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# Cigarettes vs. e-cigarettes: Passive exposure at home measured by means of airborne marker and biomarkers <sup>☆</sup>



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## ABSTRACT

**Background:** There is scarce evidence about passive exposure to the vapour released or exhaled from electronic cigarettes (e-cigarettes) under real conditions. The aim of this study is to characterise passive exposure to nicotine from e-cigarettes' vapour and conventional cigarettes' smoke at home among non-smokers under real-use conditions.

**Methods:** We conducted an observational study with 54 non-smoker volunteers from different homes: 25 living at home with conventional smokers, 5 living with nicotine e-cigarette users, and 24 from control homes (not using conventional cigarettes neither e-cigarettes). We measured airborne nicotine at home and biomarkers (cotinine in saliva and urine). We calculated geometric mean (GM) and geometric standard deviations (GSD). We also performed ANOVA and Student's *t* tests for the log-transformed data. We used Bonferroni-corrected *t*-tests to control the family error rate for multiple comparisons at 5%.

**Results:** The GMs of airborne nicotine were 0.74  $\mu\text{g}/\text{m}^3$  (GSD=4.05) in the smokers' homes, 0.13  $\mu\text{g}/\text{m}^3$  (GSD=2.4) in the e-cigarettes users' homes, and 0.02  $\mu\text{g}/\text{m}^3$  (GSD=3.51) in the control homes. The GMs of salivary cotinine were 0.38 ng/ml (GSD=2.34) in the smokers' homes, 0.19 ng/ml (GSD=2.17) in the e-cigarettes users' homes, and 0.07 ng/ml (GSD=1.79) in the control homes. Salivary cotinine concentrations of the non-smokers exposed to e-cigarette's vapour at home (all exposed  $\geq 2$  h/day) were statistically significant different than those found in non-smokers exposed to second-hand smoke  $\geq 2$  h/day and in non-smokers from control homes.

**Conclusions:** The airborne markers were statistically higher in conventional cigarette homes than in e-cigarettes homes (5.7 times higher). However, concentrations of both biomarkers among non-smokers exposed to conventional cigarettes and e-cigarettes' vapour were statistically similar (only 2 and 1.4 times higher, respectively). The levels of airborne nicotine and cotinine concentrations in the homes with e-cigarette users were higher than control homes (differences statistically significant). Our results show that non-smokers passively exposed to e-cigarettes absorb nicotine.

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## 1. Introduction

Interest towards electronic cigarettes (e-cigarettes) by the smoking population has grown in recent years (Ayers et al., 2011). There are some studies that have suggested that e-cigarettes might help smokers to reduce or eventually quit smoking (Bullen et al., 2013; Etter et al., 2011; Polosa et al., 2011; Siegel et al., 2011; Wagener et al., 2012; Brown et al., 2014), even though, other studies have

<sup>☆</sup>The research and ethics committee of the Bellvitge University Hospital provided ethical approval for the study protocol, including the informed consent form. This study meets the code of the Declaration of Helsinki.

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shown lower quitting rates among smokers who use these devices (Vickerman et al., 2013; Popova and Ling, 2013; Adkison et al., 2013; Grana et al., 2014). Moreover, e-cigarettes have sometimes been proposed as a tool for harm reduction (Cahn and Siegel, 2011; Fagerström and Bridgman, 2014). However, there is still little evidence from well-designed, large randomized controlled trials (Bullen et al., 2013). Moreover, studies on the safety and toxicity of e-cigarettes are scarce and show high variability among and within different brands, suggesting an inadequate quality control manufacture (Hadwiger et al., 2010; Trtchounian et al., 2010; Williams and Talbot, 2011). Because of the lack of sufficient data concerning their safety or efficacy, e-cigarettes have been banned through regulation in several countries such as Singapore, Brazil, Belgium, Uruguay and other countries (Convention Secretariat. WHO Framework Convention on Tobacco Control, 2012). However, e-cigarettes are freely available in other countries or are to be licensed as smoking cessation aids such as in the United Kingdom (Convention Secretariat. WHO Framework Convention on Tobacco Control, 2012; Torjesen, 2013).

Another concern recently appeared regarding the potential passive exposure to the vapour exhaled by e-cigarette users, as their use has increased in indoor places, including those with tobacco smoke-free bans (Convention Secretariat. WHO Framework Convention on Tobacco Control, 2012). Also, some private companies have banned their use in indoor workplaces. The legal status of e-cigarettes is unclear in many countries in this regard and there are very few studies about the safety of the passive exposure to e-cigarettes. Available evidence derives mainly from laboratory studies and there are few studies addressing secondhand exposure to exhaled vapours from e-cigarettes under real conditions (Burstyn, 2014). These studies, focused on airborne measurements, show that the vapour generated from e-cigarettes contains potentially toxic compounds; nevertheless, these are generally in lower amounts than those for the conventional cigarettes (Czogala et al., 2013; McAuley et al., 2012; Pellegrino et al., 2012; Schripp et al., 2013). To our knowledge, there are no studies about passive exposure to e-cigarettes under real-use conditions and, to date, these measures have never been done by means of biomarkers.

The objective of this study is to describe the passive exposure to nicotine emissions from e-cigarettes and from conventional cigarettes among non-smokers under real-use conditions, using both airborne and biological markers.

## 2. Material and methods

We conducted a study under real-use conditions about passive exposure to e-cigarettes and to conventional cigarettes using airborne markers (nicotine) and biomarkers (saliva and urine cotinine) of tobacco exposure. We recruited a convenience sample comprised of 54 non-smoker volunteers from different homes: 25 living at home with conventional smokers, 5 living with nicotine e-cigarette users, and 24 from control homes (nobody using conventional cigarettes neither e-cigarettes). The e-cigarette devices (all tank system) and the e-cigarette liquid brands (propylene glycol based liquids) were of different brands (Totally Wicked<sup>®</sup>, Puff<sup>®</sup>, and Free Life<sup>®</sup>). The only source of passive exposure to e-cigarette vapour or tobacco smoke among the participants living with the e-cigarette users or with smokers was exclusively at home during the one week period of the study, as previously accorded with the researchers. After the assessment of the exposure to secondhand smoke, the volunteers answered a detailed questionnaire of exposure to secondhand smoke which confirmed their lack of exposure in settings other than their homes (Martinez-Sanchez et al., 2009).

### 2.1. Field work

The field work was conducted between November 2011 and February 2012. We visited the volunteers' home and explained the objective and procedure of the study, provided a presentation letter, and obtained written informed consent. We installed one passive device to sample nicotine in the air of the main family room, usually the living room. After one week, we returned to the volunteers' home to collect the nicotine sampler, to collect a sample of saliva and urine, and to

administer the secondhand smoke exposure questionnaire. The research and ethics committee of the Bellvitge University Hospital provided ethical approval for the study protocol, including the informed consent form. This study meets the code of the Declaration of Helsinki.

### 2.2. Airborne marker of passive exposure (nicotine)

We sampled the nicotine in the air with a sampling device, which included a filter of 37 mm in diameter treated with sodium bisulphate (Hammond and Leaderer, 1987). It was installed suspended from the ceiling following a standard protocol: they had to hang freely in the air and not to be placed within one metre of an area where someone regularly smokes, where air does not circulate such as a corner, under a shelf or buried in curtains. After collection, nicotine was extracted from the filter in the sampling devices and analysed by gas chromatography with detection by mass spectrometry (GC/MS) at the Laboratory of the Public Health Agency of Barcelona (limit of quantification: 5 ng of nicotine in filter, equivalent to 0.02  $\mu\text{g}/\text{m}^3$  per one week of exposure) (Fernández et al., 2008; Nebot et al., 2009). The airborne nicotine concentration ( $\mu\text{g}/\text{m}^3$ ) was computed by dividing the amount of nicotine collected in the filter ( $\mu\text{g}$ ) by the flow rate ( $24 \times 10^{-6} \text{m}^3/\text{min}$ ) and allowing for the time (minutes) the filter had been exposed. Samples with nicotine concentrations below the quantification limit were assigned a value of 0.01  $\mu\text{g}/\text{m}^3$  (half of the limit of quantification), according to the 7-day exposure time.

### 2.3. Biomarkers of passive exposure (cotinine in saliva and urine)

During the second visit, 7 days after the installation of the nicotine sampling device, we obtained saliva and urine samples for cotinine analysis. Participants provided about 20 ml of urine. For the saliva sample, participants were asked to rinse their mouths and then suck a lemon candy (Smint<sup>®</sup>) to stimulate saliva production. They were asked to spit out a small amount of saliva and then to provide about 9 ml of saliva by spitting it into a funnel placed in a test tube. Both saliva and urine samples were frozen in 3 ml aliquots to  $-80^\circ\text{C}$  for storage.

The frozen samples were sent to the Bioanalysis Research Group of the IMIM (Hospital del Mar Medical Research Institute) in Barcelona. Salivary and urinary cotinine were measured by liquid chromatography coupled to tandem mass spectrometry with multiple reactions monitoring (LC/MS/MS). Urinary cotinine concentration was adjusted for urinary creatinine.

### 2.4. Data analysis

We described the airborne marker (nicotine concentrations) and biomarkers (salivary and urinary cotinine) using geometric means (GM), geometric standard deviations (GSD), medians, and interquartile ranges (IQRs) by type of home (with conventional cigarette consumption, with e-cigarette consumption, and non-smokers homes). We used the Spearman's rank correlation coefficient (*rsp*) to assess the correlation between airborne markers and biomarkers. We compared the concentrations by means of ANOVA tests and Student's *t* tests for independent samples. Due to the skewed distribution of the data we used log-transformed data for airborne nicotine, salivary and urinary cotinine to perform all the hypothesis testing.

We performed several comparisons: a) all participants exposed to conventional cigarettes vs. all participants exposed to e-cigarettes emissions, and b) all participants exposed to conventional cigarettes for two hours or more per day vs. all participants exposed to e-cigarettes emissions (all of them exposed for two hours or more). We used Bonferroni-corrected *t*-tests to control the family error rate for multiple comparisons at 5%.

## 3. Results

Salivary and urinary cotinine were highly correlated (*rsp*=0.855,  $p < 0.001$ ), and both biomarkers were highly correlated with air nicotine concentration measured at the volunteers' home during one week (*rsp*=0.731 for salivary cotinine and *rsp*=0.710 for urinary cotinine  $p$ -values  $< 0.001$ ).

Table 1 shows the airborne nicotine, salivary and creatinine-adjusted urinary cotinine concentrations. The GMs of airborne nicotine were 0.74  $\mu\text{g}/\text{m}^3$  (GSD=4.05) in the smokers' homes, 0.13  $\mu\text{g}/\text{m}^3$  (GSD=2.4) in the e-cigarettes users' homes, and 0.02  $\mu\text{g}/\text{m}^3$  (GSD=3.51) in the control homes. The GMs of salivary cotinine were 0.38 ng/ml (GSD=2.34) in the smokers' homes, 0.19 ng/ml (GSD=2.17) in the e-cigarettes users' homes, and 0.07 ng/ml (GSD=1.79) in the control homes. There was a statistically significant difference in the airborne nicotine concentrations

**Table 1**  
Airborne nicotine at home and biomarkers (salivary and urine cotinine) taken at the end of one week period.

	n	Airborne nicotine ( $\mu\text{g}/\text{m}^3$ )		Salivary cotinine (ng/ml)		Urinary cotinine (ng/mg)	
		Median (IQR)	GM (GSD)	Median (IQR)	GM (GSD)	Median (IQR)	GM (GSD)
Exposed to conventional cigarettes							
All participants	25	1.03 [0.21; 1.99]	0.74 (4.05)	0.32 [0.23; 0.63]	0.38 (2.34)	2.58 [1.13; 4.85]	2.46 (2.67)
No. of cigarettes/day smoked at home <sup>a</sup>							
1	10	0.60 [0.12; 1.86]	0.44 (4.05)	0.22 [0.15; 0.53]	0.24 (2.20)	1.46 [0.93; 3.85]	1.78 (2.39)
2–6	9	1.05 [0.63; 2.65]	1.16 (2.83)	0.30 [0.24; 0.42]	0.35 (1.71)	1.74 [1.17; 3.20]	2.05 (1.92)
$\geq 7$	4	2.38 [0.56; 7.84]	1.60 (6.16)	0.89 [0.61; 1.03]	0.81 (1.34)	5.98 [3.78; 10.18]	6.00 (1.69)
No. of hours/day exposed at home <sup>a</sup>							
1–2	17	1.05 [0.20; 1.92]	0.65 (3.90)	0.30 [0.18; 0.53]	0.30 (2.10)	1.74 [1.11–3.77]	2.10 (2.22)
$\geq 2$	6	1.90 [0.69; 4.54]	1.44 (4.31)	0.58 [0.27; 0.97]	0.51 (2.00)	2.88 [1.23–8.67]	3.10 (2.61)
Exposed to e-cigarettes							
All exposed $\geq 2$ hours/day	5	0.11 [0.06; 0.32]	0.13 (2.4)	0.24 [0.15; 0.31]	0.19 (2.17)	2.64 [0.70; 4.04]	1.75 (2.67)
Control homes <sup>b</sup>							
All participants	24	0.01 [0.01; 0.05]	0.02 (3.51)	0.05 [0.05; 0.13]	0.07 (1.79)	0.72 [0.55; 1.09]	0.70 (1.76)
Global comparison by ANOVA test							
p-value <sup>c</sup>		< 0.001		< 0.001		< 0.001	
Multiple comparisons by Student's tests							
p-value <sup>d</sup>		0.014		0.110		0.483	
p-value <sup>e</sup>		< 0.001		< 0.001		< 0.001	
p-value <sup>f</sup>		0.007		0.003		0.008	
p-value <sup>g</sup>		0.030		0.010		0.060	

Urinary cotinine adjusted for urinary creatinine.

IQR: interquartile range; GM: geometric mean; GSD: geometric standard deviations.

<sup>a</sup> The figures do not sum the total due to some missing values.

<sup>b</sup> Homes where nobody smokes or uses e-cigarettes.

<sup>c</sup> Comparison among three types of homes (conventional cigarettes, e-cigarettes, and control) by ANOVA test from log-transformed data.

<sup>d</sup> Comparison between conventional cigarettes homes and e-cigarettes homes by Student's *t* tests for independent samples from log-transformed data.

<sup>e</sup> Comparison between conventional cigarettes homes and control homes by Student's *t* tests for independent samples from log-transformed data.

<sup>f</sup> Comparison between e-cigarettes homes and control homes by Student's *t* tests for independent samples from log-transformed data.

<sup>g</sup> Comparison between conventional cigarettes homes ( $\geq 7$  cigarettes/day) and e-cigarettes homes by Student's *t* tests for independent samples from log-transformed data.

and both biomarkers according to the type of home (*p*-values of ANOVA < 0.001). There was also a statistically significant difference in airborne nicotine concentration among the three possible comparisons (homes with conventional smokers vs. control homes; homes with conventional smokers vs. homes with e-cigarette users; and homes with e-cigarettes users vs. control homes) (Table 1). There was no statistically significant differences in salivary cotinine concentrations between the non-smokers exposed to e-cigarettes' vapour at home and the non-smokers exposed to SHS from conventional cigarettes and there were statistically significant differences between both homes (conventional cigarettes and e-cigarettes) and control homes (Table 1). We found same results in the urinary cotinine concentrations (Table 1).

Salivary cotinine concentrations were statistically significant different between non-smokers exposed  $\geq 7$  cigarettes/day and non-smokers exposed to e-cigarettes, although this difference did not reach statistical significance for urinary cotinine (Table 1). All non-smokers who lived with e-cigarette users were exposed to the vapour of e-cigarettes more than 2 h per day (see Table 1).

#### 4. Discussion

This study shows similar concentrations of airborne nicotine in the control homes and in the e-cigarette's homes; both type of homes have lower concentrations than in the conventional smoker's home. E-cigarettes produce an aerosol with fewer chemical compounds than that in conventional cigarettes because they do not require combustion and hence the temperature reached is lower than those in the conventional cigarettes (Goniewicz et al., 2014; McAuley et al., 2012). Even so, the vapour generated from e-cigarettes contains potentially toxic compounds that are generally

at traced amounts (Czogala et al., 2013; McAuley et al., 2012; Pellegrino et al., 2012; Schober et al., 2013; Schripp et al., 2013).

In our study, average airborne nicotine concentration in homes with conventional smokers were approximately 5.7 times higher than in homes with e-cigarettes users. These results are in agreement with the results obtained by Czogala et al. (2013) in a laboratory study: second-hand exposure to nicotine was 10 times higher from tobacco smoke than from e-cigarettes. We did not find statistically significant differences in cotinine concentrations from the non-smokers exposed to e-cigarette vapour versus those exposed to tobacco smoke. This is also in agreement with a laboratory study from Flouris et al. (2013) that found that e-cigarettes and tobacco cigarettes generated similar effects on serum cotinine levels after a passive exposure of one hour (2.4 vs. 2.6 ng/ml respectively). Hence, this discrepancy between airborne nicotine levels and biomarkers (cotinine levels) in different laboratory studies is maintained in our study under real-use conditions. This could be because biological markers are indicative of the real internal dose exposure in any setting in the previous days, whereas the environmental measurements only determine exposure in specific places.

In our study, cotinine concentrations among the non-smokers exposed to e-cigarette users (all of them former heavy smokers) were lower than those concentrations among the non-smokers exposed to seven or more conventional cigarettes. However, these concentrations were higher than those found in non-smokers living in the control homes.

Our results should be taken with caution, because of the small number of volunteers exposed to e-cigarette users at home. In addition, although one requirement to participants was to be exposed to smoking only at home, and all participants answered a detailed questionnaire on secondhand smoke exposure in

settings other than homes, we cannot disregard non-reporting of other potential sources of exposure. The main sources of second-hand smoke exposure in Spain are private venues (homes and cars) since the current Spanish smoke-free legislation bans smoking in all indoor public and workplaces. Nevertheless, there are no reasons to expect such a recall bias in the volunteers. Also, differences within and among e-cigarette liquid and cartridges brands containing nicotine may provide different results (Williams and Talbot, 2011). Nevertheless, the results of our study add new information that should be extended with other studies assessing the real impact of the e-cigarettes exposure among non-smokers.

Despite the potential limitations, it is noteworthy that this is the first study attempting to assess passive exposure to e-cigarette vapour under a real-use condition, with real e-cigarette and cigarette users, and a long exposure time analysed (one week). Moreover, the study has also provided novel results about objective and specific biomarkers of tobacco exposure in humans exposed to e-cigarette vapour under real use conditions.

In conclusion, our data show that the levels of airborne nicotine concentrations in the e-cigarette user's homes were higher than those in the control homes, and that concentration of biomarkers among non-smokers exposed to e-cigarettes vapour and to conventional cigarettes was statistically similar. Our results show that non-smokers passively exposed to e-cigarettes absorb nicotine.

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## Competing interests

Authors declare that they have no conflicts of interest.

## Contributors

MB and JMMS conceived the study, conducted the fieldwork, prepared the database, analysed the data and drafted the manuscript. MB, JMMS, XS, MF, RPO, JAP, ES, and EF contributed substantially to the conception, design, and interpretation of data. All authors contributed to the manuscript and approved its final version. EF is the guarantor.

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