International Journal of Hygiene and Environmental Health 222 (2019) 486–493

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Passive exposure to pollutants from conventional cigarettes and new electronic smoking devices (IQOS, e-cigarette) in passenger cars

Wolfgang Schober[a,*], Ludwig Fembacher[a], Adela Frenzen[a], Hermann Fromme[a,b]

[a] Bavarian Health and Food Safety Authority, Department of Chemical Safety and Toxicology, Pfarrstrasse 3, 80538 Munich, Germany

[b] Institute and Clinic for Occupational, Social and Environmental Medicine, University Hospital, LMU Munich, Ziemssenstrasse 1, 80336 Munich, Germany

ARTICLE INFO

Keywords:
Passive exposure
IQOS
E-cigarette
Tobacco cigarette
Passenger cars
Indoor air

ABSTRACT

Smoking in car interiors is of particular concern because concentrations of potentially harmful substances can be expected to be high in such small spaces. To assess the potential exposure for occupants, especially children, we performed a comprehensive evaluation of the pollution in 7 passenger cars while tobacco cigarettes and new electronic smoking products (IQOS, e-cigarette) were being smoked. We collected data on the indoor climate and indoor air pollution with fine and ultrafine particles and volatile organic compounds while the cars were being driven. Smoking of an IQOS had almost no effect on the mean number concentration (NC) of fine particles (> 300 nm) or on the $PM_{2.5}$ concentration in the interior. In contrast, the NC of particles with a diameter of 25–300 nm markedly increased in all vehicles ($1.6–12.3 \times 10^4/cm^3$). When an e-cigarette was vaped in the interior, 5 of the 7 tested cars showed a strong increase in the $PM_{2.5}$ concentration to 75–490 $\mu g/m^3$. The highest $PM_{2.5}$ levels (64-1988 $\mu g/m^3$) were measured while tobacco cigarettes were being smoked. With the e-cigarette, the concentration of propylene glycol increased in 5 car interiors to 50–762 $\mu g/m^3$, whereby the German indoor health precaution guide value for propylene glycol was exceeded in 3 vehicles and the health hazard guide value in one. In 4 vehicles, the nicotine concentration also increased to 4–10 $\mu g/m^3$ while the e-cigarette was being used. The nicotine concentrations associated with the IQOS and e-cigarette were comparable, whereas the highest nicotine levels (8–140 $\mu g/m^3$) were reached with tobacco cigarettes. Cigarette use also led to pollution of the room air with formaldehyde (18.5–56.5 $\mu g/m^3$), acetaldehyde (26.5–141.5 $\mu g/m^3$), and acetone (27.8–75.8 $\mu g/m^3$). Tobacco cigarettes, e-cigarettes, and the IQOS are all avoidable sources of indoor pollutants. To protect the health of other non-smoking passengers, especially that of sensitive individuals such as children and pregnant women, these products should not be used in cars.

1. Introduction

Every year, about 6 million people worldwide die from the consequences of tobacco use (WHO, 2012), and smoking is still the biggest risk factor for the development and manifestation of cardiovascular and pulmonary diseases (Collaborators GBDT, 2017). Tobacco smoke is a complex mixture of numerous toxic and carcinogenic substances that are formed when tobacco is burned and is by far the most dangerous, easily preventable indoor pollutant. Convincing scientific evidence has been available for a long time from experimental and epidemiological studies, which demonstrated that passive smoking is also associated with serious health risks, including the development of lung cancer (IARC, 2004; US-DHHS, 2010, 2014). Inhaling tobacco smoke from the ambient air is particularly dangerous to children because they have a higher breathing rate per kilogram bodyweight than adults and their detoxification system is not yet fully developed (Arcus-Arth and Blaisdell, 2007; Cheraghi and Salvi, 2009). In children, passive smoking interferes with lung development and promotes the development of asthma and other respiratory diseases (Wang and Pinkerton, 2008), and in infants it increases the risk of sudden infant death syndrome (Raupach et al., 2008; US-DHHS, 2014).

Meanwhile, a number of studies have also been performed on electronic cigarettes (e-cigarettes). The results suggest that inhaling propylene glycol-containing e-cigarette aerosols may have adverse health effects, especially in the respiratory tract and cardiovascular system (Carnevale et al., 2016; Palamidas et al., 2017; Vardavas et al., 2012; Vlachopoulos et al., 2016). Vaping indoors can also release pollutants in concentrations that may pose a health risk to others (Schober

Abbreviations: DNPH, 2,4-Dinitrophenylhydrazine; PW, passenger window; VOC, volatile organic compounds

* Corresponding author.
E-mail address: wolfgang.schober@lgl.bayern.de (W. Schober).

https://doi.org/10.1016/j.ijheh.2019.01.003
Received 5 October 2018; Received in revised form 20 December 2018; Accepted 11 January 2019
1438-4639/

et al., 2014). Since the initial market introduction in 2014 of the IQOS (Philip Morris International) in Japan and Italy, this new electronic smoking device has become commercially available worldwide (Tabuchi et al., 2018). Unlike e-cigarettes, the IQOS does not use liquids but electronically heats special tobacco sticks (HEETS) up to 350 °C (heat-not-burn tobacco product), producing an aerosol that, according to the manufacturer, mainly consists of water, glycerin, and nicotine, together with other substances (e.g. flavorings). Recent research has shown that heating tobacco also produces toxic compounds (e.g. formaldehyde), which the smoker inhales together with the aerosol (Davis et al., 2019; Farsalinos et al., 2018). The extent to which these pollutants also affect the quality of indoor air and thus represent a potential health risk for passive smokers is currently unclear because scientific studies on this topic are largely lacking.

The consumption of tobacco cigarettes and e-cigarettes in car interiors is of particular concern because levels of potentially harmful substances can be expected to be high in such small spaces. The interior of a car is usually two to five cubic meters and thus only a fraction of the size of a medium-sized room (Ott et al., 2008). The situation is aggravated by the fact that children in particular are not able to simply get out of a car if someone is smoking. Experimental studies have shown that cigarette use in cars increases the concentration of atmospheric ($PM_{2.5}$, CO, airborne nicotine) and biological (cotinine/3-hydroxycotinine in plasma and urine) markers of secondhand smoke (Jones et al., 2014; Liu and Zhu, 2010; Northcross et al., 2014; Semple et al., 2012). Smoking-related $PM_{2.5}$ concentrations were found to be much higher in family cars than in hospitality venues (e.g. bars, pubs) before smoke-free legislation was adopted (Raoof et al., 2015). Therefore, to assess the potential exposure for non-smoking passengers, especially children, we performed a comprehensive study of pollutant levels during the smoking of an IQOS, an e-cigarette, and tobacco cigarettes in 7 passenger cars of different sizes. We collected data on the indoor climate and indoor air pollution caused by fine and ultrafine particles and volatile organic compounds while the vehicles were being driven.

2. Materials and methods

2.1. Study design

The indoor air quality was measured with and without smoking in 7 passenger cars. As the size of an interior directly affects the level of passive smoke exposure, we included vehicles with large, medium and small interior volumes in the study: (I) large interior volume (4–5 m^3): Skoda Octavia (built in 2015), Volvo S (1997); (II) medium interior volume (3–4 m^3): VW Golf (2006), VW Golf (2005), VW Golf (2001); and (III) small interior volume (2–3 m^3): Smart ForFour (2016), Fiat Punto (2009). All measuring instruments were stowed in a bag that was placed in the back seat behind the passenger and secured with the seatbelt to prevent it slipping. The sensors of the various devices were fed out of the bag and positioned in the area corresponding with the breathing zone of a child, if one were sitting in the back seat (Fig. 1).

We performed preliminary test drives to ensure that the measuring instruments were working reliably and did not move during driving. During these preliminary test drives, we also assessed how far open the passenger window should be to allow us to perform reliable interior measurements while at the same time simulating realistic exposure conditions when someone was smoking in the car. For this assessement, we measured the indoor concentrations of fine and ultrafine particles during smoking under different ventilation conditions. Because the pollution in the interior could be expected to be highest with tobacco cigarettes, in the preliminary test drives the passenger smoked a tobacco cigarette. Based on the indoor particle measurements, the preliminary test drives indicated that the following conditions were suitable to prevent exceptionally high pollution levels due to insufficient ventilation and at the same time to simulate a realistic ventilation behavior of smokers in a car: (I) front ventilation set at level 1 (no recirculation of air) and (II) windows on the front passenger side 2 cm or 5 cm open and all other windows closed.

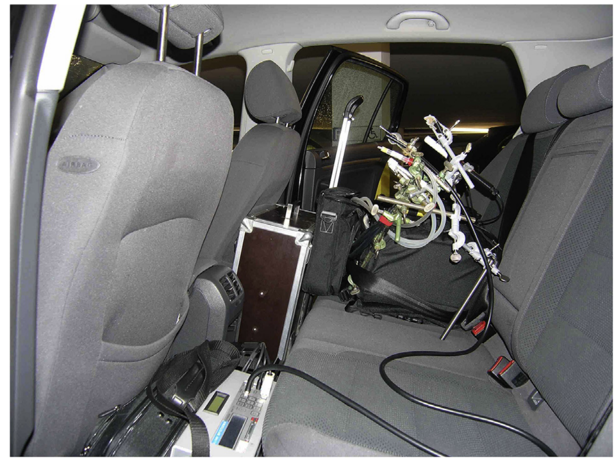

Fig. 1. The photo shows the arrangement of the measuring instruments in the back seat of the car behind the passenger seat. The sensors for determining the levels of particles and volatile organic compounds and assessing the indoor climate were placed in what would be the breathing zone of a child seated in this position.

2.2. Measurements

To keep the external exposure conditions largely comparable, all study test drives took place at the same time of day (9:00 a.m. to 1:00 p.m.) on 7 consecutive working days in November 2017 in Munich (Germany) and on the same 8.5 km circular route in the center of Munich. All vehicles took 20–23 min to complete the route on every test drive (ventilation speed: 0–50 km/h). The exposure conditions were as described above, and of the two persons in the car only the passenger smoked. We performed a total of 7 test drives per vehicle, in the following order:

Drive 1: No smoking, passenger window (PW): 5 cm open
Drive 2: Passenger smoked 2 HEETS with IQOS, PW: 5 cm open
Drive 3: Passenger smoked 2 HEETS with IQOS, PW: 2 cm open
Drive 4: Passenger continually vaped an e-cigarette, PW: 5 cm open
Drive 5: Passenger continually vaped an e-cigarette, PW: 2 cm open
Drive 6: Passenger smoked 2 tobacco cigarettes, PW: 5 cm open
Drive 7: Passenger smoked 2 tobacco cigarettes, PW: 2 cm open

By using the test conditions described above, we were able to standardize the duration of data collection by the measuring devices and use of the various smoking products and the travel times. Before the first test drive and between each test drive, all vehicle doors were opened, and the interior was fully ventilated for 10 min. During this time, we changed the desorption tubes for determining volatile organic compounds and prepared the measuring instruments for the next drive. According to the records of the German Meteorological Service (Deutscher Wetterdienst, DWD), it did not rain or snow on any of the measurement days, so we can assume that the traffic-related entry of pollutants into the interior of the test vehicles was largely comparable during the test drives.

2.3. Participants

We recruited 7 drivers (one male, 6 female), who were asked to bring their own car, and 7 passengers (one male, 6 female), who were asked to smoke while driving. Participants were recruited by sending an e-mail to everyone working at the Bavarian Health and Food Safety Authority. Only volunteers who fulfilled the inclusion criteria were invited to participate in the study, i.e. they were healthy, over 18 years old and active tobacco cigarette or e-cigarette smokers. The exclusion criteria included existing respiratory and cardiovascular diseases, pregnancy, alcohol and drug abuse at the time of the study, and, for the drivers, the lack of a valid driver's license. The ethics committee of the Bavarian Medical Association approved the study, and volunteers were enrolled after providing written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

2.4. Smoking devices

As described above, during two of the test drives the passenger used the electronic smoking device IQOS (Philip Morris International, Neuchâtel, Switzerland). The HEETS used in the IQOS consist of compressed tobacco and are electronically heated in a special holder. The resulting aerosol is inhaled by the consumer in the same way as tobacco smoke. The duration of use corresponds approximately to the time it takes to smoke a conventional tobacco cigarette, i.e. about 14 drags or 6 min. Before the next use, the holder needs to be recharged in a special charger. We used Bronze Label HEETS in this study because, according to the sales associate (IQOS Store Munich), they were the most popular at the time of the study. Bronze Label HEETS contain a special blend of tobacco with spicy flavor and have a nicotine content of 0.5 mg/HEET. None of the participants had ever used an electronic tobacco heater previously. Therefore, on the measurement day the smokers were shown how to use the IQOS and practiced changing the tobacco sticks and recharging the holder. The time needed to smoke 2 HEETS and recharge the holder once corresponded exactly with the time needed to complete the circular driving route.

The second electronic smoking device used in the study was the e-cigarette SubTwin Neo (Red Kiwi, Seevetal, Germany). This device consists of a rechargeable battery, a vaporizer, and a cartridge containing the liquid to be vaporized. The SubTwin Neo is a standard tank model with a battery capacity of 900 mAh and a vaporizer resistance of 1.2 Ω. In this study, it was used with a tobacco-flavored liquid with a nicotine content of 18 mg/ml (Dreamliner, AKRA Kotschenreuther, Langenzenn, Germany). On the measurement day, passengers who usually smoked only tobacco cigarettes were shown how to use the e-cigarette and practiced vaping.

Before each test drive, we ensured that the electronic smoking devices were charged and working properly.

During the last two test drives with each vehicle, the passenger smoked two Marlboro Red tobacco cigarettes (Philip Morris International). As declared by the manufacturer, Marlboro Red has a nicotine content of 0.8 mg/cigarette.

2.5. Puff topography

The duration of inhalation from the e-cigarette was set at four seconds. This duration was based on the findings of earlier studies on vapers' behavior, which showed that vapers typically inhale for about four seconds (Spindle et al., 2015). The duration of inhalation from the IQOS and the tobacco cigarette was set at two seconds. To standardize the duration of the inhalations the smokers were instructed to count to four or two while inhaling from a smoking product. In addition, the study investigator instructed all study participants to inhale in exactly the same way at each inhalation to ensure that the same volume of vapor or smoke was inhaled with each four- or two-second inhalation. Furthermore, the smokers were advised to drag on a smoking product about twice per minute and to inhale the vapor/smoke directly into their lungs.

2.6. Analysis of indoor air parameters

2.6.1. Indoor climate

To determine the indoor concentration of carbon monoxide (CO) and carbon dioxide (CO_2) and to measure temperature, relative humidity, and air pressure, we used the data logger Almemo 710 (Ahlborn, Holzkirchen, Germany) with the appropriate set of sensors. The logger was stowed in a bag in the back seat behind the passenger and secured in place with the seatbelt. The sensors were positioned outside the bag so that they could freely record the climate data in the car interior. Data were acquired continually (10 measurements per minute) during the 7 test drives.

2.6.2. Particle mass, particle number concentration

The number and mass concentrations ($PM_{2.5}$) of the particles released during smoking were measured continually with an optical laser aerosol spectrometer (dust measuring device 1.108, Grimm Technologies, Ainring, Germany). The measuring device continuously sucks in air via a volume-flow-controlled pump and passes it through a laser measuring chamber. The scattering signals generated by the particles as they pass through the laser are detected by a high-speed photodiode and counted by an integrated pulse-height analyzer. The laser aerosol spectrometer measures the concentration of 15 different particle sizes ranging from 300 nm to > 20 μm. Because the scattering intensity decreases with the sixth power of the particle size, optical light scattering systems cannot detect particles with a diameter < 0.1 μm. For this reason, we added a special plug-in module for measuring nanoparticles (NanoCheck 1.320, Grimm Technologies, Ainring, Germany) to the laser aerosol spectrometer. The measuring technique of the nanoparticle counter is based on a combination of a unipolar diffusion charger, an electrical conductivity measurement, and an aerosol Faraday cup electrometer and allows nanoparticles below the optical range, i.e. 25–300 nm, to be continually measured. Both particle measuring devices were placed as a measuring unit in the footwell behind the driver's seat and secured against slipping (Fig. 1). The inside air was drawn in via an antistatic hose (1.2 l/min), whose circular suction head was in the same measuring zone as the other measuring instruments. The particle load in the inside air were measured every 6 s throughout the 7 test drives.

2.6.3. Volatile organic compounds (VOC)

To determine indoor VOC, a sampling pump (Gilian GilAir Plus, Sensidyne, St. Petersburg, USA) collected 1- and 2-L air samples during each test drive. For this measurement, the room air was passed through thermal desorption tubes, with Tenax TA as the sorbent (20010-U Supelco, Sigma-Aldrich, St. Louis, USA), at a flow rate of 55 or 110 ml/min. Sampling started 1 min after the start of the test drive and lasted 18 min. The volatile compounds were then desorbed from the carrier material by thermal desorption (Shimadzu TD-20) and analyzed in a gas chromatograph-mass spectrometer (GC/MS; Shimadzu GCMS-QP2010). For the chromatographic separation, the analytes were transferred to the GC column (Optima 5 MS Accent, length 60 m x inner diameter 0.25 mm x film thickness 1 μm, Macherey-Nagel, Düren, Germany) via a focusing cryotrap tube packed with Tenax TA and quantified by a mass-selective detector. The desorption temperature was 285 °C.

2.6.4. Aldehydes/ketones

The concentration of carbonyls in the interior air was determined by the DNPH method (DNPH, 2,4-dinitrophenylhydrazine). In this method, air is passed through a DNPH cartridge and the aldehydes and ketones contained in the air sample are chemically bound to the DNPH absorber phase (hydrazone formation). The room air was collected during the test drives by a sampling pump (Gilian GilAir Plus, Sensidyne, St. Petersburg, USA) at a constant flow rate of 1.115 l/min on a LpDNPH-H10 cartridge (Sigma-Aldrich, St. Louis, USA). Sampling started 1 min after the start of the test drive and lasted 18 min. The sampled DNPH cartridges (20 L of air) were stored in the refrigerator until further processing, and the reaction products (carbonyl derivatives) were eluted with 5 ml of acetonitrile (LiChrosolv, Merck, Germany) no sooner than 24 h after sampling. A Dionex HPLC instrument (UltiMate 3000, Thermo Fisher Scientific, Waltham, USA) with a UV detector (column 1: 365 nm, column 2: 360 nm) was used for the analysis. Separation was performed either after dilution with water (1:2) over a reversed phase column SUPELCOSIL LC-18 (column 1; 250 mm × 4.6 mm, particle size 5 µm; Sigma-Aldrich, St. Louis, USA) with a gradient of water and acetonitrile or undiluted over a reversed phase column Acclaim Carbonyl C18 LC (column 2; 150 mm × 2.1 mm, particle size 2.2 µm; Thermo Fisher Scientific, Waltham, USA) with acetonitrile and aqueous ammonium acetate buffer (2 mmol/l) as the mobile phase. We had to use two different columns to improve the separation efficiency of individual substances (e.g. butyraldehyde and 2-butanone). The detection limits were 2 µg/m^3 for formaldehyde and acetaldehyde, 1.5 µg/m^3 for propionaldehyde and benzaldehyde, and 1 µg/m^3 for butyraldehyde, acetone, acrolein, and 2-butanone.

3. Results

3.1. Indoor climate

The mean levels of the indoor air parameters measured during the test drives are summarized in Table S1. During almost all test drives, the CO concentration was at background levels; it increased slightly only when tobacco cigarettes were smoked. The highest CO level was measured in the VW Golf (2005) at 8.8 ppm (control: 1.5 ppm).

3.2. Particle load of the indoor air

Fig. 2 shows a typical example of the development over time of the particle load (number and mass concentrations) in the indoor air of a car during the 7 test drives. The periods between test drives during which the vehicle was being fully ventilated are not included in the figure. The different ventilation conditions (PW open 2 cm vs. 5 cm) had no significant influence on the particle load in the car (Fig. 2). Therefore, Table 1 only shows the particle loads when the vehicles were less well ventilated while the smoking device was being used (i.e. PW 2 cm open; worst case). As can be seen in Table 1, the smoking of an IQOS had almost no effect on the mean number concentration of fine particles (> 300 nm) or on the $PM_{2.5}$ concentration in the interior. In contrast, the number concentration of particles with a diameter of 25–300 nm increased in all cars (1.6–12.3 × 10^4/cm^3) and averaged 9%–232% above background levels with no smoking (Table 1). When an e-cigarette was vaped in the interior, 5 of the 7 tested cars showed a strong increase in the $PM_{2.5}$ concentration to 75–490 µg/m^3 (control: 6–11 µg/m^3). The vaping of an e-cigarette released more larger particles (> 300 nm) than the use of an IQOS (e.g. Skoda Octavia: 2145 vs. 23 particles/cm^3, respectively), while the mean number concentrations of nanoscale particles tended to be higher for IQOS (Table 1). The highest particle loads, however, were measured while tobacco cigarettes were being smoked. With tobacco cigarettes, the mean $PM_{2.5}$ concentration increased to 64-1988 µg/m^3 (control: 4–11 µg/m^3), and the number concentrations of nanoscale particles were 1.3- to 17-fold higher than in the control test drive.

3.3. Air content of volatile organic compounds (VOC)

Table 2 shows the concentrations of VOC that were increased during the test drives with smoking. With the IQOS, the nicotine concentration increased to 4–12 µg/m^3 in 3 of the 7 cars. However, no increase in background levels of VOC was observed in any vehicle. With the e-cigarette, the concentration of propylene glycol increased in 5 car interiors to 50–762 µg/m^3, whereby the German indoor health precaution guide value for propylene glycol (RW I: 60 µg/m^3) was exceeded in 3 vehicles and the health hazard guide value (RW II: 600 µg/m^3) in one (AIR, 2017). Propylene glycol is used as a carrier in e-cigarette liquids and is responsible for the vapor produced during vaping. In 4 vehicles, the nicotine concentration also increased to 4–10 µg/m^3 while the e-cigarette was being used. The nicotine levels associated with the IQOS and e-cigarette were therefore comparable. However, the highest nicotine concentrations (8–140 µg/m^3) were reached with tobacco cigarettes. The burning of cigarette tobacco also led to pollution of the room air with 3-ethenylpyridine, the primary pyrolysis product of nicotine and a marker for passive smoke exposure. In 4 vehicles, the concentration of 3-ethenylpyridine increased to 8–14 µg/m^3. Higher levels of benzene (6–15 µg/m^3), toluene (15–46 µg/m^3), and furfural (4–29 µg/m^3) were also detected. However, levels of the other VOC were not higher with tobacco cigarettes than with the IQOS or e-cigarette and were sometimes not above the background levels measured in the control condition. Overall, we found no correlation between the different ventilation conditions (PW 2 cm vs. 5 cm open) and the VOC concentrations in the car interior. Poorer ventilation conditions did not necessarily result in more pollution in the indoor air. In addition, VOC concentrations were not highest in the cars with the smallest interior volume (2–3 m^3) but in cars with medium (3–4 m^3) and large volumes (4–5 m^3).

3.4. Interior concentration of aldehydes and ketones

Table S2 shows the concentrations of health-relevant aldehydes and ketones measured during the 7 test drives. The amounts of benzaldehyde, butyraldehyde, and acrolein in the air were below the detection limits in all sampled vehicles and are therefore not included in Table S2. In 5 of the 7 cars, the concentration of formaldehyde, acetaldehyde, and acetone increased while tobacco cigarettes were being smoked: Formaldehyde levels increased to 18.5–56.5 µg/m^3 (mean in control condition: 6.2 µg/m^3), and acetaldehyde and acetone levels increased to 26.5–141.5 µg/m^3 (mean in control condition: 5.2 µg/m^3) and 27.8–75.8 µg/m^3 (mean in control condition: 15.8 µg/m^3), respectively. If the interior was better ventilated (PW 5 cm open), concentrations of carbonyls tended to be slightly lower. The highest levels were found in vehicles with medium (3–4 m^3) and large (4–5 m^3) volumes, as follows: VW Golf (2005) > Volvo S > Skoda Octavia ≈ VW Golf (2006). In contrast to tobacco cigarettes, the IQOS and e-cigarette did not affect the concentrations of the investigated carbonyls. Apart from a few exceptions, the measurements were all in the range of the background levels in the control condition.

4. Discussion

In this exposure study, we performed a comprehensive evaluation of the concentrations of harmful chemicals in 7 passenger cars while conventional (tobacco cigarettes) and new electronic smoking products (IQOS, e-cigarette) were being smoked. To assess the potential exposure for non-smoking passengers, in particular children, we collected data on the indoor climate and indoor air pollution with fine and ultrafine particles and volatile organic compounds during real driving conditions. The measuring devices were located in the back seat behind the passenger and positioned so that they were measuring in what would be the breathing zone of a child seated in this position.

4.1. Electronic smoking devices (IQOS, e-cigarette)

Use of the e-cigarette led to an increase in the concentration of propylene glycol in 5 car interiors to 50–762 µg/m^3, whereby the German indoor health precaution guide value for propylene glycol (RW I: 60 µg/m^3) was significantly exceeded in 3 vehicles and the health hazard guide value (RW II: 600 µg/m^3) in one vehicle (AIR, 2017). Similar measurements above guide values were also observed in another exposure study on passive vapor exposure from e-cigarettes in a test

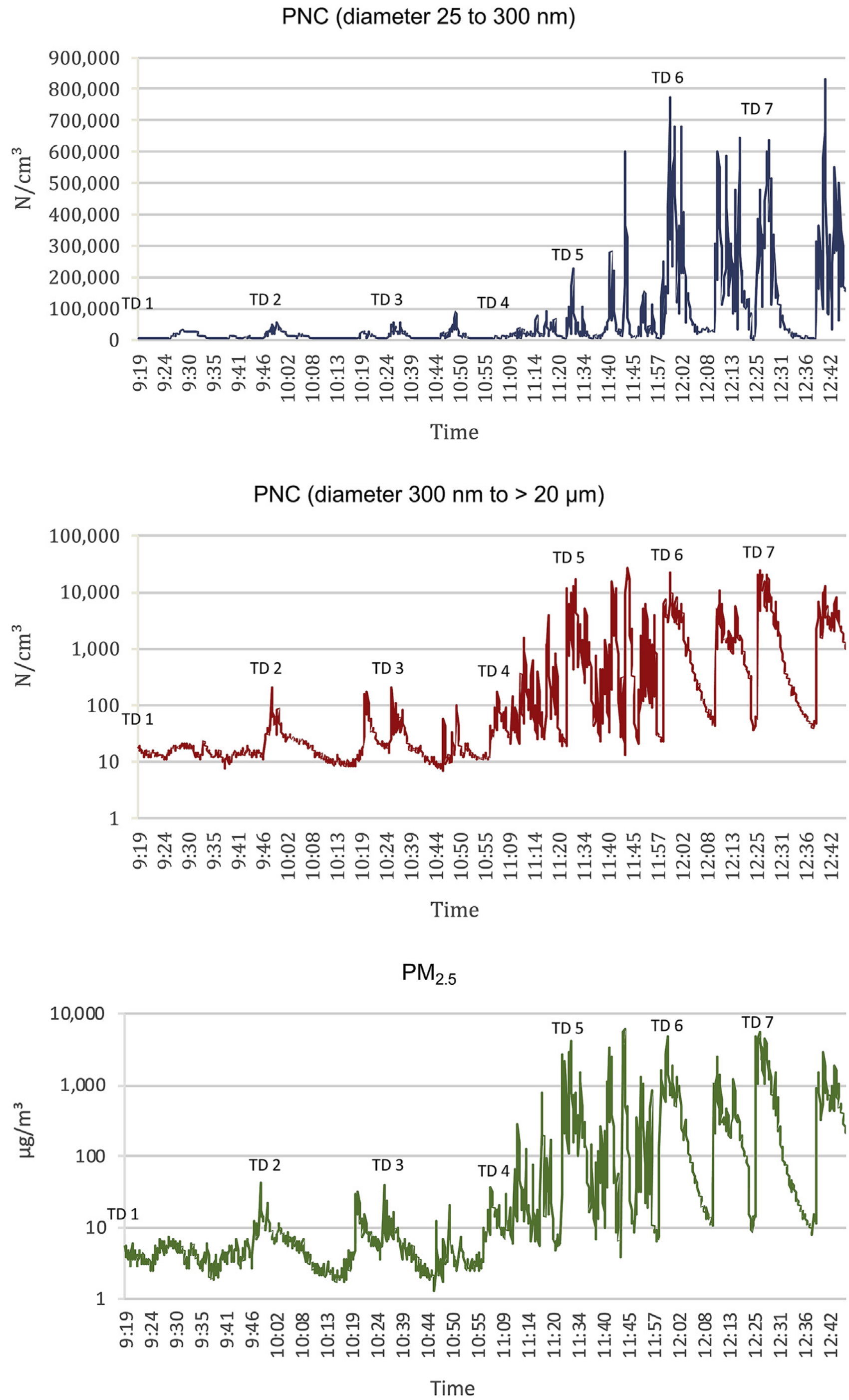

Fig. 2. A typical example of the time course of the particle load (particle number concentration, PNC; particle mass concentration, $PM_{2.5}$) in the interior of one (Skoda Octavia) of the 7 cars used in the study during the 7 20-min test drives (TDs) with no smoking (TD 1) and during the use of an IQOS (TD 2/3), e-cigarette (TD 4/5), and tobacco cigarettes (TD 6/7); the time course is shown as linear (top) and semilogarithmic (middle/bottom) representations. The periods between the test drives during which the vehicle was being fully ventilated are not shown in the figure. TD 1/2/4/6: passenger window 5 cm open; TD 3/5/7: passenger window 2 cm open.

room (Schober et al., 2014). Propylene glycol is used to absorb water and maintain moisture in some medicines, cosmetics, and foods and as a solvent in food, among other things, and is classified as safe when ingested by mouth. However, it is also used to make artificial smoke and fog, and brief exposure to propylene glycol in the air can irritate the eyes and respiratory tract (Wieslander et al., 2001). People regularly exposed to propylene glycol-containing aerosols at work (e.g. theater fog) suffer more often from respiratory irritations and impairments of lung function than non-exposed people. The most severe symptoms are shown by workers who are directly exposed to the vapors for a long time (Varughese et al., 2005). In one test drive in our study, the propylene glycol level was even 27% above the RW II (AIR, 2017). Concentrations of air pollutants above RW II can endanger the health of vulnerable people, including children. If levels exceed RW II, the basic schema for deriving guide values states that exposure should be immediately reduced (UBA, 2012).

In 4 test drives in our study, the vaping of an e-cigarette led to an increase in the nicotine concentration to 4–10 µg/m³. Similar nicotine

Table 1
Mean values of particle number concentrations (PNC; N/cm^3) of nano- and microscale particles and particle mass ($PM_{2.5}$, μg/m^3) in the car interiors (passenger window 2 cm open) with no smoking (control) and during use of an IQOS and e-cigarette (E-Cig) and two tobacco cigarettes (TC).

Car	Mean PNC (diameter 25–300 nm)	Mean PNC (diameter 300 nm to > 20 μm)	Mean PM2.5
Large interior volume			
Skoda Octavia			
Control[a]	10,491	20	6
IQOS[b]	16,726	23	6
E-Cig[c]	53,579	2145	490
TC[d]	181,487	3420	759
Volvo S			
Control[a]	20,231	41	10
IQOS[b]	22,152	90	19
E-Cig[c]	14,209	659	170
TC[d]	191,173	4168	895
Medium interior volume			
VW Golf (2006)			
Control[a]	20,675	22	7
IQOS[b]	29,044	40	11
E-Cig[c]	33,014	1362	262
TC[d]	236,167	2863	594
VW Golf (2005)			
Control[a]	73,941	40	11
IQOS[b]	123,656	144	34
E-Cig[c]	73,954	1188	269
TC[d]	193,792	9048	1988
VW Golf (2001)			
Control[a]	8434	18	7
IQOS[b]	19,554	21	6
E-Cig[c]	10,248	289	75
TC[d]	46,491	594	117
Small interior volume			
Smart ForFour			
Control[a]	17,716	14	4
IQOS[b]	25,616	21	5
E-Cig[c]	13,543	90	18
TC[d]	107,534	940	189
Fiat Punto			
Control[a]	18,626	19	9
IQOS[b]	28,827	10	4
E-Cig[c]	19,901	28	8
TC[d]	24,319	288	64

[a] Mean during a 20-min control drive with no smoking (TD 1: passenger window 5 cm open).
[b] Mean of two 6-min smoking phases with tobacco HEETS during TD 3.
[c] Mean of a continuous vaping episode during TD 5.
[d] Mean of two 6-min smoking phases with tobacco cigarettes during TD 7.

Table 2
Concentration of volatile organic compounds (VOC, μg/m^3) in the car interiors during the 7 test drives with no smoking (control) and with the use of an IQOS, an e-cigarette (E-Cig) and two tobacco cigarettes (TC) under different ventilation conditions (passenger window: 2 cm open/5 cm open). < LD: measurement was below the limit of detection (LD).

VOC	Control[a]	IQOS[b]	E-Cig[b]	TC[b]
Large interior volume				
Skoda Octavia				
Benzene	2	2/2	1/1	10/9
Propylene glycol	< LD	< LD	262/502	39/ < LD
Toluene	10	7/8	5/7	37/25
Furfural	< LD	< LD	< LD	8/9
3-Ethenylpyridine	< LD	< LD	< LD	10/10
Nicotine	< LD	< LD	4/5	68/77
Volvo S				
Benzene	6	7/3	6/2	11/15
Propylene glycol	< LD	< LD	196/226	< LD
Toluene	32	40/28	28/16	37/46
Furfural	< LD	< LD	< LD	28/13
3-Ethenylpyridine	< LD	< LD	< LD	9/14
Nicotine	< LD	< LD/6	< LD	64/105
Medium interior volume				
VW Golf (2006)				
Benzene	2	3/2	3/2	10/11
Propylene glycol	< LD	< LD	341/370	< LD/36
Toluene	6	7/7	5/8	21/31
Furfural	< LD	< LD	< LD	6/29
3-Ethenylpyridine	< LD	< LD	< LD	8/10
Nicotine	< LD	< LD/4	4/ < LD	58/88
VW Golf (2005)				
Benzene	2	< LD/1	< LD	15/9
Propylene glycol	< LD	< LD	762/611	94/58
Toluene	5	3/4	3/2	38/22
Furfural	< LD	< LD	< LD	12/8
3-Ethenylpyridine	< LD	< LD	< LD	13/9
Nicotine	< LD	12/5	10/7	140/89
VW Golf (2001)				
Benzene	< LD	< LD	< LD	< LD
Propylene glycol	< LD	< LD	50/59	< LD
Toluene	39	35/41	32/30	28/40
Furfural	< LD	< LD	< LD	< LD
3-Ethenylpyridine	< LD	< LD	< LD	< LD
Nicotine	< LD	< LD	5/ < LD	9/8
Small interior volume				
Smart ForFour				
Benzene	3	4/3	2/4	6/10
Propylene glycol	< LD	< LD	< LD	< LD
Toluene	9	8/11	7/10	15/29
Furfural	< LD	< LD	< LD	4/4
3-Ethenylpyridine	< LD	< LD	< LD	< LD
Nicotine	< LD	< LD	< LD	22/26
Fiat Punto				
Benzene	9	< LD	2/4	8/5
Propylene glycol	< LD	< LD	< LD	< LD
Toluene	35	15/11	8/26	44/18
Furfural	< LD	< LD/17	< LD	< LD
3-Ethenylpyridine	< LD	< LD	< LD	< LD
Nicotine	< LD	< LD	< LD	< LD

[a] Measurement during a 20-min control drive with no smoking (TD 1: passenger window 5 cm open).
[b] If the measured values were below the limit of detection (< LD) in both ventilation conditions, " < LD" is written only once.

levels were also observed with the IQOS smoking device (4–12 μg/m^3). Nicotine is a neurotoxin and addictive substance that leads to physical and psychological dependence (Benowitz, 2010). In animal experiments, it causes arteriosclerosis and promotes its progression (Heeschen et al., 2001; Lee and Cooke, 2011; Zhang et al., 2011). Nicotine is also teratogenic (Bruin et al., 2010) and promotes the growth of existing tumors in animal models (Heeschen et al., 2001). Earlier studies already demonstrated that the use of an e-cigarette increases the nicotine concentration of indoor air (Ballbe et al., 2014; Czogala et al., 2014; Saffari et al., 2014; Schober et al., 2014). Analyses of nicotine in saliva samples from non-smokers exposed to e-cigarette aerosols confirmed that nicotine is passively ingested when someone is vaping (Gallart-Mateu et al., 2016), although not to the extent associated with passive exposure to cigarette smoke (Jarvis et al., 1985, 2001). A recent study even provided convincing evidence for systemic nicotine uptake during passive exposure to vapor: Non-smokers who continuously inhaled e-cigarette emissions from the ambient air were found to have increased nicotine levels in saliva, serum, and urine (Melstrom et al., 2018). On the basis of these study findings, one can assume that the use of nicotine-containing e-cigarettes in car interiors is associated with a risk of systemic absorption of nicotine in non-smokers as a result of passive exposure to the vapor.

The smoking of the IQOS had almost no effect on the mean number concentration of fine particles (> 300 nm) or on the $PM_{2.5}$ concentration in the interior. In contrast, the number concentration of particles with a diameter of 25–300 nm increased in all vehicles (1.6–12.3 × 10^4/cm^3) and averaged 9%–232% above background levels without smoking. Another study on smoke exposure generated by the IQOS also described passive exposure to particles of comparable size (5.6–560 nm) (Protano et al., 2016). On the basis of the model calculations, the authors assumed that when someone uses an IQOS indoors, a high proportion (> 50%) of the submicronic particles inhaled from the ambient air reaches the alveolar region of passive smokers. In our study, we did not detect toxic carbonyls (e.g. formaldehyde), which are produced by pyrolysis during tobacco heating (Davis et al., 2019; Farsalinos et al., 2018), in any vehicle. The extent to which these compounds are formed, however, also depends on how strongly the user draws on the tobacco heater. Because none of the smokers had previously used an IQOS, the smokers may have drawn on the IQOS more cautiously, so that fewer of these substances were formed and they were not detectable in the room air.

When the e-cigarette was being vaped in the cars, we observed a sharp increase in the $PM_{2.5}$ concentration to 75–490 μg/m^3 (control: 6–11 μg/m^3). The vaping of the e-cigarette released more larger particles (> 300 nm) into the room air than the use of the IQOS. E-cigarette aerosols contain fine and ultrafine liquid particles that are formed from supersaturated propylene glycol vapor (Schober et al., 2014; Schripp et al., 2013). These particles can penetrate deep into the lungs and settle there (Manigrasso et al., 2015) and cause oxidative stress and inflammatory reactions (Cervellati et al., 2014). Irritation of the respiratory tract, dry cough, impairment of lung function, and evidence of inflammatory processes in the respiratory tract have been described as short-term effects of vaping (Pisinger and Dossing, 2014). Long-lasting inhalation of ultrafine propylene glycol droplets could be particularly harmful in the growth phase and increase the risk of asthma in children and adolescents (Choi et al., 2010). In addition, it may adversely affect the regeneration of damaged lung tissue after infection or chronic inflammation. Meanwhile, a number of experimental findings suggest that the inhalation of e-cigarette aerosols poses a health risk also for non-smokers (Fromme and Schober, 2015; IRK, 2016). Overall, in our study the use of the IQOS and e-cigarette affected the air quality in the car interiors by increasing the particle load. In the case of the IQOS, the significance of this finding for the health of passive smokers is currently unclear.

4.2. Tobacco cigarettes

The highest particle load in our study were measured while tobacco cigarettes were being smoked; with these cigarettes, mean $PM_{2.5}$ concentration in the car interiors increased to 64-1988 μg/m^3 (control: 4–11 μg/m^3). Other studies of smoke exposure inside vehicles observed comparable $PM_{2.5}$ levels. For example, measurements of particles during smoking with a window partially opened yielded $PM_{2.5}$ levels in car interiors of 47-12,150 μg/m^3 (Raoof et al., 2015). The burning of cigarette tobacco also led to a pollution of indoor air with substances typically found in tobacco smoke, such as nicotine (8–140 μg/m^3) and 3-ethenylpyridine (8–14 μg/m^3). In contrast to what one might expect, in our study the nicotine levels were not highest in the cars with the smallest interior volume. This may be because the smallest cars were the only vehicles in the study in which no tobacco cigarettes had been smoked before. In an indoor environment, nicotine from tobacco cigarette and e-cigarette aerosols can stick to various surfaces, such as fabrics, walls, windows, and floors (Goniewicz and Lee, 2015; Kuschner et al., 2011). The extent of nicotine sorption is highly affected by surface parameters, including surface area and texture, polarity, and absorbency (Petrick et al., 2010). We hypothesize that in the non-smoking cars nicotine sorption to interior objects, i.e. the seats, occurred to a greater extent than in the smoker's vehicles and contributed to a lower nicotine concentration of the room air.

We also detected increased levels of benzene (6–15 μg/m^3), toluene (15–46 μg/m^3), and furfural (4–29 μg/m^3). Similar pollution levels were also measured in the indoor air of restaurants where people smoked. In an exposure study, Bolte and coworkers (2008) measured typical combustion products of tobacco during the busiest times in 28 restaurants, pubs, and discotheques that allowed smoking. The mean concentrations of nicotine (21–227 μg/m^3), 3-ethenylpyridine (4–23 μg/m^3), and benzene (11–24 μg/m^3) were consistently in the same range as those found in the interior of cars when cigarettes are smoked. In the restaurants, the mean $PM_{2.5}$ exposure varied from 224 to 1210 μg/m^3 and the particle number concentration from 12 to 21 × 10^4 particles/cm^3, with peaks at diameters 10–500 nm. During smoking in cars, nanoscale particles (diameter 25–300 nm: 2.4–23.6 × 10^4/cm^3) were also the most common particles in the interior air. In 4 vehicles in our study, however, we measured $PM_{2.5}$ concentrations (594-1988 μg/m^3) that were significantly higher than the passive smoke exposure in restaurants where people were smoking (Bolte et al., 2008). The release of aldehydes with carcinogenic potential is highly relevant in the context of passive smoking. In our study, formaldehyde levels increased to 18.5–56.5 μg/m^3 (mean control: 6.2 μg/m^3) and acetaldehyde levels to 26.5–141.5 μg/m^3 (mean control: 5.2 μg/m^3) during smoking. Thus, formaldehyde levels in the car interiors reached levels similar to those in the study in restaurants where people were smoking (14.4–47.2 μg/m^3) (Bolte et al., 2008). With one exception, however, in all cars the concentrations of formaldehyde and acetaldehyde remained below the German indoor health precaution guide value of 100 μg/m^3 (AIR, 2016; UBA, 2013). The International Agency for Research on Cancer of the WHO classifies formaldehyde as a category 1 carcinogen (IARC, 2018). Acetaldehyde is highly toxic to the cilia. Paralysis and destruction of the ciliated epithelia on the surface of the respiratory tract results in congestion of the bronchial mucus, which reduces or suppresses the clearance process of the respiratory tract. Besides its effects on the respiratory tract, particularly on the nasal epithelia, acetaldehyde is thought to be involved in the development of lung cancer (IARC, 2018). In all vehicles, smoking of tobacco cigarettes resulted in the highest concentrations of pollutants.

5. Conclusion

The smoking of an IQOS, an e-cigarette, or tobacco cigarettes adversely affects indoor air quality through the release of fine and ultrafine particles and organic compounds. With the IQOS, the number concentration of particles with a diameter of 25–300 nm markedly increased in all passenger cars. The significance of this finding for the health of passive smokers is currently unclear. With the e-cigarette, the concentration of propylene glycol increased in 5 car interiors, whereby the German indoor health precaution guide value for propylene glycol was exceeded in 3 vehicles and the health hazard guide value in one. The use of the IQOS and an e-cigarette also led to an increase in the nicotine level in the interior which is likely associated with a risk of systemic absorption of nicotine in non-smokers. The nicotine and $PM_{2.5}$ concentrations measured in passenger cars while tobacco cigarettes are being smoked mostly exceed the pollution levels in restaurants where people are smoking. Overall, tobacco cigarettes, e-cigarettes, and the IQOS are all avoidable sources of indoor pollutants (especially nicotine and $PM_{2.5}$) that, to protect the health of the occupants, especially that of sensitive individuals such as children and pregnant women, should not be used in cars.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Acknowledgement

The authors thank all volunteers for participating in the study and Jacquie Klesing, Board-certified Editor in the Life Sciences, for editing assistance with the manuscript. The study was funded by the German Federal Ministry of Health.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://

doi.org/10.1016/j.ijheh.2019.01.003.

References

AIR, 2016. Richtwert für Formaldehyd in der Innenraumluft. Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 59, 1040–1044.

AIR, 2017. Indoor air guide value for propan-1,2-diol (propylene glycol) : communication from the Committee on Indoor Guide Values. Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 60, 1298–1304.

Arcus-Arth, A., Blaisdell, R.J., 2007. Statistical distributions of daily breathing rates for narrow age groups of infants and children. Risk Anal. 27, 97–110.

Ballbe, M., Martinez-Sanchez, J.M., Sureda, X., Fu, M., Perez-Ortuno, R., Pascual, J.A., Salto, E., Fernandez, E., 2014. Cigarettes vs. e-cigarettes: passive exposure at home measured by means of airborne marker and biomarkers. Environ. Res. 135, 76–80.

Benowitz, N.L., 2010. Nicotine addiction. N. Engl. J. Med. 362, 2295–2303.

Bolte, G., Heitmann, D., Kiranoglu, M., Schierl, R., Diemer, J., Koerner, W., Fromme, H., 2008. Exposure to environmental tobacco smoke in German restaurants, pubs and discotheques. J. Expo. Sci. Environ. Epidemiol. 18, 262–271.

Bruin, J.E., Gerstein, H.C., Holloway, A.C., 2010. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. Toxicol. Sci. 116, 364–374.

Carnevale, R., Sciarretta, S., Violi, F., Nocella, C., Loffredo, L., Perri, L., Peruzzi, M., Marullo, A.G., De Falco, E., Chimenti, I., Valenti, V., Biondi-Zoccai, G., Frati, G., 2016. Acute impact of tobacco vs electronic cigarette smoking on oxidative stress and vascular function. Chest 150, 606–612.

Cervellati, F., Muresan, X.M., Sticozzi, C., Gambari, R., Montagner, G., Forman, H.J., Torricelli, C., Maioli, E., Valacchi, G., 2014. Comparative effects between electronic and cigarette smoke in human keratinocytes and epithelial lung cells. Toxicol. In Vitro 28, 999–1005.

Cheraghi, M., Salvi, S., 2009. Environmental tobacco smoke (ETS) and respiratory health in children. Eur. J. Pediatr. 168, 897–905.

Choi, H., Schmidbauer, N., Sundell, J., Hasselgren, M., Spengler, J., Bornehag, C.G., 2010. Common household chemicals and the allergy risks in pre-school age children. PLoS One 5, e13423.

Collaborators GBDT, 2017. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: a systematic analysis from the Global Burden of Disease Study 2015. Lancet 389, 1885–1906.

Czogala, J., Goniewicz, M.L., Fidelus, B., Zielinska-Danch, W., Travers, M.J., Sobczak, A., 2014. Secondhand exposure to vapors from electronic cigarettes. Nicotine Tob. Res. 16, 655–662.

Davis, B., Williams, M., Talbot, P., 2019. iQOS: evidence of pyrolysis and release of a toxicant from plastic. Tobac. Contr. 28, 34–41.

Farsalinos, K.E., Yannovits, N., Sarri, T., Voudris, V., Poulas, K., Leischow, S.J., 2018. Carbonyl emissions from a novel heated tobacco product (IQOS): comparison with an e-cigarette and a tobacco cigarette. Addiction 113, 2099–2106.

Fromme, H., Schober, W., 2015. Waterpipes and e-cigarettes: impact of alternative smoking techniques on indoor air quality and health. Atmos. Environ. 106, 429–441.

Gallart-Mateu, D., Elbal, L., Armenta, S., de la Guardia, M., 2016. Passive exposure to nicotine from e-cigarettes. Talanta 152, 329–334.

Goniewicz, M.L., Lee, L., 2015. Electronic cigarettes are a source of thirdhand exposure to nicotine. Nicotine Tob. Res. 17, 256–258.

Heeschen, C., Jang, J.J., Weis, M., Pathak, A., Kaji, S., Hu, R.S., Tsao, P.S., Johnson, F.L., Cooke, J.P., 2001. Nicotine stimulates angiogenesis and promotes tumor growth and atherosclerosis. Nat. Med. 7, 833–839.

IARC, 2004. Tobacco Smoke and Involuntary Smoking. IARC Monogr Eval Carcinog Risks Hum, vol. 83 IARC Press, Lyon.

IARC, 2018. IARC monographs, list of classifications, volumes 1-123. http://monographs.iarc.fr/ENG/Classification/latest_classif.php.

IRK, 2016. Stellungnahme der Innenraumhygienekommission (IRK) zu elektronischen Zigaretten (E-Zigaretten). Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 59, 1660–1661.

Jarvis, M.J., Russell, M.A., Feyerabend, C., Eiser, J.R., Morgan, M., Gammage, P., Gray, E.M., 1985. Passive exposure to tobacco smoke: saliva cotinine concentrations in a representative population sample of non-smoking schoolchildren. Br. Med. J. 291, 927–929.

Jarvis, M.J., Feyerabend, C., Bryant, A., Hedges, B., Primatesta, P., 2001. Passive smoking in the home: plasma cotinine concentrations in non-smokers with smoking partners. Tobac. Contr. 10, 368–374.

Jones, I.A., St Helen, G., Meyers, M.J., Dempsey, D.A., Havel, C., Jacob 3rd, P., Northcross, A., Hammond, S.K., Benowitz, N.L., 2014. Biomarkers of secondhand smoke exposure in automobiles. Tobac. Contr. 23, 51–57.

Kuschner, W.G., Reddy, S., Mehrotra, N., Paintal, H.S., 2011. Electronic cigarettes and thirdhand tobacco smoke: two emerging health care challenges for the primary care provider. Int. J. Gen. Med. 4, 115–120.

Lee, J., Cooke, J.P., 2011. The role of nicotine in the pathogenesis of atherosclerosis. Atherosclerosis 215, 281–283.

Liu, S., Zhu, Y., 2010. A case study of exposure to ultrafine particles from secondhand tobacco smoke in an automobile. Indoor Air 20, 412–423.

Manigrasso, M., Buonanno, G., Fuoco, F.C., Stabile, L., Avino, P., 2015. Aerosol deposition doses in the human respiratory tree of electronic cigarette smokers. Environ. Pollut. 196, 257–267.

Melstrom, P., Sosnoff, C., Koszowski, B., King, B.A., Bunnell, R., Le, G., Wang, L., Thanner, M.H., Kenemer, B., Cox, S., DeCastro, B.R., McAfee, T., 2018. Systemic absorption of nicotine following acute secondhand exposure to electronic cigarette aerosol in a realistic social setting. Int. J. Hyg Environ. Health 221, 816–822.

Northcross, A.L., Trinh, M., Kim, J., Jones, I.A., Meyers, M.J., Dempsey, D.D., Benowitz, N.L., Hammond, S.K., 2014. Particulate mass and polycyclic aromatic hydrocarbons exposure from secondhand smoke in the back seat of a vehicle. Tobac. Contr. 23, 14–20.

Ott, W., Klepeis, N., Switzer, P., 2008. Air change rates of motor vehicles and in-vehicle pollutant concentrations from secondhand smoke. J. Expo. Sci. Environ. Epidemiol. 18, 312–325.

Palamidas, A., Tsikrika, S., Katsaounou, P.A., Vakali, S., Gennimata, S.-A., Kaltsakas, G., Gratziou, C., Koulouris, N., 2017. Acute effects of short term use of e-cigarettes on airways physiology and respiratory symptoms in smokers with and without airways obstructive diseases and in healthy non smokers. Tobacco Prev. Cessat. 3.

Petrick, L., Destaillats, H., Zouev, I., Sabach, S., Dubowski, Y., 2010. Sorption, desorption, and surface oxidative fate of nicotine. Phys. Chem. Chem. Phys. 12, 10356–10364.

Pisinger, C., Dossing, M., 2014. A systematic review of health effects of electronic cigarettes. Prev. Med. 69, 248–260.

Protano, C., Manigrasso, M., Avino, P., Sernia, S., Vitali, M., 2016. Second-hand smoke exposure generated by new electronic devices (IQOS® and e-cigs) and traditional cigarettes: submicron particle behaviour in human respiratory system. Ann Ig 28, 109–112.

Raoof, S.A., Agaku, I.T., Vardavas, C.I., 2015. A systematic review of secondhand smoke exposure in a car: attributable changes in atmospheric and biological markers. Chron. Respir. Dis. 12, 120–131.

Raupach, T., Radon, K., Nowak, D., Andreas, S., 2008. Passive smoking–health consequences and effects of exposure prevention. Pneumologie 62, 44–50.

Saffari, A., Daher, N., Ruprecht, A., De Marco, C., Pozzi, P., Boffi, R., Hamad, S.H., Shafer, M.M., Schauer, J.J., Westerdahl, D., Sioutas, C., 2014. Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure. Environ. Sci. Process Impact. 16, 2259–2267.

Schober, W., Szendrei, K., Matzen, W., Osiander-Fuchs, H., Heitmann, D., Schettgen, T., Jörres, R.A., Fromme, H., 2014. Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. Int. J. Hyg Environ. Health 217, 628–637.

Schripp, T., Markewitz, D., Uhde, E., Salthammer, T., 2013. Does e-cigarette consumption cause passive vaping? Indoor Air 23, 25–31.

Semple, S., Apsley, A., Galea, K.S., MacCalman, L., Friel, B., Snelgrove, V., 2012. Secondhand smoke in cars: assessing children's potential exposure during typical journey conditions. Tobac. Contr. 21, 578–583.

Spindle, T.R., Breland, A.B., Karaoghlanian, N.V., Shihadeh, A.L., Eissenberg, T., 2015. Preliminary results of an examination of electronic cigarette user puff topography: the effect of a mouthpiece-based topography measurement device on plasma nicotine and subjective effects. Nicotine Tob. Res. 17, 142–149.

Tabuchi, T., Gallus, S., Shinozaki, T., Nakaya, T., Kunugita, N., Colwell, B., 2018. Heat-not-burn tobacco product use in Japan: its prevalence, predictors and perceived symptoms from exposure to secondhand heat-not-burn tobacco aerosol. Tobac. Contr. 27, e25–e33.

UBA, 2012. Guide values for indoor air: update of the German risk assessment procedure (basic scheme). Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 55, 279–290.

UBA, 2013. Indoor air guide values for acetaldehyde. Announcement of the German Ad-hoc working group on indoor guidelines of the indoor air Hygiene committee and of the states' supreme health authorities. Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 56, 1434–1447.

US-DHHS, 2010. How Tobacco Smoke Causes Disease: the Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General. Atlanta.

US-DHHS, 2014. The Health Consequences of Smoking – 50 Years of Progress. A Report of the Surgeon General. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta.

Vardavas, C.I., Anagnostopoulos, N., Kougias, M., Evangelopoulou, V., Connolly, G.N., Behrakis, P.K., 2012. Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. Chest 141, 1400–1406.

Varughese, S., Teschke, K., Brauer, M., Chow, Y., van Netten, C., Kennedy, S.M., 2005. Effects of theatrical smokes and fogs on respiratory health in the entertainment industry. Am. J. Ind. Med. 47, 411–418.

Vlachopoulos, C., Ioakeimidis, N., Abdelrasoul, M., Terentes-Printzios, D., Georgakopoulos, C., Pietri, P., Stefanadis, C., Tousoulis, D., 2016. Electronic cigarette smoking increases aortic stiffness and blood pressure in young smokers. J. Am. Coll. Cardiol. 67, 2802–2803.

Wang, L., Pinkerton, K.E., 2008. Detrimental effects of tobacco smoke exposure during development on postnatal lung function and asthma. Birth Defects Res. C Embryo. Today 84, 54–60.

WHO, 2012. WHO global report: mortality attributable to tobacco. http://apps.who.int/iris/bitstream/10665/44815/1/9789241564434_eng.pdf.

Wieslander, G., Norbäck, D., Lindgren, T., 2001. Experimental exposure to propylene glycol mist in aviation emergency training: acute ocular and respiratory effects. Occup. Environ. Med. 58, 649–655.

Zhang, G., Marshall, A.L., Thomas, A.L., Kernan, K.A., Su, Y., LeBoeuf, R.C., Dong, X.R., Tchao, B.N., 2011. In vivo knockdown of nicotinic acetylcholine receptor alpha1 diminishes aortic atherosclerosis. Atherosclerosis 215, 34–42.