

# **Quantitative evaluation of nicotine and particulate matter exposure for passive- and non-smokers via a nicotine passive sampler and a particulate matter sensor**

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### **Abstract**

Passive smoking poses a major hazard to the health of non-smokers. Cigarette combustion emits environmental tobacco smoke (ETS) that contains various pollutants, including volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons, and particulate matter with particles <2.5 µm in aerodynamic diameter (PM<sub>2</sub>,). Therefore, to assess the risk of passive smoking, it is necessary to determine the exposure levels to ETS compounds caused by passive smoking. However, it is difficult to assess exposure to ETS compounds by excluding the effects of other sources of pollution. In this study, we assessed the individual exposure levels to ETS compounds using a nicotine passive sampler and  $PM<sub>2.5</sub>$  sensor in 258 non-smokers. Median nicotine and PM<sub>2.5</sub> concentrations were 0.065 and 7.5 µg m<sup>-3</sup>, respectively. The median nicotine concentration was nearly identical to that found in non-smoking areas (0.05  $\mu$ g m<sup>-3</sup>). The median PM<sub>2.5</sub> concentrations were below the standard value for indoor  $PM_{2.5}$  concentrations (12 μg m<sup>-3</sup>). These results indicated that the effect of passive smoking was rather modest. Nicotine concentrations in individuals exposed to passive smoking indoors were significantly higher than in those not exposed to passive smoking. Nicotine exposure from domestic passive smoking was twice that from non-domestic passive smoking. There was no significant difference in  $PM_{2.5}$  exposure between passive smoking in domestic and non-domestic settings. Moreover, it was suggested that passive smoking was equivalent to the act of smoking  $2.4 \times 10^{-3}$  cigarettes per day.

**Keywords** Passive smoking · Passive sampler · Particulate matter sensor · LC-MS/MS · Personal exposure

# **Introduction**

Passive smoking is a health concern for non-smokers. The emissions resulting from tobacco combustion are referred to as environmental tobacco smoke (ETS). The exposure of

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non-smokers to ETS has been observed in numerous countries (WHO [2007\)](#page-6-0). In fact, a survey conducted across 132 countries revealed that 30–87% and 53–98% of youth were exposed to ETS at home and in public places, respectively (Group [2006\)](#page-6-1).

The prevalence of smoking among individuals has shown a consistent decline over the past three decades. Specifically, the proportion of male smokers has decreased from 60% in 1992 to 27.1% in 2019, whereas the corresponding figures for female smokers have decreased from 13 to 7.6% during the same period. Additionally, the implementation of the Health Promotion Act in 2020 aimed to restrict smoking in public places in accordance with WHO recommendations. Consequently, the risk of smoking among passive smokers is expected to decrease accordingly; however, there have been no quantitative studies on the amount of passive smoke. Because outdoor smoking can increase as

indoor smoking areas decrease, the investigation of passive smoking outdoors is important.

ETS contains various contaminants, which include volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), and particulate matter with an aerodynamic diameter < 2.5  $\mu$ m (PM<sub>2.5</sub>). Indeed, passive smoking contributes an additional 14–50 µg d<sup>-1</sup> to the average daily intake of benzene for individuals (Nazaroff and Singer [2004](#page-6-2)), constituting 20% of personal exposure. ETS compound emissions from smoking have been reported as follows: VOCs, 14 (*m*-cresol)–2,390 (isoprene) µg cig<sup>−</sup><sup>1</sup> (Singer et al. [2003](#page-6-3)), nicotine, 1,660 µg cig<sup>-1</sup> (Singer et al. [2003\)](#page-6-3); PAHs, 16.1 (dibenz[a, h]anthracene)–2,526 (naphthalene) µg cig<sup>−</sup><sup>1</sup> (Lu and Zhu [2007](#page-6-4)); and PM, 15.6 mg cig<sup>-1</sup> (Bi et al. [2005](#page-6-5)). Although numerous studies have reported ETS exposure, observing individual ETS exposure is difficult to quantify because of the simultaneous pollution of the atmosphere by other sources. For example, cooking (Masuda et al. [2020](#page-6-6)), burning (Bootdee et al. [2016;](#page-6-7) Dambruoso et al. [2014](#page-6-8); Gustafson et al. [2008](#page-6-9)), road traffic (Harrison et al. [2021](#page-6-10)), and vehicle exhaust gases (Li et al. [2018](#page-6-11)) are potential sources of VOCs, PAHs, and PM. Therefore, a method for estimating ETS concentrations that excludes contributions from other pollution sources is required to accurately assess the risk of passive smoking.

<span id="page-1-0"></span>

Nicotine is a tobacco-specific ETS compound. Moreover, the nicotine concentration in ETS is 3–18 times that of other tobacco-specific compounds, such as myosmine and 3-ethenylpyridine (Singer et al. [2003\)](#page-6-3). Therefore, nicotine serves as an ideal ETS marker, considering the relatively low ETS concentration associated with passive smoking. The assessment of personal nicotine exposure can facilitate the estimation of ETS exposure.  $PM<sub>2.5</sub>$  is also present at high concentrations in ETS, and smoking status can be confirmed via real-time  $PM<sub>2.5</sub>$  monitoring.

In this study, we aimed to determine the levels of nicotine and  $PM<sub>2.5</sub>$  exposure among passive smokers and non-smokers in Japan. A nicotine passive sampler and PM sensor were used to determine the personal exposure to nicotine and  $PM<sub>2</sub>$  for 258 subjects from October to December 2022. The subjects specified the time and location they were exposed to passive smoking. The assessment of passive smoking was conducted using self-report measures. Personal nicotine and  $PM<sub>2.5</sub>$  exposure levels were analyzed in relation to the environmental conditions in which they were exposed to passive smoking. Finally, we estimated the extent to which passive smoking could be converted into active smoking.

# **Materials and methods**

### **Chemicals**

(−)-Nicotine was obtained from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan). Nicotine- $d_3$  was obtained from Cambridge Isotope Laboratories Inc. (Tewksbury, MA, USA) and used as an internal standard. Sodium hydrogen sulfate monohydrate (Kanto Chemical Co. Inc., Tokyo, Japan) was used as an adsorbent for the passive sampler. Sodium hydrate (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), ultrapure water (Millipore Sigma, Burlington, MA, USA), methanol (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), and acetonitrile (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan) were used as eluents for cleaning and extraction in liquid chromatography-mass spectrometry (LC-MS/MS).

### **Passive smoking survey**

An internet-based questionnaire was sent to 5,390 individuals, and 258 potential subjects were selected. The subjects were non-smokers who were exposed to passive smoking. Passive smoking was determined based on self-reports. In addition, we ensured that there were no biases regarding sex, location, and occupation (Table [1](#page-1-0)). Passive nicotine samplers and PM sensors were distributed to the subjects. The subjects wore the nicotine passive samplers and PM sensors for 24 h and then returned them to us. The subjects specified the time and location they were exposed to passive smoking while wearing the samplers during the 24-h period via self-report measures. The survey was conducted between October and December 2022.

#### **Nicotine passive sampler**

A nicotine passive sampler, which we specifically developed to monitor atmospheric particulate nicotine with high sensitivity, was used in this study (Noro et al. [2023](#page-6-12)). The size of the sampler, including the clip, was  $36 \times 70 \times 30$  mm, and its weight was 30 g. The sampler comprised a sodium hydrogen sulfate-impregnated filter and a perforated cover. This sampler could measure the nicotine concentration while minimizing the influence of the wind. Sampling rates of the sampler were  $(1.17 \pm 0.05) \times 10^{-6}$  m<sup>3</sup> min<sup>-1</sup> for both gaseous and particulate nicotine (Noro et al. [2023\)](#page-6-12). After sampling, nicotine was extracted from the filters in the samplers using glass tubes containing 5 mL of a nicotine- $d_3$ solution (1.00  $\mu$ g L<sup>-1</sup>) and ultrasonic irradiation for 10 min. The extracts were centrifuged, and the supernatants were stored in LC vials for LC-MS/MS analysis.

### **LC-MS/MS apparatus**

Nicotine concentrations were determined using an UltiMate 3000 liquid chromatograph (Thermo Fisher Scientific, Inc., Waltham, MA, USA) interfaced with a TSQ Endura triple quadrupole mass spectrometer in the ESI mode. Liquid chromatographic separation was conducted using a cation exchange column (ZORBAX 300-SCX; 2.1 mm × 150 mm, 5 μm) obtained from Agilent Technologies Inc. (Santa Clara, CA, USA), which allowed for a large-volume injection (100 µL) into the column. LC-MS/MS conditions have been described previously (Noro et al. [2023](#page-6-12)).

### **PM sensor**

 $PM<sub>2.5</sub>$  concentrations were measured using "PM2.5 Monitor Pro," which was acquired from Yaguchi Electric Corp. (Ishinomaki, Miyagi, Japan). This apparatus was originally developed by Ishigaki et al. (Ishigaki et al. [2017\)](#page-6-13) and is not commercially available. The sensor consisted of a laser light-emitting diode, a photodiode sensor, a fan, an amplifier, and a universal serial bus encoder. The size of the sampler was  $80 \times 40 \times 30$  mm, and its weight was 67 g. The battery and data logger were built-in, and the data acquisition cycle was six times per minute.

#### **Quality assurance and quality control**

Blank samples were extracted using a sodium hydrogen sulfate solution (5 g L<sup>-1</sup>) containing nicotine- $d_3$  (1.00 µg L<sup>-1</sup>), as opposed to using ultrapure water containing nicotine- $d_3$ . They were treated in the same manner as the samples. The nicotine calibration curve was linear over the entire range of standard concentrations (0.01. 0.03, 0.10, 0.30, 1.00, 2.00, and 10.00  $\mu$ g L<sup>-1</sup>; coefficient of determination > 0.99). Peaks were identified by comparing the retention times of the samples and the standard when the signal-to-noise ratio exceeded 3 and quantified when the quantification-to-confirmation ion ratio remained within 15% of the theoretical value.

### **Results and discussion**

### **Nicotine and PM2.5 concentrations**

Personal nicotine and  $PM<sub>2.5</sub>$  exposure concentrations were obtained for 258 and 194 samples, respectively. The number of  $PM_{2.5}$  samples collected was less than 258 because some monitors stopped working during the sampling process.

Personal nicotine exposure concentrations were below the detection limit in 28 of the 258 samples (11%). The ability to observe passive smoking in 89% of the subjects indicated that this sampler was useful for effectively conducting surveys on passive smoke exposure. In contrast, the  $PM<sub>2.5</sub>$  readings on the monitor consistently remained above 0. The measurement range of the monitor extended up to 999  $\mu$ g m<sup>-3</sup>. Although there were a few instances where the recorded values exceeded this upper limit, these data points were included in the analysis because of the relatively small number of instances.

The personal exposure distribution was almost log-normal (Fig. [1\)](#page-3-0), which was consistent with previous reports (Wallace [1986](#page-6-14)). The mean, standard deviation, maximum value, and minimum value of nicotine concentrations were 0.228, 0.600, 6.16, and 0.01  $\mu$ g m<sup>-3</sup>, respectively. Its median value was  $0.065 \mu g$  m<sup>-3</sup>. No significant difference in nicotine levels was observed among age, sex, and occupation, indicating that any potential bias among the subjects was negligible (Figs. [2](#page-3-1) and [3\)](#page-4-0). The atmospheric nicotine concentrations were comparable to those observed in residential and restaurant settings  $(0.06-37 \mu g m^{-3})$  (Noro et al. [2023](#page-6-12)). The observed nicotine concentration of 64% in this study was higher than that in non-smoking areas (0.05  $\mu$ g m<sup>-3</sup>), implying that passive smoking increased ETS inhalation for non-smoking individuals (IARC [2004](#page-6-15)).

The mean, standard deviation, maximum value, and minimum value of  $PM<sub>2.5</sub>$  concentration were 11.1, 14.3, 136,

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**Fig. 2** Nicotine concentrations: (**A**) age and gender, (**B**) occupations, and (**C**) conditions of passive smoking. \*\*: *p*<0.005, ns: not significant

<span id="page-4-0"></span>



and 0.64  $\mu$ g m<sup>-3</sup>, respectively. Its median value was 7.5  $\mu$ g  $m^{-3}$ . No significant differences in PM<sub>2.5</sub> concentrations were observed among age, sex, and occupation, indicating that any potential bias among the subjects was negligible (Figs. [2](#page-3-1) and [3](#page-4-0)).

Based on the administered questionnaire, the subjects were categorized into four groups: individuals who were not exposed to passive smoke during the measurement period (N), individuals who were exposed to passive smoke indoors (I), individuals who were exposed to passive smoke outdoors (O), and individuals who were exposed to passive smoke both outdoors and indoors (IO). Nicotine concentrations in Group I were significantly higher than those in Group N (Fig. [2](#page-3-1)), but there was no significant difference between  $PM_2$ , concentrations in Groups I and N (Fig. [3](#page-4-0)). The results suggest that indoor exposure to passive smoking significantly increases ETS inhalation, whereas  $PM<sub>2.5</sub>$  is not affected by indoor passive smoking. To investigate indoor exposure in more detail, we investigated whether exposure occurred at home. There were no significant differences in nicotine and  $PM<sub>2.5</sub>$  concentrations between Group N and Groups O and IO (Figs. [2](#page-3-1) and [3\)](#page-4-0).

#### **Domestic passive smoking**

A total of 23 participants reported that their cohabiting partner was a smoker and that smoking occurred within their shared residence at the time of the survey. A comparison was made between the nicotine or  $PM<sub>2.5</sub>$  personal exposure concentrations with and without passive smoking at home (domestic versus non-domestic, respectively) (Fig. [4\)](#page-5-0). Nicotine non-domestic passive smoking had a median value of 0.068 µg m<sup>−</sup><sup>3</sup> , whereas that of domestic passive smoking was 0.136  $\mu$ g m<sup>-3</sup>, which was twice that of nicotine nondomestic passive smoking. There was a significant difference in personal nicotine exposure levels between subjects who were exposed to secondhand smoke at home and those who were not. In contrast, there was no significant difference in  $PM<sub>2.5</sub>$  personal exposure concentrations between subjects exposed to domestic passive smoking and those exposed to non-domestic passive smoking. The median value of  $PM<sub>2.5</sub>$ non-domestic passive smoking was 7.1  $\mu$ g m<sup>-3</sup>, whereas that of domestic passive smoking was 8.3  $\mu$ g m<sup>-3</sup>, which was only 1.2 times higher than that of non-domestic passive smoking. Secondhand tobacco smoke simultaneously contains large amounts of nicotine and  $PM<sub>2.5</sub>$ . The reason why PM<sub>2.5</sub> concentrations did not increase significantly as a

<span id="page-5-0"></span>

**Fig. 4** Nicotine (left panel) and  $PM_2$ <sub>5</sub> (right panel) concentrations for individuals exposed to domestic and non-domestic passive smoking. \*\*:  $p < 0.005$ , ns: not significant

result of smoking at home is thought to be because smokers have grown more considerate of non-smokers, such as by smoking near ventilation fans or balconies. The significantly higher personal nicotine exposure levels in homes may be because of exposure to residual nicotine on the surfaces of indoor materials, such as walls. High concentrations of nicotine are occasionally detected in rooms that were previously used for smoking because of the gradual vaporization of nicotine onto indoor materials.

### **Environmental tobacco smoke (ETS) inhalation**

The nicotine intake of non-smokers was calculated as follows:

$$
DI_n = C_n V \tag{1}
$$

where  $DI_n$  ( $\mu$ g d<sup>-1</sup>) represents the daily nicotine intake and  $V(m<sup>3</sup> d<sup>-1</sup>)$  denotes the inhalation rate. *V* was assumed to be 17.3 m<sup>3</sup> d<sup>-1</sup> in this study (USEPA [2011\)](#page-6-17). In addition, the nicotine emission from smoking was  $1,660 \,\mu g \text{ cig}^{-1}$  (Singer et al.  $2003$ ). The mean  $DI_n$  value for non-smokers exposed to indoor passive smoking was 3.9 µg; therefore, passive smoking was equivalent to smoking  $2.4 \times 10^{-3}$  cigarettes per day.

### **Comparison between the PM2.5 concentrations of passive smoking and non-smoking indoors in domestic settings**

Not only was there no significant difference observed between the domestic and non-domestic  $PM_{2.5}$  exposure concentrations, but both median  $PM<sub>2.5</sub>$  concentrations in those exposed to domestic  $(8.3 \mu g m^{-3})$  and non-domestic

passive smoking (7.1  $\mu$ g m<sup>-3</sup>) were lower than the standard value of indoor  $PM_{2.5}$  concentration (12 µg m<sup>-3</sup>) (USEPA [2023](#page-6-16)).

### **Conclusion**

The nicotine passive sampler and PM monitor used in this study enabled quantitative measurement of the amount of passive smoke at very low concentrations. The results of a passive smoking survey of a total of 258 people revealed that median nicotine and  $PM<sub>2.5</sub>$  concentrations were 0.065 and 7.5  $\mu$ g m<sup>-3</sup>, respectively. In Japan, the Health Promotion Act was enforced in April 2020. Consequently, smoking is substantially restricted in public places and also prohibited in universities. Moreover, indoor and outdoor smoking is regulated. The low levels of passive smoke in this study are thought to be the result of the effectiveness of various regulations. This consciousness is also expanding within households, and one possible explanation is that smokers have become more considerate of non-smokers by smoking near ventilation fans or on balconies. Consequently, the nicotine exposure from domestic passive smoking was only twice that from non-domestic passive smoking. Furthermore, no significant difference was observed between the levels of  $PM_{2.5}$  exposure from passive smoking in domestic and non-domestic settings. Furthermore, it was suggested that passive smoking was equivalent to the act of smoking  $2.4 \times 10^{-3}$  cigarettes per day.

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**Author contributions** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Saria Hoshino, Kazushi Noro, Miyu Moriya and Ayana, Komatsu. The first draft of the manuscript was written by Saria Hoshino and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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**Data availability** The datasets generated during and/or analysed during the current study are not publicly available due to privacy policy but are available from the corresponding author on reasonable request.

#### **Declarations**

**Ethics approval and consent to participate** This survey was approved by the Ethics Committee of the University of Shizuoka (code: 2–41). Informed consent to participate in the study were obtained from all participants.

**Consent for publication** Consent to publish was obtained from all par-

#### ticipants.

**Competing interests** Dr. Amagai received the scholarship funding from Japan Tobacco Inc.

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### **References**

- <span id="page-6-5"></span>Bi X, Sheng G, Feng Y, Fu J, Xie J (2005) Gas- and particulate-phase specific tracer and toxic organic compounds in environmental tobacco smoke. Chemosphere 61:1512–1522
- <span id="page-6-7"></span>Bootdee S, Chantara S, Prapamontol T (2016) Determination of PM2.5 and polycyclic aromatic hydrocarbons from incense burning emission at shrine for health risk assessment. Atmospheric Pollution Res 7:680–689
- <span id="page-6-8"></span>Dambruoso P, de Gennaro G, Di Gilio A, Palmisani J, Tutino M (2014) The impact of infield biomass burning on PM levels and its chemical composition. Environ Sci Pollut Res Int 21:13175–13185
- <span id="page-6-1"></span>Group TGC (2006) A cross country comparison of exposure to secondhand smoke among youth. Tob Control 15:ii4
- <span id="page-6-9"></span>Gustafson P, Ostman C, Sallsten G (2008) Indoor levels of polycyclic aromatic hydrocarbons in homes with or without wood burning for heating. Environ Sci Technol 42:5074–5080
- <span id="page-6-10"></span>Harrison RM, Allan J, Carruthers D, Heal MR, Lewis AC, Marner B, Murrells T, Williams A (2021) Non-exhaust vehicle emissions of particulate matter and VOC from road traffic: a review. Atmos Environ 262:118592
- <span id="page-6-15"></span>IARC (2004) Tobacco smoke and involuntary smoking. World Health Organization, Lyon, France
- <span id="page-6-13"></span>Ishigaki Y, Tanaka K, Pradada H, MAtsumoto Y, Maruno Y (2017) Citizen sensing for environmental risk communication. CYBER, Balcerona, Spain
- <span id="page-6-11"></span>Li Q, Kim M, Liu Y, Yoo C (2018) Quantitative assessment of human health risks induced by vehicle exhaust polycyclic aromatic hydrocarbons at Zhengzhou via multimedia fugacity models with cancer risk assessment. Sci Total Environ 618:430–438
- <span id="page-6-4"></span>Lu H, Zhu L (2007) Pollution patterns of polycyclic aromatic hydrocarbons in tobacco smoke. J Hazard Mater 139:193–198
- <span id="page-6-6"></span>Masuda M, Wang Q, Tokumura M, Miyake Y, Amagai T (2020) Risk assessment of polycyclic aromatic hydrocarbons and their chlorinated derivatives produced during cooking and released in exhaust gas. Ecotoxicol Environ Saf 197
- <span id="page-6-2"></span>Nazaroff WW, Singer BC (2004) Inhalation of hazardous air pollutants from environmental tobacco smoke in US residences. J Expo Sci Environ Epidemiol 14:S71–S77
- <span id="page-6-12"></span>Noro K, Komatsu A, Moriya M, Kai Y, Wang Q, Miyake Y, Amagai T (2023) Development of a passive sampler for analysis of nicotine in non-smoking areas. Microchem J 190:108735
- <span id="page-6-3"></span>Singer BC, Hodgson AT, Nazaroff WW (2003) Gas-phase organics in environmental tobacco smoke: 2. Exposure-relevant emission factors and indirect exposures from habitual smoking. Atmos Environ 37:5551–5561
- <span id="page-6-16"></span>USEPA (2023) National Ambient Air Quality Standards (NAAQS)
- <span id="page-6-17"></span>USEPA (2011) Exposure factors handbook. National Center for Environmental Assessment Office of Research and Development U.S. Environmental Protection Agency Washington, DC 20460
- <span id="page-6-14"></span>Wallace LA (1986) Personal exposures, indoor and outdoor air concentrations, and exhaled breath concentrations of selected volatile organic compounds measured for 600 residents of New Jersey, North Dakota, North Carolina and California†. Toxicol Environ Chem 12:215–236
- <span id="page-6-0"></span>WHO (2007) Protection from exposure to second-hand tobacco smoke. Policy recommendations

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