



Impacts of exhaled aerosol from the usage of the tobacco heating system to indoor air quality: A chamber study

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HIGHLIGHTS

- The impact of using tobacco heating system on indoor air was investigated.
- The pollutant levels were significantly lower compared to conventional cigarettes.
- Exhaled particles evaporated fast as opposed to those of conventional cigarettes.
- Number of users was the most important factor affecting indoor air quality.

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ABSTRACT

Aerosol particle, carbonyl, and nicotine concentrations were analysed as pollutants affecting indoor air quality during the usage of electrically-heated tobacco product - the Tobacco Heating System (THS). Quantitative experimental variables included THS use intensity as number of parallel users (1, 3, or 5), distance to the bystander (0.5, 1, or 2 m), as well as environmental conditions in a chamber: ventilation intensity as air changes per hour (0.2, 0.5, or 1 h⁻¹), and relative humidity (RH, 30, 50 or 70%). The real-time particle number (PNC), CO and CO₂ concentration, as well as off-line acetaldehyde, formaldehyde, nicotine, and 3-ethenylpyridine concentration was measured during and after the active usage. Use of THS resulted in a statistically significant increase of several analytes including nicotine, acetaldehyde, PM_{2.5}, and PNC as compared to the background. The obtained levels were significantly lower (approximately 16, 8, 8 and 28 times for nicotine, acetaldehyde, PNC and PM_{2.5}, respectively) compared to the levels resulting from conventional cigarette (CC) smoking under identical conditions. The maximum 30 min concentration of PNC (4.8×10^5 #/cm³), as well as maximum concentration of PNC (9.3×10^6 #/cm³) suggest that the intensive use of THS in a confined space with limited ventilation might cause substantially elevated aerosol concentrations, although these particles appeared as highly volatile ones and evaporated within seconds. Generally, the usage intensity (number of simultaneous users) prevailed as the most important factor positively affecting pollutant variations; another important factor was the distance to bystander.

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1. Introduction

Conventional cigarettes (CCs) were the most commonly used tobacco product in most countries up to the recent decade. The current tobacco sector is becoming tremendously complex with the rapid emergence and popularity of alternative products (Navas-Acien, 2018). The first widespread alternative were electronic

cigarettes (ECs) – devices electrically heating and vaporizing a liquid solution to produce an inhalable aerosol, typically containing nicotine, flavourings, and other compounds (Nayir et al., 2016). Another viable approach to reduce the levels of hazardous substances associated with cigarette burning smoke is the generation of nicotine-containing aerosol by heating tobacco in reduced temperatures as opposed to burning, thus entitling the process as “heat-not-burn” (HnB), and the product as Tobacco Heating System (THS) or Tobacco Heating Product (THP). The first commercial HnB, Premier™ (R. J. Reynolds, Winston-Salem, NC, USA), was introduced in 1988, followed by Eclipse™ (R. J. Reynolds) and Accord™

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(Philip Morris) in the 1990s, Heat Bar™ (Philip Morris) in 2007, and IQOS™ (Philip Morris International, Lausanne, Switzerland) in 2016. British American Tobacco has recently developed a THP comprising an electrical heating device, commercially known as Glo™, and consumable tobacco rods, commercially known as KentNeostiks™ referred as THP1.0 (Proctor, 2018).

The mainstream aerosol produced by tobacco fillers and the mainstream aerosol of IQOS were shown to contain almost the same amount of nicotine as those of conventional combustion cigarettes (Bekki et al., 2017). The THS was shown to deliver nicotine to the aerosol at levels higher than ECs but lower than CCs when tested using Health Canada Intense puffing regime (Farsalinos et al. (2017)). At the same time, significantly lower concentrations of harmful and potentially harmful constituents (HPHCs) (Schaller et al., 2016; Jaccard et al., 2017) and tobacco-specific nitrosamines (TSNAs, Bekki et al., 2017) were found in the aerosol of THS (as compared to the mainstream smoke of reference cigarette 3R4F). The reduction of constituents in the mainstream aerosol of THS (IQOS) in comparison with a reference cigarette 3R4F was more than 90%: carbon monoxide (>97.00%), volatile organic compounds (VOCs), aromatic amines, hydrogen cyanide, phenol, and polycyclic aromatic hydrocarbons (PAHs) (>98%) (Li et al., 2018). The mainstream aerosol of another type of HnB - THP1.0 – was also shown to have overall average reduction of 97.5% for the abbreviated list of HPHCs of smoke specified by US Food and Drug Administration Tobacco Products Scientific Advisory Committee for reporting in cigarette smoke (excluding nicotine) in comparison with the CC (Forster et al., 2018).

Investigations performed by governmental institutions confirmed findings of tobacco companies and independent researchers. Mallock et al. (2018) reported that the yields of the carbonyl compounds in the mainstream THS 2.2 aerosol were reduced by 80–96%, VOCs and SVOCs reduced by 97–99% compared to a reference cigarette 3R4F (Schaller et al., 2016). Having performed a systematic review of 31 publication on HnB Simonavicius et al. (2018) concluded that although limited by methodological heterogeneity, findings were largely similar for independent and industry-funded studies.

Although previous studies have reported many data on the mainstream aerosol, the data on the second hand HnB aerosol is still very limited. The comparison between the background and THS environmental aerosol samples generated by smoking machines in an environmentally controlled room showed a statistically significant increase in concentration of only five compounds (nicotine, acetaldehyde, toluene, benzene, and solanesol) (Mottier et al., 2016). The concentrations of most measured indoor air constituents during the use of THS in an environmentally controlled room simulating “Office”, “Residential”, and “Hospitality” environments were similar to background levels (with the exception of acetaldehyde and nicotine) and for most analytes were an order of magnitude lower than found in assessments with the CC (Mitova et al., 2016). PAHs were reported to be mostly non-detectable in the particulate emission of organic matter from THS. Metal concentrations were similar to the background levels and lower during THS usage compared to both ECs and CCs. Aldehydes were higher in comparison with the EC environmental aerosol, however the levels were substantially lower compared to CCs (Ruprecht et al., 2017). Markers of environmental tobacco smoke (RSP, UVPM, FPM, solanesol, nicotine, 3-ethenylpyridine), toluene, carbon monoxide, propylene glycol, glycerol, and triacetin were below the limit of detection or the limit of quantification in simulated non-smoking and smoking environments after using of electrically-heated tobacco product referred to as the Novel Tobacco Vapour (NTV) product, while the concentrations of ammonia, carbonyls, and total volatile organic compounds were found at the same levels in the

chamber without NTV use (Ichitsubo et al., 2018). Submicronic particles (SMPs) were four-times higher during smoking CCs than those released by ECs and THS, and remained high for at least 1 h, while SMPs values returned immediately similar to background for ECs and THS (Protano et al., 2016).

The above studies mostly aimed at the quantification of levels (average values) of aerosol particles or gaseous compounds in indoor air during the usage of HnB devices. At the same time, no data are yet available on the time-resolved patterns of dispersion of aerosol in a room under varying environmental conditions. The aim of this study was to assess temporal and spatial variations of exhaled THS aerosol in a chamber, based on a highly time resolved aerosol concentration and particle size distribution measurements supplemented by averaged values of tobacco specific gaseous air pollutants. This data were regressed against environmental conditions, such as ventilation rate, relative humidity, THS usage intensity, and distance of a user to the bystander indicating important factors affecting the potential exposure.

2. Methods

2.1. The experimental design

The experiment aimed to research the quantitative effects of environmental variables including ventilation intensity (V) as air changes per hour (0.2, 0.5, or 1), THS use intensity (I) as number of parallel users (1, 3, or 5), relative humidity (RH, 30, 50 or 70%), and distance to the bystander (D , 0.5, 1, or 2 m) onto pollutant concentration variations in a chamber. The experimental plan with variables and responses is provided in supplementary material (Fig. S1, Table. S1). Totally 30 experimental runs were carried out with THS and three with CC.

2.2. Indoor chamber

A test chamber (the floor area of 13 m² and a volume of 35.8 m³) representing a standard room was adapted for the purpose to evaluate levels of various gaseous pollutants, aerosol particle concentration and size distribution at a location of potential exposure of an occupant in a room. The walls, floor and ceiling of the chamber were fabricated using conventional construction materials, such as painted dry-wall, PVC lining, and a panel ceiling. Supply and exhaust airflow via in-ceiling air diffusers were controlled using an air handling unit (GOLD 04, Swegon AB, Sweden). The supply air temperature during the experiments was set to $+22 \pm 2$ °C. Relative humidity (RH) was regulated in the range of 30–70% using air humidification system (ES4, NORDMANN Engineering AG, Basel, Switzerland). Cleaning of the chamber before each experimental day was done by water based floor mopping. The outdoor air was conditioned in a heat exchanger and treated with two steps of filtration: an F7 class filter (based on EN 779:2012 inside the handling unit and subsequently a high efficiency particulate air filter (HEPA 13, General Filter, Italy). Gaseous organic pollutants were removed by a fixed active carbon bed installed after the air handling unit. One multi-nozzle air supply diffuser of 0.5 × 0.5 m with plenum box was used for the in-ceiling air supply. The air change rate inside of the chamber was checked before and after of each day experiments via the duct air velocity measurements (Innova 1221, Lumasense, Denmark). Additionally, the air change rate was verified using CO₂ tracer gas decay method (ASTM, 2000) by CO₂ meter (7545 IAQ-CALC, TSI Inc., USA) before and after the measurement campaign. The effectiveness of purging of the chamber between runs was additionally tested using metal oxide VOC sensors (iAQ-2000, ams AG, Austria).

Bystander. A “dummy” of a rectangular geometry was installed

in the chamber to simulate a seated person with the inclusion of “legs”. The surface area of the “dummy” was equal to 1.7 m² covered with a textile fabric. The surface temperature of the dummy was maintained in the range of +31 °C to +34 °C, similar to the human body surface temperature. The dummy was seated on a chair near a wall. The aerosol samples were drawn through a copper inlet tube and divided to sampling instruments, which were positioned immediately outside of the chamber in order to minimize particle losses due to diffusion and evaporation processes.

2.3. Analytics

Particles. The real time size-segregated particle concentration was determined using the electrical low pressure impactor (ELPI+, Dekati Ltd., Finland), at a flow rate of 10 l/min. ELPI+ divides aerosol particles to 15 fractions (from 0.006 µm to 10.0 µm). This instrument utilises the cascade impaction principle and has a direct-reading capability. Real-time concentrations of aerosol samples were registered at 1 s temporal resolution. Additionally, for the process control a scanning mobility particle sizer (SMPS) (3910, TSI Inc., USA) classified aerosol particles across 13 size bins from 10 to 420 nm based on the electrical mobility diameter during 60 s, or was used as a counter for a single size bin at a 1 s resolution, with the flow rate of 1 l/min. SMPS measures particles using electrical classification by radial differential mobility analyser and optical counting using isopropanol-based condensation particle counter, resolution in terms of concentration is 1 #/cm³.

The verification of particle size distribution (PSD) as measured by the particle instruments was conducted by generating an aerosol of Polystyrene Latex (PSL) particles of 0.3 µm and 1.0 µm in the chamber, using an atomizer (Collison Nebulizer, CH Technologies, USA), Inc. and passing the flow through an aerosol neutralizer (3054, TSI Inc, USA).

Carbonyls. Concentration of formaldehyde and acetaldehyde was estimated following the ASTM D5197 - 03 procedure. This method involves drawing air (pump Universal PCXR8, SKC Inc., USA) through a cartridge containing silica gel coated with 2,4-dinitrophenylhydrazine (DNPH) reagent (SKC Inc.). The DNPH derivatives were analysed for parent aldehydes utilizing high performance liquid chromatography (HPLC).

Nicotine and 3-ethenylpyridine. The method was based on ISO 18145 procedure, i.e. the collection of nicotine by adsorption on a sorbent resin (XAD®-4, 7 × 70-mm size, 2 sections, 40/80 mg sorbent, 20/40 mesh, SKC Inc.), extraction of nicotine from the sorbent resin and determination by gas chromatography-mass spectrometry (GC-MS-QP2010 Ultra, Shimadzu Corp., Japan). The standard procedure was modified by using a mass spectrometry detection instead of nitrogen selective detection.

Microclimate parameters, carbon dioxide and carbon monoxide. The values of carbon dioxide (CO₂) and carbon monoxide (CO), together with temperature and relative humidity levels were continuously recorded by appropriate sensors (7545 IAQ-CALC, TSI Inc., USA). The instrument used a low-drift NDIR sensor for CO₂ (range from 0 to 5000 ppm, accuracy ±3.0% of reading or ±50 ppm, resolution 1 ppm) and electrochemical sensor for CO (range 0–500 ppm, accuracy ±3.0% of reading or ±3 ppm, resolution 0.1 ppm). The meters were factory calibrated before each measurement campaign and additionally inter-compared every third day of experiments.

2.4. Experimental procedure

The experiment was realized as a D-optimal design, available via experiment planning package Modde 10 (MKS Umetrics, Sweden), supplemented with additional experiments aiming to compare or

validate main experimental runs. The experiment plan included 20% of replicates.

The real-time particle number concentration (PNC) and particle size distribution (PSD) obtained from the aerosol instruments were further analysed for maximum and mean concentration values during the entire experimental run and after the active period of the usage, as well as recalculated to particle mass concentration for the PM_{2.5} fraction (particles having aerodynamic diameter of less than 2.5 µm). Additionally, off-line carbonyls (acetaldehyde and formaldehyde), off-line nicotine and 3-ethenylpyridine; and real-time CO₂ concentration were entered as responses to the model.

The concentration of pollutants before the experiment was monitored initially for 30 min to assure adequately low background concentration. A background conditions with human presence but no product use were monitored afterwards – 30 min; under intensity of three THS users – background conditions were evaluated with three human subjects; 5 THS users – background conditions with five THS users; the experimental chamber was purged at least for 30 min after each measurement session; ACH of 8 h⁻¹ and portable air cleaners (KC-A60, Sharp Corporation; MC70L, Daikin; Therapy Air, Zepter International, Ciuzas et al. (2016)) were used to reach the background levels for both the aerosol particles and VOCs (PNC – 300–500 #/cm³ or VOCs –500-600 ppm of CO₂ equivalents).

A human subject entered the chamber and used the THS according to ad libitum regime, until full consumption of a single stick (12 puffs on average). The aerosol concentration was monitored for sufficient time to reach a lower asymptote of the exponential decay.

The experiment was performed in the identical sequence every day, only changing relative humidity, air change rate, as well as the THS use intensity.

Pollution generated by the smoking of a conventional cigarette (CC, Marlboro Gold) was investigated for the comparison with THS-generated pollution. The experiment was run at 50% RH, 0.5 ACH, at 2 m distance to the bystander, and 1 cigarette smoking intensity, representing the “medium” exposure conditions. Totally three experimental runs were carried out. The evaluation of background conditions, sampling duration and analytes measured were identical as in case of THS experiments.

A volunteer checklist was issued before the experiments to ensure proper clothing and hygiene products, thus minimizing background pollution. Each study participant was thoroughly inspected and the potential risk assessed by the research personnel before the experiment.

2.5. Data processing and analysis

Temporal variation of particle number concentration and particle size distribution. The measured distributions were based on particle number concentration (unit particles/cm³ or #/cm³). The PSD was based on the number density (concentration) distribution function, which represented particle concentration normalised to the particle size bin where it was measured, i.e., the number of particles per volume of air with sized between D_p and dD_p. This is usually expressed mathematically as $D_p = dN/d\log D_p$ (#/cm³).

Regression modelling of factors affecting dispersion of particles. Results were fitted to a regression model to obtain effects of air changes per hour, distance between bystander and user, and intensity of THS use (number of human subjects using THS). Multiple linear regression (interaction) model was employed in order to obtain linear functions, relating experimental variables and responses. This process was used to determine the significant process factors affecting the variations of pollutant concentrations between runs. The obtained models were assessed for their coefficient of determination (R²), predictive squared correlation coefficient (Q²),

model validity, and reproducibility.

Normalisation of data with respect to chamber size. The measured concentrations were normalised aiming at the adequate comparison of measured concentrations with the results from other studies. Conditions suggested by CEN/TS 16516 standard (CEN standards, 2010) i.e. chamber volume of 30 m³ and air change rate of 0.5 as well as for the number of test products used in each study, according to the following formula:

$$C_{\text{normal}} = C_{\text{measured}} \times (V \times \text{ACH}) / (V_{\text{st}} \times \text{ACH}_{\text{st}}).$$

3. Results and discussion

3.1. Particle and gaseous pollutant levels

General descriptive statistics of analytes investigated under various conditions is summarized in Table 1. The usage of THS resulted in nicotine, acetaldehyde, particle number and mass concentrations significantly above the background. The highest coefficient of variation (suggesting stronger influence of experimental conditions), was observed in case of PM₁₀, PM_{2.5}, PNC, as well CO₂, nicotine, and acetaldehyde. The maximum 30 min concentration of fine particulate matter as PM_{2.5} (635.7 µg/m³) and PNC (4.8 × 10⁵ #/cm³), as well as 1 s maximum concentration of PM_{2.5} (109.8 mg/m³) and PNC (9.3 × 10⁶ #/cm³) suggest that the intensive use of THS in a confined space with limited ventilation might cause substantially elevated particle concentrations. On the other hand, such high maximum concentrations only occur for a very short period of time (5–7 s), as impacted by a directional exhalation from the user to a bystander. Moreover, due to high volatility of particles (as described in subsequent sections) it is unlikely that average particle mass concentration would be substantial as measured by reference filter-based method. At the same time, the maximum concentrations of formaldehyde (16.3 µg/m³) and acetaldehyde (12.4 µg/m³) fell within the range of the mean concentrations observed in residential and public environments (Kaunelienė et al., 2018). High maximum value of CO₂ indicated that numerous presence of users in the chamber caused increased CO₂ levels, which were not efficiently diluted by the air change applied.

Smoking of the CC resulted in the significant increase above the background (i.e. background subtracted) of all measured analytes (Table 2), including formaldehyde (16.6 µg/m³), acetaldehyde (25.3 µg/m³), nicotine (28.0 µg/m³), 3-EP (3.2 µg/m³), CO (0.94 ppm), PM_{2.5} (158.1 µg/m³), PMC₁₀ (174.0 µg/m³), and PNC (6.6 × 10⁵ #/cm³). Such levels are higher (from several times to an order of magnitude) compared to the usage of THS.

Aiming at the adequate comparison of measured concentrations with the results from other studies the measured concentrations were normalised as described in Section 2.5. The calculations are summarized in Table S2. The normalised median nicotine concentration (0.5 µg/m³) during the usage of THS in our study was similar to the median concentrations (0.6, 0.7, and 0.6 µg/m³) in the “Office”, “Residential” and “Hospitality” simulations, representing different ventilation regimes (Mitova et al., 2016). The median concentration of PM_{2.5} (2.9 µg/m³) also ranged similarly to Ruprecht et al. (2017) (2.3 µg/m³). The mean PNC in our study, however, was an order of magnitude higher (9.4 × 10⁴ #/cm³) in comparison with 9.8 × 10³ #/cm³ as normalised from Ruprecht et al. (2017). High variation of PNC among studies may be affected by multiple factors, including but not limited to differences in puffing topography, chamber size and measurement instrumentation. In a medium-sized room chamber such as in this study, the distance from emission source to the measurement site is shorter, preventing minimizing impacts of particle deposition and evaporation. High volatility of the exhaled particles (containing up to 76% of water, Mitova et al. (2016)) causes rapid evaporation to nucleation mode size range thus possibly not measured efficiently by various particle detection techniques.

The normalised median concentration of formaldehyde (19.8 µg/m³) during the smoking of CC was in good correspondence with the median concentrations (15.0, 13.7, and 16.2 µg/m³) in the “Office”, “Residential”, and “Hospitality” simulations, respectively (Mitova et al., 2016) and was in the same range with the mean concentration (21.9 µg/m³) from Ruprecht et al. (2017). Similar tendency was also observed for acetaldehyde, with the median (30.2 µg/m³) being close to 30.6, 32.3, and 30.6 µg/m³ (Mitova et al., 2016), as well as 38.9 µg/m³ from Ruprecht et al. (2017). The median nicotine concentration (33.4 µg/m³) was higher than in the “Office” (18.1 µg/m³) and “Residential” (11.2 µg/m³), but close to “Hospitality” (32.0 µg/m³) simulation (Mitova et al., 2016). The normalised mean PM_{2.5} (188.7 µg/m³) was slightly lower than the mean (273.8 µg/m³) from Ruprecht et al. (2017), but PNC was an order of magnitude higher (7.8 × 10⁵ #/cm³) than the mean (6.7 × 10⁴ #/cm³) from Ruprecht et al. (2017), similarly to THS. Generally, our data obtained at well controlled conditions confirms earlier findings (Mitova et al. (2016; Ruprecht et al. (2017))) on the important pollutants related to the usage of the THS and CC.

3.2. Highly time resolved aerosol concentration

The temporal variation patterns of aerosol concentration (as PNC) under varying conditions (distance to the bystander, varying intensity, relative humidity, and product type) as measured during the experiments is presented in Fig. 1. Graphs represent the time

Table 1

Descriptive statistics for air quality parameters during the use of THS, summarizing 30 sampling runs under various conditions (use intensity, distance, air change rate, and relative humidity). The averaging time of particle number and mass concentrations corresponds to the sampling duration of gaseous compounds (30 min).

	Background ^a (Mean ± StDev)	Mean	StDev	95% conf. Interval	Median	Min value	5th percentile	25th percentile	75th percentile	95th percentile	Max value
PNC, #/cm ³	8.5 × 10 ² ± 7.9 × 10 ²	2.1 × 10 ⁵	3.1 × 10 ⁵	2.7 × 10 ³	1.1 × 10 ⁵	8.7	1.4 × 10 ⁴	7.9 × 10 ⁴	3.0 × 10 ⁵	4.5 × 10 ⁵	4.8 × 10 ⁵
PM _{2.5} , µg/m ³	4.2 ± 8.6	200.0	2339.4	19.8	11.4	0.0	2.6	5.3	32.5	119.4	635.7
PM ₁₀ , µg/m ³	43.2 ± 117.1	1105	17000	144.2	19.3	0.0	3.1	5.9	35.5	188.7	874.9
CO ₂ , ppm	794 ± 274	831	304	5.6	697	474	530	610	1008	1465	1960
CO, ppm	0.1 ± 0.2	0.11	0.17	0.003	0.00	0.00	0.00	0.00	0.20	0.50	0.80
Formaldehyde, µg/ m ³	12.0 ± 2.8	11.0	3.7	1.4	10.9	3.6	5.0	7.9	14.4	15.7	16.3
Acetaldehyde, µg/ m ³	3.2 ± 1.2	5.7	2.8	1.1	4.9	1.4	2.0	3.6	7.1	10.9	12.0
Nicotine, µg/m ³	2.2 ± 1.9	5.1	3.3	1.2	0.6	1.7	1.8	2.5	6.7	12.3	13.9
3-EP, µg/m ³	0.6 ± 0.2	0.7	0.2	0.1	0.3	0.3	0.4	0.5	0.7	1.1	1.1

^a Human background.

Table 2
Descriptive statistics for air quality parameters during the use of THS vs Conventional cigarette, under identical experimental conditions (single user, 0.5 ACH, 2 m distance to a bystander, and 50% RH).

	Background ^a (Mean ± StDev)	Mean	StDev	95% conf. Interval	Median	Min value	5th percentile	25th percentile	75th percentile	95th percentile	Max value
PNC, #/cm ³	THS $8.9 \times 10^2 \pm 5.4 \times 10^2$	8.0×10^4	3.2×10^5	6.2×10^2	8.6×10^4	3.6×10^2	2.6×10^4	7.3×10^4	9.7×10^4	1.0×10^5	1.1×10^5
	CC $3.1 \times 10^2 \pm 2.7 \times 10^2$	6.6×10^5	2.6×10^5	7.1×10^3	7.8×10^5	4.2×10^2	3.2×10^4	6.8×10^5	8.2×10^5	8.5×10^5	9.2×10^5
PM _{2.5} , µg/m ³	THS 3.3 ± 4.1	5.7	7.6	0.2	5.6	0.4	2.6	3.5	6.8	8.7	311.5
	CC 1.3 ± 8.4	159.4	57.1	1.5	169.8	0.2	22.8	148.9	192.8	225.5	796.1
PM ₁₀ , µg/m ³	THS 7.5 ± 6.0	8.3	54.9	1.5	5.7	0.4	2.7	3.7	7.0	9.2	2352
	CC 5.8 ± 21.1	179.8	191.2	5.1	171.5	0.2	28.7	150.9	195.4	232.1	4937
CO ₂ , ppm	THS 620 ± 58	644	65	3.7	647	501	537	597	690	754	793
	CC 580 ± 63	610	57	3.2	613	498	511	568	651	699	767
CO, ppm	THS 0.01 ± 0.03	0.01	0.02	0.001	0.00	0.00	0.00	0.00	0.00	0.10	0.10
	CC 0.01 ± 0.02	0.95	0.41	0.02	1.00	0.00	0.00	0.90	1.20	1.40	1.60
Formaldehyde, µg/m ³	THS 14.2 ± 0.3	14.1	0.4	1.06	14.1 ^b						
	CC 10.9 ± 0.8	27.5	2.2	5.34	27.5 ^b						
Acetaldehyde, µg/ m ³	THS 3.3 ± 0.1	3.6	0.4	0.94	3.6 ^b						
	CC 3.6 ± 0.8	28.9	2.6	6.51	28.9 ^b						
Nicotine, µg/m ³	THS 1.4 ± 0.1	1.81	0.14	0.35	1.81 ^b						
	CC 1.6 ± 0.3	29.6	1.8	4.39	29.6 ^b						
3-EP, µg/m ³	THS 0.5 ± 0.1	0.56	0.03	0.09	0.56 ^b						
	CC 0.5 ± 0.1	3.7	0.3	0.65	3.7 ^b						

^a Human background.

^b Median value was assumed to be equal to mean value assuming normal distribution of data.

span of 10 min, starting at the beginning of the usage and including both “active” and “after” (post usage) period of each run. The distributions of PNC as box plots under various experimental conditions are presented in the supplementary material (Fig. S2).

3.2.1. Distance

The usage of THS at a close proximity of a bystander resulted in a distinct pattern of aerosol variation, which included a rapid and significant increase in particle concentration by several orders of magnitude from the background, and then dropping back at the same rate after several seconds (Fig. 1(A)). The duration of the visible peaks was on average around 6–8 s, which corresponded to the duration of exhalation of puff plus the time for the travel of aerosol to the sampler. Such pattern of temporal variation was evident only at a distance of 0.5 m from the bystander, where the bystander experienced direct puff into a breathing zone. Such pattern is similar to the one observed in our earlier study with electronic cigarettes (Martuzevicius et al., 2018).

An increasing distance from the bystander resulted in diminishing visibility of peaks (puffs), which were not observable at a distance of 2 m (with one user, ACH of 1 h⁻¹ and RH of 30%). The distance factor resulted in a significantly higher mean PNC (4.2 times) during the active usage (9.7×10^4 and 2.3×10^4 for 0.5 and 2 m, respectively). At the same time, a longer distance had no significant effect to PNC levels during the after usage period (~370 s from the beginning of puffing), which were at comparable levels (7.0×10^4 to 7.5×10^4 for 0.5 and 2 m, respectively).

An evident decrease in PNC levels for 2 m distance was possibly caused by several factors: a dispersion of particles in a room while travelling across; the deposition of aerosol particles on surrounding surfaces; and partial evaporation of aerosol particles to gaseous phase compounds. The exposure of bystander was greatly influenced by the direction of the exhalation of the puff; however, for longest tested distance this factor had a minor impact.

3.2.2. Intensity

The number of parallel users of THS (further referred to as the usage intensity) had a direct impact to the concentration of aerosol particles near the bystander and in the chamber. PNC levels from five users were significantly higher comparing with THS emission from one user (Fig. 1(B)). The figure displays the comparison of users located at 2 m from the bystander, while the ventilation and

RH were at minimum (0.2 h⁻¹, and 30%, respectively). Average PNC in case of five users was 27 times (mean of 2.0×10^4 and 5.4×10^5 #/cm³) higher under “active” period and 8 times (mean of 5.9×10^4 and 4.7×10^5 #/cm³) higher under “after” period. Such multiplied increase of the PNC generated by 5 users reflects a more rapid of fill up of the chamber with exhaled aerosol, thus a more effective transport of particles to the bystander. In case of one user, 2 m distance seems to be sufficiently long for particles to disperse and not reach bystander, thus the concentration of PNC is naturally underestimated.

The usage intensity is also a relatively ambiguous factor, since it depends on the topography of smoking/usage. It can vary with the inhaled puff duration, hold-in-body duration, or exhaled puff duration. A quantitative influence of the usage topography may be attributed to a random error of the experiment, especially in case of the far distance from the bystander.

3.2.3. Relative humidity

Temporal variation of PNC (from THS) under two different relative humidity levels (30% vs. 70%) are presented in Fig. 1(C). The figure reflects PNC variations in case of a single user, ACH of 1 h⁻¹, and 2 m distance. The longer travel distance to the bystander was expected to provide sufficient time for aerosol particles to react with ambient moisture.

Having identical conditions at different levels of RH, the PNC levels under “active” period also varies over the time in different patterns (Fig. 1(C)), indicating higher mean PNC levels (1.9 times as from 7.2×10^4 to 3.7×10^4 for 30 and 70%, respectively) and fluctuations at 30% RH. This can be attributed to the fact that particle deposition velocity increases with air relative humidity (Han et al., 2011); therefore, at RH of 70% we cannot identify individual puffs that are clearly visible under RH of 30%. At the same time, PNC levels under “after” period (which started from ~360 s and lasted until 1180 s) were 1.3 time higher at 70% RH and varied from 8.2×10^4 to 1.1×10^5 for 30 and 70%, respectively. Lower PNC levels at dry air conditions (30%) under “after” period could be observed due to a faster aerosol particle evaporation at the relatively lower partial pressure of water vapour in the air.

3.2.4. Product type: THS vs. CC

The variation of PNC during the use of THS was distinctly different as compared to the usage of CC under the identical

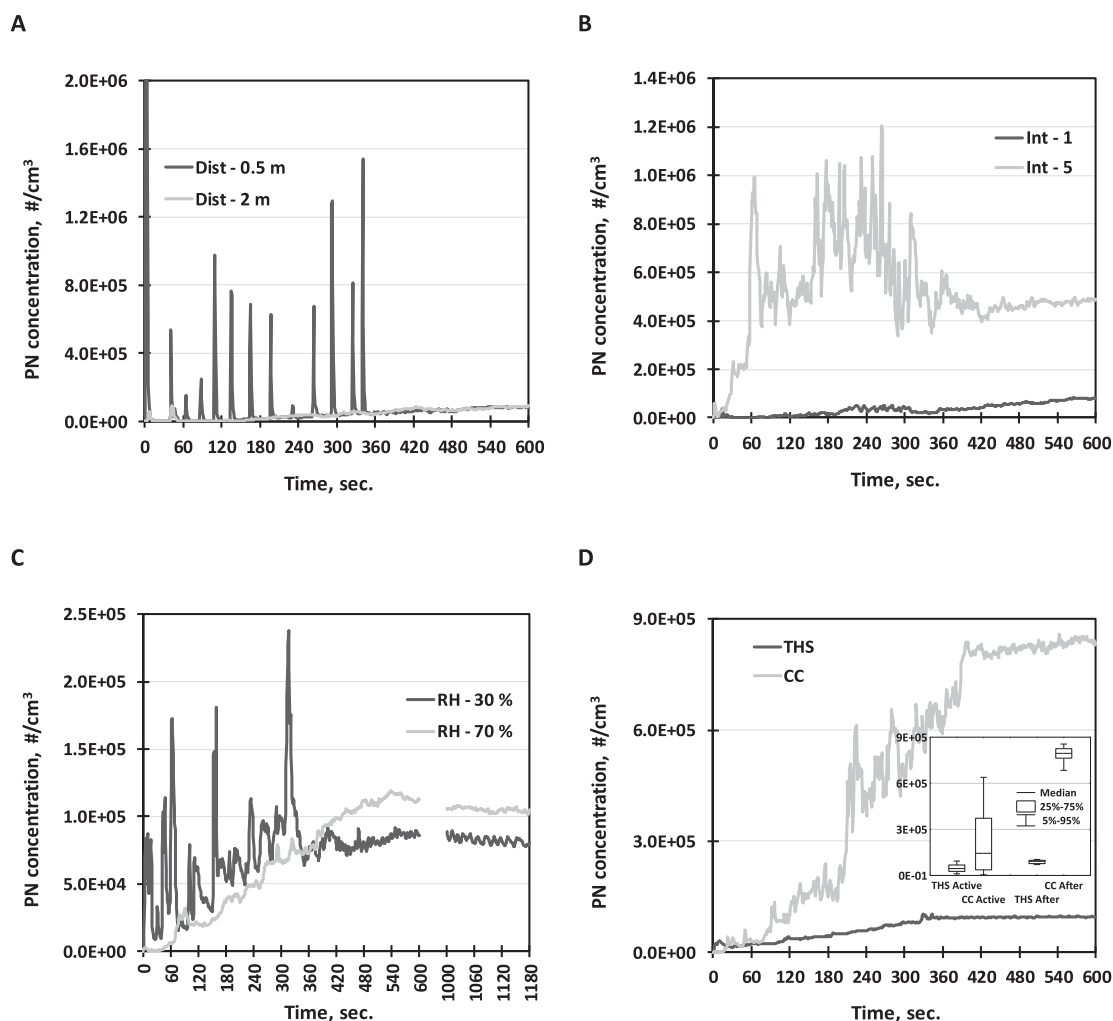


Fig. 1. Temporal variation of particle number concentration while using the THS: (A) The effect of distance from the bystander 0.5 m vs. 2 m (I-1, V-1, RH-70); (B) One user vs five simultaneous users (D-2, V-0.2, RH-30); (C) RH 30% vs. 70% (D-2, I-1, V-1); (D) THS vs. CC (I-1, D-2, V-0.5, RH-50). The inset of (D) represents summarized distributions of PNC during active usage and after usage periods.

conditions (intensity – 1 user, distance 2 m, ACH – 0.5 h^{-1} , and RH – 50%) (Fig. 1(D)). PNC was in the same range during 60 s from the start of the experiment. Then at approx. 90 s from the start, PNC rapidly increased for CC and it remained an order of magnitude higher compared to THS. The noise component of the time series was also different, representing higher fluctuations in case of CC, while THS produced a relatively smooth curve. Coefficient of variation resulted in 0.5–0.82 during “active” period for THS and CC, respectively. During the entire “active” period CC generated 5.6 times higher ($2.8 \times 10^5 \text{ #/cm}^3$) concentration than THS ($4.9 \times 10^4 \text{ #/cm}^3$), while under “after” period an even greater 8.5 times difference ($8.0 \times 10^5 \text{ #/cm}^3$ vs. $9.5 \times 10^4 \text{ #/cm}^3$) was observed (Fig. 1(D) inset as boxplots). Such patterns in aerosol concentration variations may be attributed to the volatility of particles. In case of THS, the concentration does not rise similarly to CC since the particles evaporate (transfer from droplet to gaseous phase) faster than they accumulate in the air of chamber.

The mainstream particles of THS have been shown as highly volatile (Pacitto et al., 2018), while exhaled aerosol is expected to have even lower content of non-volatile matter. This phenomena is similar to that registered with electronic cigarettes (Zhao et al.,

2017; Martuzevicius et al., 2018). At a closer distance, real-time aerosol instrumentation is capable in registering peaks for both THS and CC, but at a further distance, volatile particles may not reach the bystander, in case of low usage intensity and low ambient humidity.

3.3. Particle size distribution

Generally, the particle size distribution (PSD) obtained during the usage of the tested THS exhibited a unimodal distribution, having a mode at the smallest particle diameter of ELPI+. The shape of the distribution was comparable for both THS and CC (Fig. 2). The main difference resulted from the overall particle levels, with the CC producing an order of magnitude higher particle concentrations across all measured size bins. Moreover, the CC also produced higher amount of particles in the range $0.38\text{--}0.60 \mu\text{m}$, whilst in case of THS, no particles were registered both during the period of active usage, and post-usage period.

The PSD of the aerosol was also comparatively similar during the peak of the concentration, except to that in a channel $0.25\text{--}0.38 \mu\text{m}$, reflecting a presence of these “larger” particles in

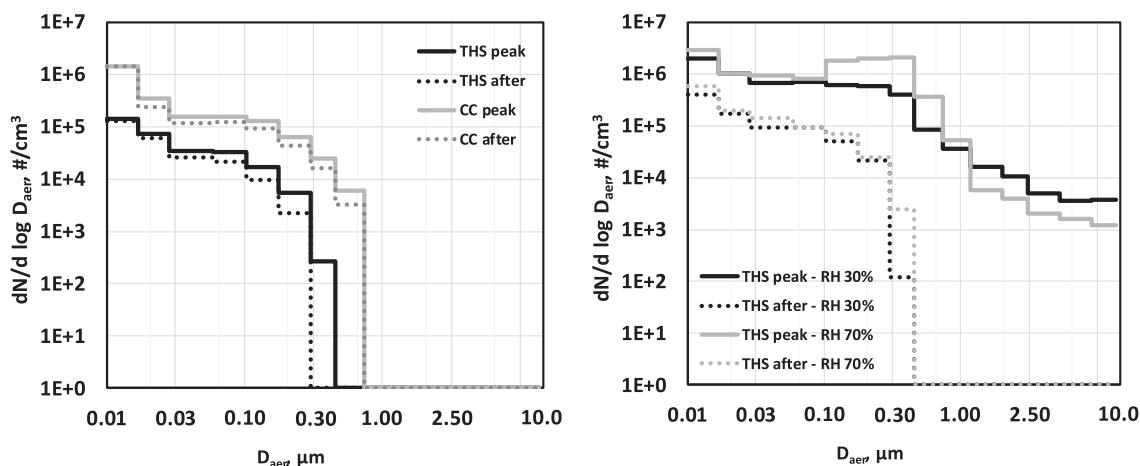


Fig. 2. Particle size distribution (PSD) of indoor aerosol during the use of THS. (A) A comparison against conventional cigarette (distance to bystander 2 m, number of users 1, RH 50%, ventilation 0.5 ACH), (B) Effect of the relative humidity in the room to the PSD (distance to bystander 0.5 m, number of users 5, ventilation 0.5 ACH).

the directly exhaled aerosol, but not present later, possibly due to high volatility of these particles. Fig. 2(A) presents data from the 2 m distance of bystander to the user, thus particles have sufficient time to undergo transformations (evaporation, agglomeration, settling) while travelling across the room.

The PSDs obtained during this experiment are in line with that obtained during our earlier experiments with the usage of electronic cigarettes, with respect to a mode at 100–300 nm (Martuzevicius et al., 2018). At the same time, a high concentration of nucleation mode particles is apparent. We expect that ELPI + here is capable in registering particles, which rapidly evaporate from the accumulation mode to nucleation mode, considering high volatility of these particles (i.e., droplets).

Fig. 2(B) presents a specific case of PSDs as affected by a relative humidity (30% vs 70%). These measurements were taken at the extreme conditions of five simultaneous users and close distance to a bystander (0.5 m). This resulted in a concentration an order of magnitude higher during the peak, when the direct exhalation of users had substantial effect at a close distance. Here, larger particles are also present. At the same time, the increase in RH resulted in a more clear mode at 0.10–0.38 μm , representing accumulation mode resulting in the growth of particles (or delayed shrinkage on the other hand) due to ambient humidity.

3.4. Screening the factors affecting the variation of pollutant concentration

The experimental data (Table S3) were fitted to the regression model, thus providing information on the relationship and the significance of process factors to the various pollution estimates. Table 3 depicts qualitative estimates on important factors affecting pollutant concentrations. Generally, the usage intensity (number of simultaneous users) prevailed as the most important factor positively affecting pollutant variations. This was valid for pollutants that have been associated with the usage of THS (Kaunelienė et al., 2018; Mitova et al., 2016), including particles, nicotine, and acetaldehyde, while 3-EP and formaldehyde were not impacted. During the “active” period, the difference between one and five users reached up to one order of magnitude, while in the “after” period the difference was up to 4 times higher (Fig. S2). At the same time, maximum particle mass concentration did not depend on the number of users, since a single user exhaling directly to the bystander may have caused higher variation than five users located further, as confirmed by the negative influence of the distance

factor. Nicotine and acetaldehyde are among gaseous pollutants resulting from the usage of THS. At the same time, formaldehyde and 3-EP were not affected. The positive relationship of CO_2 to number of users may be likely associated to the increase of exhaled CO_2 as related to increased presence of humans in the room.

The distance to a bystander was an important factor in case of $\text{PM}_{2.5}$ mean values – the further the user, the lower the concentration. At the same time, increasing distance resulted in higher PNC values in the “after” period, indicating the chamber-related dispersion patterns of fine aerosol, resulting in a more efficient transfer of small particles from the further distance after the active usage was over.

The combined effect of these two factors on pollutant concentrations is presented in Fig. 3. $\text{PM}_{2.5}$ concentration was directly affected by both distance and usage intensity. For example, a single user at a close distance to the bystander may generate average concentration of ca. $200 \mu\text{g}/\text{m}^3$, while at 2 m distance the concentration is reduced more than four times to $<50 \mu\text{g}/\text{m}^3$. Yet again, five users at a further distance may increase the concentration twice (up to $100 \mu\text{g}/\text{m}^3$), while at a closer distance the increase may be eight-fold. Similar effect was applicable to nicotine, where at a far distance one user resulted in $2 \mu\text{g}/\text{m}^3$, while five users at a close distance increase potential exposure by 5 times. PNC during “after” period and acetaldehyde depended only on number of users, with potential exposure increasing 2–3 fold having one to five users in the room.

The air change rate appeared to be not a significant factor in the ranges that it was operated (up to 1 ACH). Apparently, such ventilation intensity was not able to efficiently remove rather intensive emission of pollutants. PNC was more sensitive to changes in ACH, since it is mainly determined by a presence of sub-micrometre particles, which efficiently travel with the ventilation air.

The relative humidity has significantly positively impacted $\text{PM}_{2.5}$ concentration variation in the “after” period. Increasing humidity resulted in higher vapour pressure around the exhaled volatile droplet particles, thus sustaining their existence and preventing rapid evaporation, and shifting particle size to an accumulation range (thus increasing particle mass), as confirmed by increased mode of PSD in Fig. 2(B). At the same time, effects of relative humidity to formaldehyde and acetaldehyde may be related to the measurement artefacts. The RH has been indicated as an important factor while sampling aldehydes by 2,4-DNPH impregnated silica cartridges (Mabilia et al., 2010). While dry conditions prevent the efficient uptake of aldehydes, increased

Table 3

The significance of process factors to the responses (pollutant concentrations) during the usage of THS in a chamber based on the interaction regression model. ++ denotes the most important positive factor (highest value among obtained), + less important positive factor, - a negative factor, - a most important negative factor, 0 – factor not statistically significant.

	PNC Mean (All)	PNC Mean (After)	PM _{2.5} mean (All)	PM _{2.5} mean (After)	PM _{2.5} max	Nicotine 3-EP	Formaldehyde ^a	Acetaldehyde	CO ₂
Air Change Rate (ACH)	-	-	0	0	0	0	0	0	0
Number of Simultaneous Users (Int)	++	++	+	++	0	++	0	++	+
Relative humidity (RH)	0	0	0	+	0	0	++	+	0
Distance to bystander (Dist)	0	+	-	0	-	-	0	0	0
ACH*Int	-	-	0	0	0	0	0	0	0
ACH*RH	0	0	0	0	0	+	+	0	0
ACH*Dist	0	0	0	0	0	+	+	0	0
Int*RH	0	0	+	+	0	0	0	0	0
Int*Dist	+	+	0	0	0	0	0	0	0
RH*Dist	+	0	0	0	0	0	+	0	0

^a Low validity and low percent of the variation of the response according to cross validation.

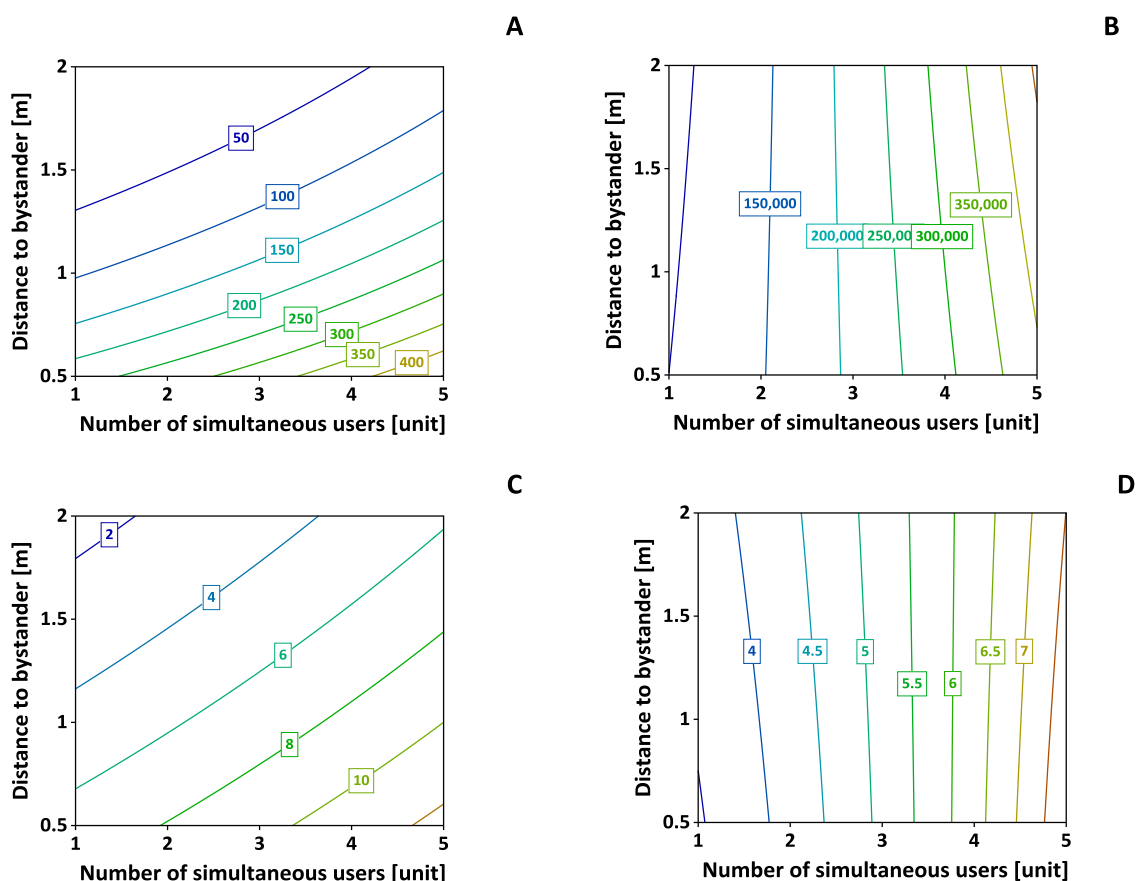


Fig. 3. The joint effects the number of simultaneous users and the distance to a bystander on pollutant concentrations at the scenario $V = 0.2$; $RH = 30$: (A) Mean $PM_{2.5}$ concentration, $\mu g/m^3$; (B) Mean PNC during “After” period, $\#/cm^3$; (C) Nicotine, $\mu g/m^3$; (D) Acetaldehyde, $\mu g/m^3$.

humidity potentially results in increased sorption on highly hydrophilic silica.

The interaction between process parameters has not revealed a dramatic synergistic nor antagonistic effect in the used setup. The explanation of the observed significant interactions are difficult to explain mechanistically. The positive effect of Intensity*Relative humidity to $PM_{2.5}$ concentration variations was apparently caused with the growth of particles at the increasing concentration. Intensity*Distance positively affected submicrometric particle number variations, related to the particle transport and dispersion within the chamber.

4. Conclusions

Use of THS resulted in statistically significant increase of several analytes including nicotine, acetaldehyde, PN and $PM_{2.5}$ concentrations. The obtained levels were significantly lower (approximately 16, 8, 8, and 28 times for nicotine, acetaldehyde, PN and $PM_{2.5}$ concentrations, respectively) if compared to the levels caused by conventional cigarette (CC) smoking under identical conditions. The maximum concentrations of formaldehyde ($16.3 \mu g/m^3$) and acetaldehyde ($12.4 \mu g/m^3$) fell within the range of the mean concentrations observed in residential and public environments. The

maximum 30 min concentration of PNC ($4.8 \times 10^5 \text{ \#/cm}^3$), as well as maximum concentration of PNC ($9.3 \times 10^6 \text{ \#/cm}^3$) suggest that the intensive use of THS in a confined space with limited ventilation might cause substantially elevated aerosol concentrations, although these particles appeared as highly volatile ones and evaporated within seconds. At the same time, exhaled THS aerosol particles (differently from CC) evaporated faster than they accumulated in the air of chamber, which was confirmed by the highest concentration of particles at nucleation mode.

Generally, the usage intensity (number of simultaneous users) prevailed as the most important factor positively affecting pollutant variations; another important factor was the distance to bystander. Under identical conditions, the mean PNC in case of five users was 27 times higher during the usage and 8 times higher after the usage compared to one user. The distance factor resulted in a significantly higher mean PNC (4.2 times) at a distance of 0.5 m in comparison to 2 m during the active usage. At the same time, a longer distance had no significant effect to PNC levels during the after usage period, which were at comparable levels for both distances. The air change rate appeared to be not a significant factor in the ranges that it was operated (up to 1 ACH). Apparently, such ventilation intensity was not able to efficiently remove rather intensive emission of pollutants during 30 min period, requiring prolonged ventilation at maximum regimes.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.chemosphere.2019.02.095>.

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