that particle-bound trace metals in mainstream smoke can be efficiently retained by the cigarette's filter, particularly in the case of arsenic. Other factors could also play a role, such as higher temperature, oxygen concentration and mass-transfer rates in mainstream vs. sidestream emissions, all of which could alter combustion conditions leading to the formation of different species in each case.

In a simple box model, the simulated scenario computed the emissions from smoking one cigarette per hour, between 7 am and 9 pm, in a space volume of V = 20, 40, 60, 80 and 100 m^3 and for three different air exchange values, λ = 0.1, 0.3 and 0.5 h^{-1}. Figure S1 (Supporting Information) illustrates the curves obtained for Cd, As, Cr and Mn for a particular set of conditions (V = 40 m^3 and λ = 0.3 h^{-1}). Compared with the other three metals, Cd is predicted to remain airborne longer due to its lower deposition rate, resulting in a higher θ_i^{THS}.

The integrated results (14-h average concentration) for all tested V and λ values corresponding to Cd, As, Cr and Mn are presented in Figure 2. We did not include selenium and beryllium in this analysis because their relatively low emission rates suggested that these elements did not represent a significant health hazard. Estimated indoor levels of Se and Be were far lower than the corresponding cancer and/or non-cancer reference levels.

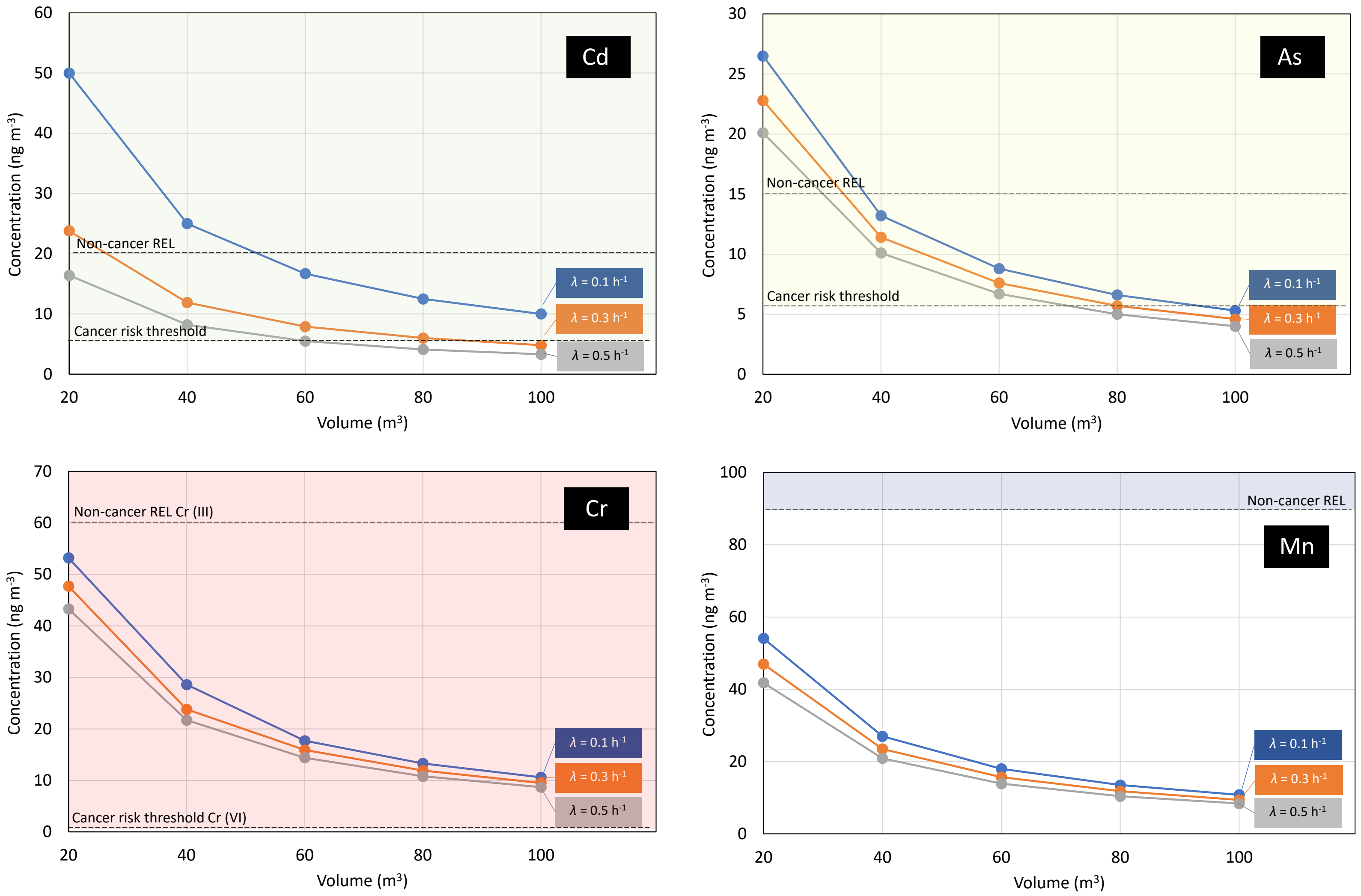

Figure 2. Predicted indoor air concentration of Cd, As, Cr and Mn as a function of the indoor space volume and the air change rate (λ), for typical residential values of these parameters. The dotted lines correspond to the cancer risk threshold and the non-cancer chronic reference exposure level.

In all cases, the indoor concentration decreased with increasing V and λ values. In the case of cadmium, we also observed a marked effect due to changes in the air exchange rate, which were not present for the other elements. This is due to the fact that Cd remains airborne for a longer time than most other metal traces. The predicted indoor concentrations for Cd, As and Cr where higher than the corresponding cancer risk thresholds in almost all modeled scenarios, suggesting that long-term exposure to SHS and THS may contribute to incremental cancer incidence in non-smokers. In the case of chromium, it should be noted that the threshold corresponds only to the hexavalent form of this element, and our analysis does not allow us to determine the oxidation state. When compared with non-cancer RELs, cadmium and arsenic levels exceeded their corresponding reference levels only for the most extreme cases of poor ventilation rates and small space volume. Such conditions are rarely found in most cases, so this analysis suggests that the impact of SHS and THS on non-cancer effects from inhalation is minor. Non-cancer RELs for trivalent chromium and manganese were not exceeded in any of the simulated scenarios. In summary, nonsmokers' exposure to SHS and THS in homes may contribute to negative health impacts due to inhalation of cadmium, arsenic and chromium traces.

***Predicted trace metal concentration in public smoking venues*.** The airborne concentration of Cd, As, Cr and Mn were calculated using equation 4 for the conditions reported in each of the surveyed 17 bars, and are plotted in Figure 3. Under these conditions, the presence of fresh smoke predominated, and for that reason elements with the highest emission rates were present at the highest concentrations. By contrast, cadmium was present at lower levels than the other elements, owing to its relatively lower emission rate. In virtually all the considered venues, the predicted Cd, As and Cr levels where higher than the cancer risk thresholds, in agreement with the above-described findings for the home environment. In addition, except for Mn, the other three elements exceeded, at least in some of the bars, the non-cancer REL. In the case of arsenic, most conditions estimated for the surveyed bars led to airborne concentrations that were higher than the non-cancer REL (15 ng m^{-3}).

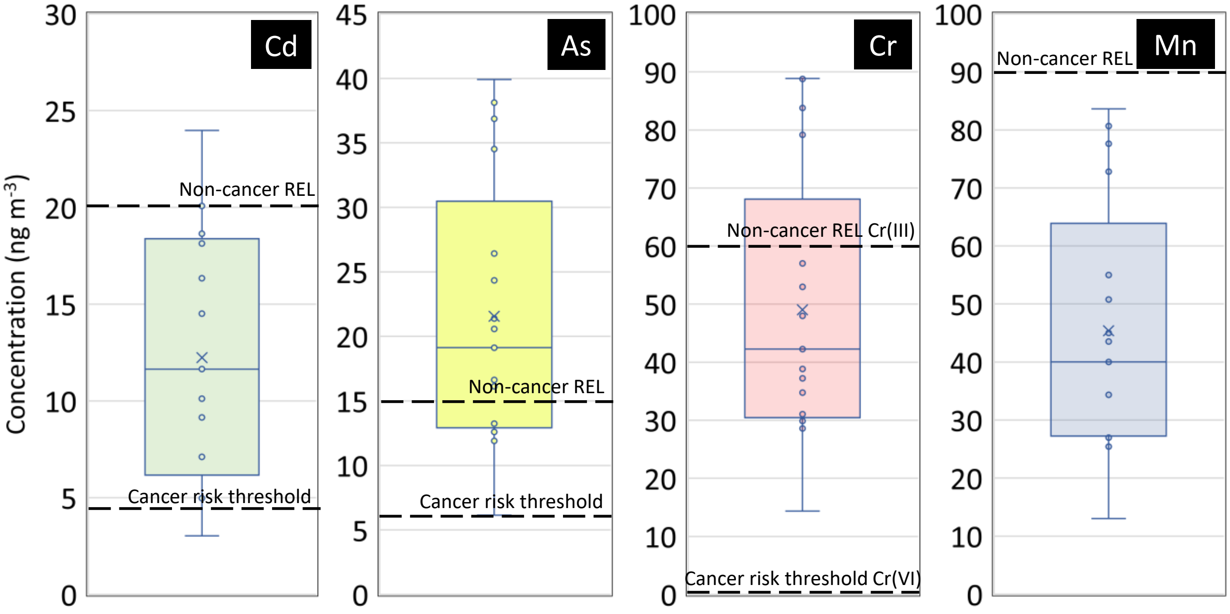

Figure 3. Indoor air concentration of Cd, As, Cr and Mn predicted for conditions reported in 17 different smoking bars. The dotted lines correspond to the cancer risk threshold and the non-cancer chronic reference exposure level.

Implications to indoor environmental quality and health**.** This study illustrated the presence of metal traces in secondhand and thirdhand smoke at levels that, in some cases, may result in nonsmokers' chronic exposures to higher than acceptable doses. Smoking may be their single source, or contribute to the overall exposure burden if these contaminants are also generated by other indoor sources and/or infiltrate from outdoor air. This analysis was limited to inhalation exposures to airborne metal contaminants. However, in smoking environments these trace metals will also be present on indoor surfaces and in dust particles, and occupants are likely to be exposed to harmful levels of trace metals through multiple pathways. For that reason, the analysis presented here does not represent the total thirdhand exposure burden. Our results suggest that intake of metal traces via dermal uptake and dust ingestion are likely to contribute to the total toxicant dose. Further studies are warranted to better understand the integrated impact of toxic metal traces present in secondhand and thirdhand tobacco smoke. Similarly, understanding the long-term mass balance of these contaminants is needed to characterize their indoor fate and transport. Given their potential persistence, it is important to assess the efficacy of ventilation, vacuuming and cleaning as removal mechanisms.

Associated Content

The Supporting Information provides additional experimental details, including: a description of analytical methods and QA/QC for metal trace analysis; instrument settings, calibration ranges and detection limits; the predicted air concentration of Cd, As, Cr and Mn in a representative scenario; and physical characteristics of bars used in this analysis.

Acknowledgement

This study was supported by the University of California's Tobacco Related Disease Research Program (UC-TRDRP) THS Consortium grant T32PT5965 (PI: Destaillats). The Lawrence Berkeley National Laboratory operates under the U.S. Department of Energy contract DE-AC02-05CH11231. The authors thank Marion Russell and Lara Gundel for their support.

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