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Exposure to secondhand aerosol from electronic cigarettes at homes: A real-life study in four European countries

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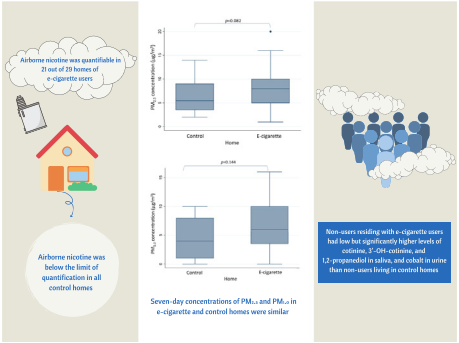
HIGHLIGHTS

- This multi-country study assessed exposure to e-cigarette aerosol at home.
- E-cigarette use emits pollutants and may impair indoor air quality.
- Airborne nicotine was quantifiable in 21 out of 29 e-cigarette users' homes.
- E-cigarette non-users living with e-cigarette users absorbed e-cigarette emission.
- Further studies are needed to guide smoke-free policy in private settings.

GRAPHICAL ABSTRACT



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ABSTRACT

Electronic cigarette (e-cigarette) use emits potentially hazardous compounds and deteriorates indoor air quality. Home is a place where e-cigarettes may frequently be used amid its increasing prohibition in public places. This study assessed the real-life scenario of bystanders' exposure to secondhand e-cigarette aerosol (SHA) at home. A one-week observational study was conducted within the TackSHS project in four countries (Greece, Italy, Spain, and the United Kingdom) in 2019 including: 1) homes of e-cigarette users living together with a non-user/non-smoker; and 2) control homes with no smokers nor e-cigarette users. Indoor airborne nicotine, $PM_{2.5}$, and $PM_{1.0}$ concentrations were measured as environmental markers of SHA. Biomarkers, including nicotine and its metabolites, tobacco-specific nitrosamines, propanediol, glycerol, and metals were measured in participants' saliva and urine samples. E-cigarette use characteristics, such as e-cigarette refill liquid's nicotine concentration, e-cigarette type, place of e-cigarette use at home, and frequency of ventilation, were also collected. A total of 29 e-cigarette users' homes and 21 control homes were included. The results showed that the seven-day concentrations of airborne nicotine were quantifiable in 21 (72.4 %) out of 29 e-cigarette users' homes; overall, they were quite low (geometric mean: 0.01 μg/m^3; 95 % CI: 0.01–0.02 μg/m^3) and were all below the limit of quantification in control homes. Seven-day concentrations of $PM_{2.5}$ and $PM_{1.0}$ in e-cigarette and control homes were similar. Airborne nicotine and PM concentrations did not differ according to different e-cigarette use characteristics. Non-users residing with e-cigarette users had low but significantly higher levels of cotinine, 3′-OH-cotinine and 1,2-propanediol in saliva, and cobalt in urine than non-users living in control homes. In conclusion, e-cigarette use at home created bystanders' exposure to SHA regardless of the e-cigarette use characteristics. Further studies are warranted to assess the implications of SHA exposure for smoke-free policy.

1. Introduction

The widespread use of electronic cigarettes (e-cigarettes) in Europe and other parts of the world has led to the growing occurrence of exposure to secondhand e-cigarette aerosol (SHA), especially among young people (World Health Organization, 2020; European Commission, 2021). In the United States (US), exposure to SHA in indoor or outdoor public places was reported by nearly one in three middle- and high-school students in 2018 (Dai, 2020). In Europe, 16.0 % of bystanders (e-cigarette non-users) reported exposure to SHA, at least weekly, in 2017–2018, in any indoor setting (Amalia et al., 2021a). The prevalence was higher among smokers who did not use e-cigarettes, with 19.7 % were exposed to SHA in smoke-free indoor places, according to a survey in six European countries in 2016 (Tigova et al., 2019).

Previous studies assessing SHA exposure with objective markers have identified particle pollution such as fine (e.g., $PM_{2.5}$ and $PM_{1.0}$) and ultrafine (e.g., $PM_{0.1}$) particulate matter, and chemical compounds, including nicotine, volatile organic compounds, propanediol, glycerol, metals, formaldehyde, acetaldehyde, tobacco-specific nitrosamines (TSNAs), and flavourings in SHA (Fernández et al., 2015; van Drooge et al., 2019). These substances were found to increase in concentration as a result of e-cigarette use in indoor environments and could be absorbed by bystanders through inhalation and dermal exposure (Kuga et al., 2020; Bekö et al., 2018). Airborne nicotine has been detected in higher concentrations after e-cigarette use by human volunteers in experimental studies in offices or rooms (Czogala et al., 2014; Schober et al., 2014; Visser et al., 2019; Melstrom et al., 2017) and in some observational studies inside homes of e-cigarette users, (Ballbè et al., 2014) in e-cigarette convention events, (Johnson et al., 2018; Chen et al., 2018) e-cigarette shops, (Son et al., 2020; Li et al., 2021) and even in their neighbouring businesses (Li et al., 2021). Nicotine and its metabolites, such as cotinine and trans-3′-hydroxycotinine (3′-OH-cotinine), have been identified in biological samples (i.e., serum, saliva or urine) of e-cigarette non-users who were exposed to SHA (Czogala et al., 2014; Ballbè et al., 2014; Melstrom et al., 2018) suggesting that nicotine is systemically absorbed by non-user bystanders. The concentration of $PM_{2.5}$ also substantially increased while e-cigarettes were used in locations such as rooms, (van Drooge et al., 2019; Czogala et al., 2014; Melstrom et al., 2017; Volesky et al., 2018; Amalia et al., 2021b; Schripp et al., 2013) homes, (Fernández et al., 2015; Savdie et al., 2020) cars, (Amalia et al., 2021b; Savdie et al., 2020; Schober et al., 2019) e-cigarette events, (Soule et al., 2017) and e-cigarette shops (Son et al., 2020; Li et al., 2021). Another major concern pertaining to SHA was the presence of metal elements (e.g., aluminium, silver, arsenic, iron), propanediol and glycerol in e-cigarette aerosols, which were absent or found only in a small amount in conventional cigarette smoke (Schober et al., 2014; Schripp et al., 2013; Schober et al., 2019; Zhao et al., 2020).

As pollutants in SHA may impair indoor air quality and biomarkers of exposure to these pollutants have been found in biological samples of e-cigarette non-users, the possibility of adverse health effects in exposed bystanders has been a matter of discussion. Exposure to SHA from short-term use of e-cigarettes may cause reduced respiratory function, headache, and irritation symptoms of eyes, nose, and airways among e-cigarette non-users (Tzortzi et al., 2018; Tzortzi et al., 2020; Johnson et al., 2019). It may also provoke respiratory inflammation in chronic obstructive pulmonary disease patients, (Rosenkilde Laursen et al., 2021) and exacerbate asthma symptoms in youth with asthma (Bayly et al., 2019a).

Although e-cigarette use and exposure to SHA among non-users at homes have been less frequently reported than in public places (e.g., workplaces, restaurants), (Amalia et al., 2021a; Majmundar et al., 2019) exposure to SHA in homes has been found to be extensive. A multi-country study in Europe reported the median duration of SHA exposure of 43 min/day at home among non-users (Amalia et al., 2021a). Qualitative studies revealed that the home is a location where e-cigarette use by both young people and adults commonly occurred (Robertson et al., 2019; Wadsworth et al., 2016; Alexander et al., 2019).

The above evidence underscores the importance of assessing involuntary exposure to pollutants from SHA at homes. However, there is still limited knowledge on the objective level of such exposure in a real-life situation since the available evidence has been derived mainly from laboratory or controlled study designs. Thus, this paper aims to comprehensively characterise environmental and individual exposure to SHA in real-life conditions at homes.

2. Materials and methods

2.1. Study design

An observational study was performed to examine the environmental and individual exposure to SHA in two types of households: e-cigarette users' homes and control homes. The study was conducted in Greece (Athens), Italy (Milan), Spain (Barcelona), and the United Kingdom (UK, Edinburgh) within the course of 1 week for each home between June and September 2019. This study was developed under the TackSHS project, which comprehensively assessed the impact of secondhand smoke (SHS) and SHA on the European population (Fernández et al., 2020).

2.2. Ethical issues

An ethics and research committee from each participating country approved this study (local protocol references, Greece: 086; Italy: INT 5/19; Spain: PR002/19; UK: NICR 18/19 037). The project was registered at www.clinicaltrials.gov (NCT04140630). All participants were properly informed about the potential risks of taking part in this study, and all of them provided written consent.

2.3. Participants

In each participating country, we recruited participants from both types of households. For each e-cigarette user's home (e-cigarette homes), we included one exclusive e-cigarette user and one non-user of any tobacco or nicotine products who resided in the same household. From each control home, that is, a household where no one used e-cigarettes or any tobacco or nicotine products, we enrolled one participant (non-user).

Non-users in both home types were eligible to participate if they were: a) aged 18 or over, b) a never user of e-cigarettes or a former e-cigarette user for more than 1 month, and c) a never user of any tobacco or nicotine products or a former user for more than 1 month. E-cigarette users were eligible to participate if they were: a) aged 18 or over, b) a daily e-cigarette user at home (at least during 1 month prior to the study), and c) a never or former user of any other tobacco or nicotine products (at least 1 month prior to the study). The exclusion criteria for all participants were being regularly exposed to SHS or SHA in places other than home or having another e-cigarette or tobacco user in the same household. We aimed to recruit 20 e-cigarette homes and 5 control homes in each country, summing to 80 e-cigarette homes (160 participants) and 20 control homes (20 participants) from the four countries, but logistical reasons prevented the achievement of the target sample size. Nevertheless, based on a previous pilot study, (Ballbè et al., 2014) our final sample size still allowed us to detect differences in the environmental and biological markers according to different home types.

Participants were recruited through advertisements in social networks, databases of previous e-cigarette studies and personal contacts of the research teams. All participants who agreed to participate received a gift card of a local cultural store to acknowledge their participation.

2.4. Measurements

2.4.1. Environmental measurements

Airborne nicotine: Gas-phase nicotine was measured with passive sampling, using nicotine samplers of 37 mm in diameter containing a filter treated with sodium bisulphate, a method developed by Hammond and Leaderer that has been used in previous studies (Hammond and Leaderer, 1987; Arechavala et al., 2018). The nicotine concentrations ($\mu g/m^3$) were determined using gas chromatography–mass spectrometry at the laboratory of the Public Health Agency of Barcelona (ASPB). The time-weighted average nicotine concentrations were quantified by dividing the amount of nicotine extracted from the filter by the volume of air sampled (estimated flow rate of 24 mL/min multiplied by the minutes the filter had been exposed). The procedure has a limit of quantification (LOQ) of 5 ng per filter, which is equivalent to 0.02 $\mu g/m^3$ of nicotine per 7 days of exposure.

Particulate matter (PM): The real-time $PM_{2.5}$ and $PM_{1.0}$ concentrations at 10-s interval were measured with an air quality monitoring device (AirVisual Pro, IQAir), a low-cost indoor air quality device that measures several environmental parameters, including $PM_{1.0}$, $PM_{2.5}$, temperature and humidity. It uses an internally-developed advanced light-scattering laser sensor that illuminates a laser within a measuring chamber and counts the irradiated light reflected from the microscopic particulate matter. The number of particles is processed by AirVisual together with the airflow during the measurement to provide the PM concentrations in $\mu g/m^3$.

We performed preliminary tests to evaluate the performance of the devices, and the results showed no temperature and relative humidity interferences, negligible zero and span drift, and calibration factors close to 1, thus, no modifications from the manufacturer were needed. We calibrated every instrument in SHS, operating them in parallel with governmental Beta Attenuation reference monitors as reference (Beijing US Embassy BAM monitor, with US EPA and TUV certificates). AirVisual sensors have been found to be highly correlated (r^2 of average daily measurements was 0.959) (IQAir, 2021).

In this study, the device's screen was covered with opaque cardboard to avoid any feedback to the participants about the air quality measured in the house. PM data were downloaded to a local computer from the monitors' internal memory for statistical analyses.

2.4.2. Biological measurements

The personal exposure to SHA was assessed by quantifying e-cigarette aerosol-related biomarkers in saliva and urine samples of e-cigarette users and non-users from both home types. The samples were stored at −20 °C in a freezer and sent in dry ice to the laboratory at IMIM-Hospital del Mar Medical Research Institute and the University of Granada (UG), respectively, for analyses. This study determined the concentrations of nicotine, cotinine, 3′-OH-cotinine, nornicotine, TSNAs (N′-nitrosonornicotine; NNN, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNK, and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; NNAL), propanediol (1,2-propanediol; 1,2-PD and 1,3-propanediol; 1,3-PD), (Wallace et al., 2021) and glycerol in saliva and urine samples using liquid chromatography-tandem mass spectrometry. Analysis of 27 metal elements in urine samples only was performed on an Agilent 8900 triple-quadrupole inductively coupled plasma-mass spectrometry (Agilent Technologies, Santa Clara, CA, USA). Suitable certified reference material [Seronorm (Sero, Billingstad, Norway) Trace Elements Urine L1 and L2 (references 210605, 210705)] was reanalysed together with a blank and an intermediate calibration standard every 12 samples. The list of metals analysed is provided in Supplementary Table 1. The LOQ for each biomarker is presented in Table 3 and Supplementary Table 1.

2.4.3. Observational data

Questionnaire: Information on sociodemographic profile (i.e., sex, age, and highest education level attained) and the self-rated overall health status (categorised as good, fair, and poor) of the participants were collected from the interview using an ad hoc questionnaire during a home visit. From the answers of the users, data on duration of being an e-cigarette user, type of e-cigarette commonly used (categorised as 1st generation or 'cig-a-like', 2nd generation or 'vape pens', 3rd generation or 'Mods', and 4th generation or 'Pods'), self-reported nicotine concentration in the refill liquid of e-cigarette (refill liquid, also known as e-liquid) commonly used, place of e-cigarette use at home (categorised as everywhere, only indoor places, and only outdoor places), and use of ventilation during e-cigarette use (categorised as never, sometimes, and always) were obtained.

Diary: information on the cooking time at home was registered by e-cigarette users and non-users every day in the given diary since PM is also emitted during cooking process. Data on the use of other potential combustions sources (e.g., candles, incense) were also collected, although participants were asked to avoid their use during the fieldwork. Daily reminders were sent via SMS to prompt the participants to fill in the diary.

2.5. Fieldwork

The fieldwork was conducted in the e-cigarette and control homes over seven consecutive days. A researcher visited the homes on the first and last days of the period. During the first visit, participants provided written informed consent to participate in this study, and sampling devices for airborne nicotine and PM were installed in the home's main room. Airborne nicotine was collected using a passive nicotine sampler that was installed and hung for 1 week in a location where air circulated adequately, at least two metres from any airflow and 1 m away from an open window or any ventilation system. The PM monitoring device was placed >30 cm away from the wall and the floor. The PM monitoring device was switched on and left in the participants' house for a week. During the visit, the researchers also interviewed the participants using an ad hoc questionnaire and collected the e-cigarette user's and non-users saliva sample into a test tube, using a lemon candy to stimulate salivation, when needed, until reaching the amount of at least 4 mL of saliva.

During the subsequent 7 days, participants completed the diary every day and PM concentrations were continuously measured by the monitoring device. On the last day, the researcher switched off and collected the PM monitoring device, the passive nicotine sampler, and the diary. At this time point, 20 mL urine samples were also collected from the participants in Italy and Spain.

2.6. Statistical analysis

The descriptive statistics of the sociodemographic and health profile of users and non-users from e-cigarette and control homes were calculated. We estimated the geometric means (GM) and associated 95 % confidence interval (95 % CI) for airborne nicotine concentrations and median and interquartile range (IQR) for $PM_{2.5}$ and $PM_{1.0}$ concentrations according to home types. We also stratified the airborne nicotine and PM concentrations in e-cigarette homes by characteristics related to e-cigarette use, such as refill liquid's nicotine level, e-cigarette device types, place of use and ventilation during e-cigarette use at home. For the PM concentrations, we excluded the values corresponding to cooking times recorded in the diary as the concentrations increased dramatically. We performed the Mann-Whitney *U* test to calculate differences in e-cigarette and control homes concentrations and the Kruskal-Wallis test for differences in concentrations in different conditions related to e-cigarette use.

We also estimated the GM and 95 % CI concentrations of each biomarker in saliva and urine according to the group of participants (i.e., users, non-users, and controls). *P*-values to compare the estimates between groups of participants were computed using the Mann-Whitney *U* test.

To determine the GM and 95 % CI estimates of airborne nicotine and biomarker concentrations, we performed Tobit regression of log-transformed concentrations, with the LOQ as the lower limit. This imputation method was chosen because it takes into account values under LOQ, as done in previous studies assessing indoor second- and third-hand smoke (Semple et al., 2019; Whitehead et al., 2009).

We performed the aforementioned non-parametric statistical tests, Mann-Whitney U test and Kruskal-Wallis test, due to the small sample sizes and the predominantly very low concentrations of most of the environmental and biological markers measured and thus, highly skewed to the right or log-normally distributed (Ott, 1990). All analyses were performed with STATA 14.0, and the significance level was set at p-value <0.05.

3. Results

3.1. Demographic and e-cigarette use profile

Table 1 shows the sociodemographic and health profile distribution of the participants from the four countries. In total, 79 participants, including 29 users and 29 non-users from e-cigarette homes, and 21 non-users from control homes (controls), were enrolled. Most of the users (67.9 %) were male, while non-users (75.0 %) and controls (66.7 %) were mostly female. Most of the participants (50.6 %) were aged 30–49 years; the median age for users, non-users, and controls were 43.1, 41.7, and 41.3 years, respectively. Almost all the participants (74 participants; 96.1 %) considered themselves in good or fair health.

Users reported that they had used the e-cigarette for a median duration of 36 months (interquartile range, IQR: 19–54 months) by the time of the study, most of them (n = 18; 64.3 %) used the 3rd generation of e-cigarette (e.g., Eleaf, Vaporesso), and one user used the 4th generation (Juul). The median nicotine concentration in the refill liquids used by e-cigarette users was 3 mg/mL, ranging from 0 to 20 mg/mL.

Table 1
Sociodemographic and health characteristics of electronic cigarette (e-cigarette) users and non-users living in e-cigarette users' homes and control participants living in e-cigarette non-users' homes in four European countries. TackSHS Study, 2019.

Total	Total N (%)	Users N (%)	Non-users N (%)	Controls N (%)
	79 (100.0)	29 (100.0)	29 (100.0)	21 (100.0)
Country				
Greece	25 (31.6)	10 (34.5)	10 (34.5)	5 (23.8)
Italy	14 (17.7)	4 (13.8)	4 (13.8)	6 (28.6)
Spain	21 (26.6)	8 (27.6)	8 (27.6)	5 (23.8)
United Kingdom	19 (24.1)	7 (24.1)	7 (24.1)	5 (23.8)
Sex[a]				
Male	33 (42.9)	19 (67.9)	7 (25.0)	7 (33.3)
Female	44 (57.1)	9 (32.1)	21 (75.0)	14 (66.7)
Age (years)[a]				
15–29	10 (13.0)	3 (10.7)	2 (9.5)	5 (17.9)
30–49	39 (50.6)	14 (50.0)	12 (57.2)	13 (46.4)
≥50	28 (36.4)	11 (39.3)	7 (33.3)	10 (35.7)
Highest education level[a]				
Primary school	2 (2.6)	1 (3.6)	1 (3.6)	0 (0.0)
Secondary school	20 (26.0)	13 (46.4)	7 (25.0)	0 (0.0)
University or similar	55 (71.4)	14 (50.0)	20 (71.4)	21 (100.0)
Overall health status[a,b]				
Good	61 (79.2)	22 (78.6)	22 (78.6)	17 (81.0)
Fair	13 (16.9)	4 (14.3)	5 (17.8)	4 (19.0)
Poor	3 (3.9)	2 (7.1)	1 (3.6)	0 (0.0)

[a] Total 77 participants because two participants did not provide this information.
[b] Self-reported health status.

3.2. Environmental markers

The concentration of airborne nicotine throughout 7 days of observation was quantifiable in 21 out of 29 e-cigarette homes and in none of the control homes. The GM of seven-day airborne nicotine concentration in e-cigarette homes was 0.01 μg/m^3 (95% CI: 0.01–0.02 μg/m^3), while the concentrations in control homes were all below the LOQ.

Fig. 1a shows that the median (8.00 μg/m^3; IQR: 5.00–10.00 μg/m^3) $PM_{2.5}$ concentration in e-cigarette homes during the observation week was not significantly different than that of in control homes (median: 5.50 μg/m^3; IQR: 3.50–9.00 μg/m^3; $p = 0.082$). Likewise, the concentration of $PM_{1.0}$ in e-cigarette homes (Fig. 1b) shows a similar pattern (median: 6.00 μg/m^3; IQR: 3.50–10.00 μg/m^3 vs median: 4.00 μg/m^3; IQR: 1.00–8.00 μg/m^3).

The seven-day airborne nicotine, $PM_{2.5}$, and $PM_{1.0}$ levels in e-cigarette homes did not vary by any of the e-cigarette use characteristics examined (Table 2).

3.3. Biomarkers

3.3.1. Comparison between non-users and control participants

Table 3 shows that the concentrations of nicotine metabolites, except nornicotine, of non-users were significantly higher than those found in control participants only in saliva samples. Although the salivary nicotine concentration of non-users was lower than that of control participants (0.17 vs 0.28 ng/mL, respectively), more samples (19 out of 21) from control participants than from non-users (18 out of 29) were below the LOQ. Also, non-users had lower proportions of saliva samples whose concentrations of cotinine and 3′-OH-cotinine were <LOQ compared to control participants. The GM concentration of salivary 1,2-PD in non-users (8.05 nmol/mL; 95 % CI: 4.70–13.78 nmol/mL) was almost twice ($p < 0.001$) of that in control participants (4.84 nmol/mL; 95 % CI: 2.80–8.37 nmol/mL). The concentrations of all urinary biomarkers among non-users also presented in Table 3 were similar to those of control participants. Out of 27 metal elements analysed in urine (Supplementary Table 1), cobalt was the only metal showing a GM concentration in non-users higher (0.60 μg/L; 95 % CI: 0.19–1.86 μg/L; $p = 0.031$) than that in control participants (0.22 μg/L; 95 % CI: 0.12–0.38 μg/L).

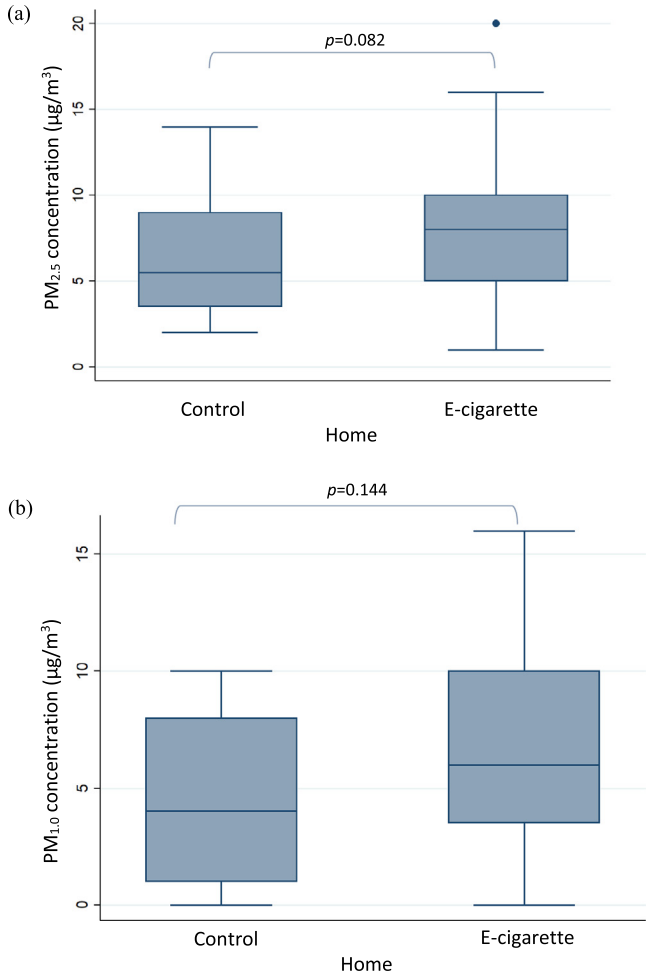

Fig. 1. Seven-day $PM_{2.5}$ (a) and $PM_{1.0}$ (b) concentrations (μg/m^3) in homes of electronic cigarette users ($n = 29$) and control homes ($n = 21$). p-Value was calculated with Mann-Whitney U test. TackSHS Study, 2019.

3.3.2. Comparison between e-cigarette users and non-users or control participants

Compared to e-cigarette users, the concentrations of salivary and urinary nicotine as well as all its metabolites of non-users and control participants were all significantly lower. 1,2-PD was the only humectant biomarker found at a consistently higher level in both biological samples of users than that of non-users and control participants. Additionally, no significant difference was found in concentrations of TSNAs between users and non-users or controls in both saliva and urine, except for salivary NNN, where a higher concentration was identified in the saliva of users compared to that of non-users ($p = 0.032$). We found similar concentrations of metals in the urine of users, non-users, and control participants.

4. Discussion

This observational study evaluated bystanders' exposure to SHA at home environment by measuring the concentration of indoor airborne markers and biomarkers. Our findings show low but quantifiable concentrations of airborne markers in homes of e-cigarette users, while airborne nicotine levels were all unquantifiable in control homes. Our study also found higher levels of cotinine, 1,2-PD, and cobalt in biological samples taken from bystanders compared to control participants.

Although we were not able to identify whether airborne nicotine was detected in e-cigarette users' homes at levels significantly higher than in control homes, the fact that this marker was higher than LOQ in 72 % of e-cigarette user's homes as opposed to 0 %, as was the case in control homes, indicates that e-cigarette use at home might increase airborne nicotine concentrations and have the potential to contaminate indoor air. As nicotine is a specific marker for the consumption of any nicotine-containing product, and participants were not using any other form of nicotine-containing products at home, the source of this pollutant was likely the aerosol exhaled by the e-cigarette users. The fact that we did not find significant differences in airborne nicotine concentrations between e-cigarette and control homes may be partly due to the methodology used to collect the marker in the gas phase, which may underestimate the true concentration. A previous study noted that the largest increase of airborne nicotine from e-cigarette use is in the particle phase compared to the gas phase (van Drooge et al., 2019).

Our results agree with further evidence that e-cigarette use at home impairs air quality. Using the same observation period (7 days), sampling and analysis method, Ballbè et al. reported a significantly higher concentration of airborne nicotine in homes of e-cigarette users (0.11 μg/m^3) compared to control homes (0.01 μg/m^3) (Ballbè et al., 2014). Expectedly, they are lower than those found in public settings where e-cigarette use is more intense, with levels ranging from 1.1 to 124.7 μg/m^3 in e-cigarette conventions, (Johnson et al., 2018; Chen et al., 2018) and from 0.9 to 3.3 μg/m^3 inside e-cigarette shops (Son et al., 2020; Li et al., 2021).

Similar to our study (8 μg/m^3; IQR: 5–10 μg/m^3), a previous observational study detected a median $PM_{2.5}$ concentration of 9.88 μg/m^3 in an e-cigarette user's home (IQR: 8.84–11.96 μg/m^3), not significantly different from control homes (Fernández et al., 2015). Although found in a relatively low concentration, the peaks of $PM_{2.5}$ level observed in that study were concurrent with e-cigarette puffs, (Fernández et al., 2015; Volesky et al., 2018)

Table 2
Seven-day concentrations (μg/m^3) of airborne nicotine, $PM_{2.5}$, and $PM_{1.0}$ in 29 homes of electronic cigarette (e-cigarette) users by different e-cigarette use characteristics. TackSHS Study, 2019.

	Airborne nicotine			$PM_{2.5}$			$PM_{1.0}$		
	N[a]	Geometric mean (95 % CI)	*p*-Values[b]	N[a]	Median (IQR)	*p*-Values[b]	N[a]	Median (IQR)	*p*-Values[b]
Type of e-cigarettes			0.314			0.337			0.294
1st generation	3	0.02 (0.01–0.08)		3	10.00 (7.00–16.00)		3	10.00 (5.00–14.00)	
2nd generation	6	0.02 (0.01–0.03)		4	4.50 (3.00–9.50)		4	1.75 (0.00–7.75)	
3rd generation	18	0.00 (0.00–0.05)		18	7.50 (5.00–10.00)		18	5.50 (4.00–9.00)	
4th generation	1	0.02[d]		1	10.00		1	9.00	
Nicotine concentration (mg/mL)[c] in refill liquid			0.310			0.581			0.668
0	1	<LOQ		1	5.00		1	4.00	
>0–<6	10	0.02 (0.01–0.04)		9	7.00 (5.00–14.00)		9	5.00 (3.50–12.00)	
≥6	8	0.01 (0.00–0.05)		8	7.50 (5.50–9.50)		8	5.50 (3.50–7.50)	
Not reported	10	0.02 (0.01–0.03)		11	10.00 (6.00–13.00)		11	9.00 (5.00–12.00)	
Place of e-cigarette use at home			0.827			0.296			0.299
Everywhere	15	0.01 (0.00–0.04)		13	7.00 (5.00–13.00)		13	5.00 (4.00–12.00)	
Only indoors	13	0.02 (0.01–0.02)		13	8.00 (6.00–10.00)		13	6.00 (5.00–9.00)	
Only outdoors	1	<LOQ		1	2.00		1	0.00	
Use of ventilation during e-cigarette use			0.981			0.073			0.068
Never	7	0.02 (0.01–0.03)		6	9.50 (9.00–14.00)		6	9.00 (6.00–12.00)	
Sometimes	10	0.01 (0.01–0.03)		9	6.00 (5.00–7.00)		9	4.00 (2.00–5.00)	
Always	12	0.01 (0.00–0.06)		12	9.00 (5.50–13.00)		12	6.50 (4.50–12.50)	

IQR: interquartile range; CI: confidence interval; LOQ: limit of quantification.
[a] Not all characteristics add up to 29 due to missing data.
[b] Kruskal-Wallis test.
[c] As reported by the participants.
[d] Tobit regression was not applied due to insufficient observations.

indicating that e-cigarette users exhaled $PM_{2.5}$ in the aerosol. However, the study did not employ ad libitum use of e-cigarette and did strictly control the environment.

We could not detect differences between concentrations of $PM_{2.5}$ and $PM_{1.0}$ in e-cigarette and control homes, probably because the study was conducted in a natural situation in which users use the product sporadically. One experimental study including three subjects using e-cigarettes concurrently for 2 h has described increased PM concentration during e-cigarette use compared to background measurements (Schober et al., 2014). Also, the similar PM concentration in control and e-cigarette homes may be due to the high decay rates of e-cigarette aerosol that may not increase the 24-h and one-week PM concentrations (Schober et al., 2019; Wallace et al., 2021). The rapid decay of PM from SHA might be attributable to the quick evaporation of the e-cigarette aerosol, as propanediol and glycerol are its main components, in addition to deposition on the surfaces and removal by ventilation (Schober et al., 2019). Furthermore, the e-cigarette aerosol size distribution alters in the human lungs and leads to the exhalation of ultrafine particles, which were not captured in the current study, owing to deposition of the liquid particle in the lungs and evaporation into the environment (Schripp et al., 2013). Additionally, our study excluded PM values recorded during cooking times that may dramatically elevate the level of PM at home, an approach that may also partly explain the low concentration of PM found in our study, but more realistic than other studies not considering this factor.

Despite the relatively low concentration of indoor pollutants found in this study, our findings still show increased concentrations of nicotine in e-cigarette homes compared to the control homes in natural conditions, which indicate that e-cigarette use at home generates SHA and might involuntarily expose other people to the pollutants. Furthermore, previous research demonstrated that PM and nicotine emitted from e-cigarette use indoors may drift to adjacent rooms and the outdoor environment, resulting in an air quality deterioration of smoke- and aerosol-free areas (Li et al., 2021). Both PM and airborne nicotine from e-cigarette use are deposited on the floor, windows, clothes, and other indoor surfaces, which might raise concern over their thirdhand exposure potential (Schober et al., 2019; Goniewicz and Lee, 2015).

Interestingly, we observed no variation of airborne nicotine and PM concentrations across different e-cigarette use characteristics which, under controlled conditions in previous research, has been found to influence the concentration of both markers from e-cigarette emission (Melstrom et al., 2017; Zhao et al., 2018). More observational studies using larger sample sizes are needed to identify the determinants of SHA exposure at homes under real conditions.

The higher concentrations of salivary cotinine and 3′-OH-cotinine found in bystanders in our study suggest that the airborne nicotine in SHA was absorbed by bystanders, confirming preliminary studies (Bekö et al., 2018; Ballbè et al., 2014). These studies found a higher concentration of urinary cotinine in bystanders, while our study did not find any significant increase in the concentration of any nicotine metabolites in urine. Differences might be attributed to the inter-individual variability in the nicotine and cotinine metabolism, which are affected by factors including race, gender, age, genetic variances, diet, or medications (Benowitz et al., 2009).

Although some TSNAs (i.e., NNN, NNK) were previously detected in saliva samples, (Pérez-Ortuño et al., 2016) our study did not find differences in TSNAs concentrations in saliva or urine between non-users in e-cigarette homes and non-users in control homes. Previous observational studies did not detect any TSNAs in the urine sample of bystanders attending e-cigarette events, (Johnson et al., 2019) nor found NNAL at a significant level in the urine of non-users living with e-cigarette users (Martínez-Sánchez et al., 2019). NNK was detected in children who lived with e-cigarette users but at a level not different from children living with non-users (Quintana et al., 2021). Future studies need to explore the extent of TSNAs systemic absorption among bystanders exposed to SHA.

We also identified refill liquid's humectant component, 1,2-PD, in saliva samples of bystanders at a significantly higher level than that was found in control participants. It is well known that 1,2-PD and glycerol are the most abundant constituents in refill liquid (≥80 % of refill liquid mass), (Dai et al., 2018) and have been identified in elevated concentrations in e-cigarette users' plasma (National Academies of Sciences, 2018). Our findings also agree with a previous study demonstrating increased 1,2 PD concentrations in car interiors during e-cigarette use to levels exceeding the German indoor health precaution guide (60 μg/m^3) (Schober et al., 2019; Fromme et al., 2019). The heating of 1,2-PD and glycerol by e-cigarette use has been found to form toxic thermal degradation by-products, such as acrolein, formaldehyde, acetaldehyde, and propylene oxide (Conklin et al., 2018; Sleiman et al., 2016). As solvents are the main constituents of refill liquids, the harmful by-products are

Table 3
Concentrations of biomarkers in saliva and urine samples of electronic cigarette (e-cigarette) users and non-users living in e-cigarette users' homes and control participants living in e-cigarette non-users' homes. TackSHS Study, 2019.

Biomarkers		Saliva						Urine[a]					
		Users (N = 29)	Non-users (N = 29)	Controls (*N* = 21)	*p*-Values[b]	*p*-Values[c]	*p*-Values[d]	Users (*N* = 12)	Non-users (N = 12)	Controls (*N* = 11)	*p*-Values[b]	*p*-Values[c]	*p*-Values[d]
Nicotine (LOQ: 0.50 ng/mL)	Number of samples < LOQ	1	18	19				1	5	3			
	Geometric Mean (95 % CI)	63.76 (15.28–266.01)	0.17 (0.04–0.70)	0.28 (0.14–0.59)	0.023	<0.001	<0.001	67.52 (10.82–421.39)	0.61 (0.20–1.80)	0.63 (0.48–0.82)	0.777	<0.001	<0.001
Cotinine (LOQ: 0.10 ng/mL)	Number of samples < LOQ	1	7	10				0	0	0			
	Geometric Mean (95 % CI)	33.54 (10.01–112.34)	0.24 (0.09–0.60)	0.00 (0.00–0.12)	0.003	<0.001	<0.001	96.93 (12.49–752.07)	1.04 (0.28–3.87)	0.33 (0.19–0.57)	0.242	0.003	<0.001
3′-OH-cotinine (LOQ: 0.04 ng/mL)	Number of samples < LOQ	2	12	18				0	0	0			
	Geometric Mean (95 % CI)	9.03 (2.56–31.82)	0.02 (0.00–0.12)	0.00 (0.00–0.01)	0.002	<0.001	<0.001	345.18 (45.68–2608.01)	3.61 (0.85–15.35)	1.36 (0.54–3.42)	0.325	0.001	<0.001
Nornicotine (LOQ: 0.10 ng/mL)	Number of samples < LOQ	6	27	21				2	7	8			
	Geometric Mean (95%CI)	0.71 (0.33–1.53)	0.01 (0.00–0.12)	<LOQ	0.224	<0.001	N/A	4.87 (0.69–34.31)	0.06 (0.01–0.34)	0.07 (0.00–0.14)	0.347	0.003	0.001
NNN (LOQ: 1.00 pg/mL)	Number of samples < LOQ	21	27	21				11	11	10			
	Geometric Mean (95%CI)	0.39 (0.09–1.69)	0.02 (0.00–4.94)	<LOQ	N/A	0.032	N/A	0.70 (0.31–1.59)	0.84 (0.57–1.25)	0.65 (0.23–1.80)	0.900	0.952	0.900
NNK (LOQ: 2.00 pg/mL)	Number of samples < LOQ	27	28	21				12	12	11			
	Geometric Mean (95%CI)	0.04 (0.00–106.71)	<LOQ	<LOQ	N/A	N/A	N/A	<LOQ	<LOQ	<LOQ	N/A	N/A	N/A
NNAL (LOQ: 0.50 pg/mL)	Number of samples < LOQ	26	28	21				9	10	10			
	Geometric Mean (95%CI)	0.00 (0.00–0.68)	0.00 (0.00–93.89)	<LOQ	0.395	0.165	N/A	0.13 (0.01–1.73)	0.13 (0.01–1.76)	0.23 (0.04–1.42)	0.528	0.569	0.306
1,2-PD (LOQ: 3.00 nmol/mL)	Number of samples < LOQ	2	7	6				0	0	0			
	Geometric Mean (95%CI)	100.23 (37.39–268.67)	8.05 (4.70–13.78)	4.84 (2.80–8.37)	<0.001	<0.001	<0.001	294.90 (95.48–910.80)	19.68 (7.99–48.46)	17.89 (7.70–41.54)	0.951	0.003	0.002
1,3-PD (LOQ: 3.00 nmol/mL)	Number of samples < LOQ	17	24	15				5	6	9			
	Geometric Mean (95%CI)	2.56 (1.11–5.91)	0.11(0.00–4.21)	0.61 (0.01–4.68)	0.424	0.050	0.200	3.88 (0.94–16.04)	2.95 (1.17–7.45)	4.90 (2.36–10.15)	0.314	0.504	0.755
Glycerol (LOQ: 10.00 nmol/mL)	Number of samples < LOQ	1	3	3				0	2	0			
	Geometric Mean (95%CI)	293.40 (119.85–718.26)	88.85 (50.71–155.70)	51.88 (20.63–130.50)	0.512	0.034	0.020	38.67 (22.54–66.32)	28.52 (15.80–51.50)	48.89 (36.36–65.72)	0.295	0.644	0.325

Abbreviations: LOQ: limit of quantification; NNN: N′-nitrosonornicotine; NNK: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; 1,2-PD: 1,2-propanediol; 1,3-PD: 1,3-propanediol; SD: standard deviation; NA: not applied.

[a] Urine samples were collected from participants in Italy and Spain only.

[b] Non-users vs. controls calculated using Mann-Whitney *U* test.

[c] Users vs. non-users calculated using Mann-Whitney *U* test.

[d] Users vs. controls calculated using Mann-Whitney *U* test.

expected to be present in SHA regardless of limits imposed on individual nicotine, additives, and/or flavourings.

Regarding metals, previous studies have also found cobalt in serum and urine of e-cigarette users, even at similar concentrations as found in combustible cigarette smokers (Zhao et al., 2020). Cobalt has been detected in refill liquids, suggesting that the cobalt found in human fluids of e-cigarette users was inhaled from e-cigarette aerosol (Zhao et al., 2020). Our study indicates that bystanders may also be exposed to the metal element present in SHA from e-cigarette use at home. To our knowledge, this is the first study that determined metal elements in e-cigarette non-users biological samples. Although cobalt is a biologically essential element part of vitamin B_{12}, excessive exposure may pose various adverse health effects, from allergic skin and respiratory reactions to neurological (hearing and visual impairment), cardiovascular, and endocrine diseases (Leyssens et al., 2017).

Our findings support the importance of comprehensively assessing the consequences of e-cigarette use at home for air quality and bystanders while recommending banning e-cigarette use in the presence of other people. Previous research indicates that young people living with e-cigarette users were 11 times more likely to be exposed to SHA compared to those not living with users of any tobacco products, (Bayly et al., 2019b) and they can gain more access to e-cigarettes stored at home which might pose safety risks (Kirkcaldy et al., 2019).

E-cigarette use inside homes is common when people perceive that SHA is less harmful than SHS and when there is no e-cigarette use restriction at home (Tzortzi et al., 2020; Bayly et al., 2019b; Kirkcaldy et al., 2019; McMillen et al., 2018; Agaku et al., 2020; Drehmer et al., 2019; Brose et al., 2017). In fact, private environments, including homes, have been described as the least protected place from SHA by the national legislation of European countries (Amalia et al., 2021c). Although voluntary rules on e-cigarette use at home are not common, some studies suggest that such restriction might effectively tackle exposure to SHA. In the US, people who lived within households with voluntary e-cigarette use restrictions had lower odds and frequency of e-cigarette use, while those who worked in workplaces with a total prohibition of e-cigarette use had significantly reduced likelihood of SHA exposure (Azagba et al., 2020).

Our study was limited by the convenience sampling of participants, which restricts the generalisation of our results but was the most efficient method to identify and enrol e-cigarette users. Nevertheless, we included participants from different countries with different sociodemographic contexts, increasing the sample's variability. We cannot disregard that the airborne sampling devices inside homes might have created a social-desirability bias where e-cigarette users might have changed their behavior (e.g., not using e-cigarette in a room where the devices were placed). Additionally, environmental and biological markers can originate from other sources, such as outdoor factors, indoor sources, common personal care products, and diet. It is also possible that some substances in candies may interfere with some biomarkers analysed. However, we analysed the same candies for propanediol and glycerol in a previous study that proved no interference in the analysis of these compounds (Amalia et al., 2021b). Other potential sources of metals were explored in the questionnaire, including some occupations (soldering, metalworking and other metal trades), hobbies (oil painting, mock-up construction, welding, etc.), having tattoos or piercings, and diet. However, the metal concentrations in urine found in this study were very low, and thus, we did not control for these factors in our analyses. Additionally, we used control participants to control for those complex confounders. We also acknowledge that this study is limited by the nature of self-reported data on e-cigarette use characteristics (e.g., refill liquid's nicotine concentration, e-cigarette type, place of e-cigarette use at home) and the lack of information on e-cigarette use duration at home. However, our intention was to describe and compare SHA exposure in e-cigarette users' and non-users homes, regardless of the variations in e-cigarette use, including the length of e-cigarette use at home. Furthermore, we did not take into account the air exchange rate that might affect the concentration of indoor airborne markers. Nevertheless, this study included variability across homes by sampling homes from different countries for 7 days and incorporating the information on the frequency of room ventilation during e-cigarette use.

Notwithstanding the mentioned limitations, the present study is the first multi-country study that simultaneously examined environmental and personal exposure to SHA at homes using a non-interventional study design with a relatively long observation period. The complexity of the study design enables us to see a comprehensive picture of the real-life scenario. Most of the e-cigarette users recruited (64 %) were using the 'mod' system of the 3rd generation of e-cigarettes which was the popular e-cigarette model in the market at the time of the study (Zare et al., 2018). Additionally, there were similar characteristics of participants across different groups (i.e., users, non-users, controls), which made them comparable. We also minimised the distortion in PM measurement by taking into account the cooking activity because it is a prominent source of PM indoors. The same protocol was followed in the four countries, and training was centrally provided by the coordinating centre. Moreover, the same devices for PM and airborne nicotine sampling were centrally purchased and delivered to the four countries as well as all the materials for biological samples' collection. Finally, all the analytical procedures were performed according to the nature of the sample in each of the accredited laboratories (airborne nicotine at ASPB, nicotine, other nicotine-related compounds, and humectants in saliva and urine at IMIM, and metals in urine at UG).

5. Conclusion

There were no meaningful differences in airborne nicotine and PM concentrations measured in e-cigarette users' homes and control homes during a week. Nevertheless, airborne nicotine was not detected in control homes at all. In contrast, there were significant differences in some biomarkers measured in bystanders, including nicotine, 1,2-PD, and metal elements. These results show that the bystanders in this study were exposed to SHA. While the potential and extent of long-term effects of this exposure cannot be determined yet, further research focusing on the chemical characteristics of the aerosol and the development of methods to measure it in both particle and gas phases in real-life scenarios is warranted.

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CRediT authorship contribution statement

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Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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