EXHIBIT

tabbies

1

Vaping-Passive; literature search 8-31-19 and 12-11-19
Lee's Summit Health Education Advisory Board

1. https://www.mdpi.com/1660-4601/16/9/1525

Int J Environ Res Public Health. 2019 Apr 30;16(9). pii: E1525. doi: 10.3390/ijerph16091525.

The Health Risks of Electronic Cigarette Use to Bystanders.

Visser WF[1], Klerx WN[2], Cremers HWJM[3], Ramlal R[4], Schwillens PL[5], Talhout R[6].

Abstract

This works aimed to assess the health risks of e-cigarette use to bystanders. The exhaled breath of 17 volunteers was collected while they were vaping, and the levels of nicotine, propylene glycol, glycerol, formaldehyde, acetaldehyde, acrolein, tobacco-specific nitrosamines (TSNAs), and heavy metals were analyzed. Increased levels of nicotine, propylene glycol, TSNAs and copper were found in the exhaled breath of the volunteers. From these measurements, bystander exposure was estimated for two different scenarios: (1) A non-ventilated car with two e-cigarette users and (2) a ventilated office with one e-cigarette user. Our results show that **bystanders may experience irritation of the respiratory tract as a result of exposure to propylene glycol and glycerol. Systemic effects of nicotine should also be expected if nicotine-containing e-liquid is used, including palpitations, and an increase of the systolic blood pressure. Furthermore, due to the presence of TSNAs in some e-liquids, an increased risk of tumors could not be excluded for the 'car' scenario. While e-cigarette use can clearly have effects on the health of bystanders, the risks depend on the rate of ventilation, dimensions of the room, and vaping behavior of the e-cigarette user.** The presence of TSNAs in e-liquids can be avoided, which will prevent the most serious effect identified (increased risk of tumors).

KEYWORDS:

bystanders; electronic cigarettes; health risks; second hand vaping

PMID: 31052162

PMCID: PMC6539638

DOI: 10.3390/ijerph16091525 [Indexed for MEDLINE]

Free PMC Article

EXHIBIT

tabbies

2

2. https://www.ncbi.nlm.nih.gov/pubmed/31775282

Toxics. 2019 Nov 25;7(4). pii: E59. doi: 10.3390/toxics7040059.

Evaluation of Second-Hand Exposure to Electronic Cigarette Vaping under a Real Scenario: Measurements of Ultrafine Particle Number Concentration and Size Distribution and Comparison with Traditional Tobacco Smoke.

Palmisani J, Di Gilio A, Palmieri L, Abenavoli C, Famele M, Draisci R, de Gennaro G.

Abstract

The present study aims to evaluate the impact of e-cig second-hand aerosol on indoor air quality in terms of ultrafine particles (UFPs) and potential inhalation exposure levels of passive bystanders. E-cig second-hand aerosol characteristics in terms of UFPs number concentration and size distribution exhaled by two volunteers vaping 15 different e-liquids inside a 49 m^3 room and comparison with tobacco smoke are discussed. High temporal resolution measurements were performed under natural ventilation conditions to simulate a realistic exposure scenario. Results showed a systematic increase in UFPs number concentration (part cm^{-3}) related to a 20-min vaping session (from 6.56×10^3 to 4.01×10^4 part cm^{-3}), although this was one up to two order of magnitude lower than that produced by one tobacco cigarette consumption (from 1.12×10^5 to 1.46×10^5 part cm^{-3}). E-cig second-hand aerosol size distribution exhibits a bimodal behavior with modes at 10.8 and 29.4 nm in contrast with the unimodal typical size distribution of tobacco smoke with peak mode at 100 nm. **In the size range 6-26 nm, particles concentration in e-cig second-hand aerosol were from 2- (Dp = 25.5 nm) to 3800-fold (Dp = 9.31 nm) higher than in tobacco smoke highlighting that particles exhaled by users and potentially inhaled by bystanders are nano-sized with high penetration capacity into human airways.**

KEYWORDS:

electronic cigarettes; indoor air quality; second-hand aerosol; size distribution; tobacco smoke; ultrafine particles

PMID: 31775282

DOI: 10.3390/toxics7040059 **Free full text**

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3. https://www.ncbi.nlm.nih.gov/pubmed/302829104r

Int J Environ Res Public Health. 2018 Oct 3;15(10). pii: E2172. doi: 10.3390/ijerph15102172.

Environmental Electronic Vape Exposure from Four Different Generations of Electronic Cigarettes: Airborne Particulate Matter Levels.

Protano C[1], Avino P[2], Manigrasso M[3], Vivaldi V[4], Perna F[5], Valeriani F[6], Vitali M[7].

Abstract

Electronic cigarettes (e-cigs) were introduced into the market in 2006 and their technological features have evolved substantially over time. Currently, there are four different generations of e-cigs that are broadly considered less harmful than the use of combusted tobacco products although passive exposure to aerosols often occurs in public spaces and indoor environments. **The study aim was to evaluate the levels of airborne particulate matter (PM) emitted during the use of all the four generations of e-cigs,** testing different use modalities. PM_{10}, PM□, $PM_{2.5}$ and PM□ were measured through a Dusttrak ™ II Aerosol Monitor, for a total of 20 independent experiments. **All tested e-cigs devices produced PM during their use**, and PM_{10} was almost made of PM□ size fraction. In addition, we observed a progressive increase in PM emission from the first to the fourth generation, and an upward trend of PM□ emitted by the fourth generation e-cig with an increase in the operating power. The results showed that, **whatever the model adopted, passive vaping does occur.** This finding **supports the need for legislative interventions to regulate the e-cigs use in public places and other enclosed environments, in order to protect the health of any subject who is potentially exposed.**

KEYWORDS:
electronic cigarettes; environmental electronic vape exposure; particulate matter
PMID: 30282910 PMCID: PMC6210766 DOI: 10.3390/ijerph15102172
[Indexed for MEDLINE] **Free PMC Article**

4. https://www.ncbi.nlm.nih.gov/pubmed/31112510

Rev Environ Health. **2019 Jun** 26;34(2):105-124. doi: 10.1515/reveh-2019-0012.

Electronic cigarettes in the indoor environment.

Marcham CL1, Springston JP2.

Abstract

The use of electronic cigarettes (e-cigarettes or "vaping") has seen an unprecedented increase worldwide. Vaping has been promoted as a beneficial smoking cessation tool and an alternative nicotine delivery device that contains no combustion by-products. However, nicotine is highly addictive, and the increased use of nicotine-containing e-cigarettes among teens and individuals who are not in need of smoking cessation may lead to overall greater nicotine dependence in the population. Furthermore, available research indicates that vaping solutions and their emissions may contain much more than just nicotine, including aerosolized flavorings, propylene glycol (PG), and other intentional and unintentional contaminants. These materials could present undefined potential health hazards to both e-cigarette users and bystanders, the full extent of which is not well understood at this time. Whereas e-cigarette usage and exposures may lower some or most of the risks associated with conventional cigarette use, the health effects of nicotine and aerosol exposures from e-cigarettes are not well understood. **Research indicates that vaping aerosols are not benign, especially for nearby people in areas with limited ventilation and people with compromised health conditions.** In addition, e-juice liquids have already been responsible for an increase in accidental poisonings in children. **Because the magnitude of health and safety hazards that vaping may present to nonusers remains unclear, it is prudent to manage and control vaping in indoor locations where smoking is currently restricted.** Based on a review of current scientific information, the **American Industrial Hygiene Association (AIHA) recommends that e-cigarettes should be considered a source of aerosols, volatile organic compounds (VOCs), and particulates in the indoor environment that have not been thoroughly characterized or evaluated for health risk or safety.**

PMID: 31112510 DOI: 10.1515/reveh-2019-0012

5. https://www.ncbi.nlm.nih.gov/pubmed/28766331

Environ Sci Technol. 2017 Aug 15;51(16):9271-9279. doi: 10.1021/acs.est.7b00710. Epub 2017 Aug 2.

Emissions from Electronic Cigarettes: Assessing Vapers' Intake of Toxic Compounds, Secondhand Exposures, and the Associated Health Impacts.

Logue JM[1], Sleiman M[1,2], Montesinos VN[3], Russell ML[1], Litter MI[3,4], Benowitz NL[5], Gundel LA[1], Destaillats H[1].

Abstract

E-cigarettes likely represent a lower risk to health than traditional combustion cigarettes, but they are not innocuous. Recently reported emission rates of potentially harmful compounds were used to assess intake and predict health impacts for vapers and bystanders exposed passively. Vapers' toxicant intake was calculated for scenarios in which different e-liquids were used with various vaporizers, battery power settings and vaping regimes. For a high rate of 250 puff day^{-1} using a typical vaping regime and popular tank devices with battery voltages from 3.8 to 4.8 V, users were predicted to inhale formaldehyde (up to 49 mg day^{-1}), acrolein (up to 10 mg day^{-1}) and diacetyl (up to 0.5 mg day^{-1}), at levels that exceeded U.S. occupational limits. Formaldehyde intake from 100 daily puffs was higher than the amount inhaled by a smoker consuming 10 conventional cigarettes per day. Secondhand exposures were predicted for two typical indoor scenarios: a home and a bar. Contributions from vaping to air pollutant concentrations in the home did not exceed the California OEHHA 8-h reference exposure levels (RELs), except when a high emitting device was used at 4.8 V. In that extreme scenario, the contributions from vaping amounted to as much as 12 µg m^{-3} formaldehyde and 2.6 µg m^{-3} acrolein. Pollutant concentrations in **bars** were modeled using indoor volumes, air exchange rates and the number of hourly users reported in the literature for U.S. bars in which smoking was allowed. Predicted contributions to indoor air levels were higher than those in the residential scenario. Formaldehyde (on average 135 µg m^{-3}) and acrolein (28 µg m^{-3}) exceeded the acute 1-h exposure REL for the highest emitting vaporizer/voltage combination. Predictions for these compounds also exceeded the 8-h REL in several bars when less intense vaping conditions were considered. Benzene concentrations in a few bars approached the 8-h REL, and diacetyl levels were close to the lower limit for occupational exposures. The integrated health damage from passive vaping was derived by computing disability-adjusted life years (DALYs) lost due to exposure to secondhand vapor. Acrolein was the dominant contributor to the aggregate harm. DALYs for the various device/voltage combinations were lower than-or comparable to-those estimated for exposures to secondhand and thirdhand tobacco smoke.PMID: 28766331

DOI: 10.1021/acs.est.7b00710

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6. https://www.ncbi.nlm.nih.gov/pubmed/22672560

EXHIBIT

6

Indoor Air. 2013 Feb;23(1):25-31. doi: 10.1111/j.1600-0668.2012.00792.x. Epub 2012 Jul 2.

Does e-cigarette consumption cause passive vaping?

Schripp T[1], Markewitz D, Uhde E, Salthammer T.

Abstract

Electronic cigarette consumption ('vaping') is marketed as an alternative to conventional tobacco smoking. Technically, a mixture of chemicals containing carrier liquids, flavors, and optionally nicotine is vaporized and inhaled. The present study aims at the determination of the release of volatile organic compounds (VOC) and (ultra)fine particles (FP/UFP) from an e-cigarette under near-to-real-use conditions in an 8-m(3) emission test chamber. Furthermore, the inhaled mixture is analyzed in small chambers. **An increase in FP/UFP and VOC could be determined after the use of the e-cigarette. Prominent components in the gas-phase are 1,2-propanediol, 1,2,3-propanetriol, diacetin, flavorings, and traces of nicotine. As a consequence, 'passive vaping' must be expected from the consumption of e-cigarettes.** Furthermore, the inhaled aerosol undergoes changes in the human lung that is assumed to be attributed to deposition and evaporation.

PRACTICAL IMPLICATIONS:

The consumption of e-cigarettes marks a new source for chemical and aerosol exposure in the indoor environment. To evaluate the impact of e-cigarettes on indoor air quality and to estimate the possible effect of passive vaping, information about the chemical characteristics of the released vapor is needed.

PMID: 22672560 DOI: 10.1111/j.1600-0668.2012.00792.x
[Indexed for MEDLINE]

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7. https://www.ncbi.nlm.nih.gov/pubmed/?term=Characterisation+of+mainstream+and+passive+vapours

Int J Hyg Environ Health. 2015 Jan;218(1):169-80. doi: 10.1016/j.ijheh.2014.10.001. Epub 2014 Oct 13.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Characterisation+of+mainstream+and+passive+vapours

Int J Hyg Environ Health. 2015 Jan;218(1):169-80. doi: 10.1016/j.ijheh.2014.10.001. Epub 2014 Oct 13.

Characterisation of mainstream and passive vapours emitted by selected electronic cigarettes.

Geiss O[1], Bianchi I[2], Barahona F[2], Barrero-Moreno J[2].

Abstract

Electronic cigarettes have achieved growing popularity since their introduction onto the European market. They are promoted by manufacturers as healthier alternatives to tobacco cigarettes, however debate among scientists and public health experts about their possible impact on health and indoor air quality means further research into the product is required to ensure decisions of policymakers, health care providers and consumers are based on sound science. This study investigated and characterised the impact of 'vaping' (using electronic cigarettes) on indoor environments under controlled conditions using a 30m(3) emission chamber. **The study determined the composition of e-cigarette mainstream vapour in terms of propylene glycol, glycerol, carbonyls and nicotine emissions using a smoking machine with adapted smoking parameters.** Two different base recipes for refill liquids, with three different amounts of nicotine each, were tested using two models of e-cigarettes. Refill liquids were analysed on their content of propylene glycol, glycerol, nicotine and qualitatively on their principal flavourings. Possible health effects of e-cigarette use are not discussed in this work. **Electronic cigarettes tested in this study proved to be sources for propylene glycol, glycerol, nicotine, carbonyls and aerosol particulates.** The extent of exposure differs significantly for active and passive 'vapers' (users of electronic cigarettes). Extrapolating from the average amounts of propylene glycol and glycerol condensed on the smoking machine filter pad to the resulting lung-concentration, estimated lung concentrations of 160 and 220mgm(-3) for propylene glycol and glycerol were obtained, respectively. Vaping refill liquids with nicotine concentrations of 9mgmL(-1) led to vapour condensate nicotine amounts comparable to those of low-nicotine regular cigarettes (0.15-0.2mg). In chamber studies, peak concentrations of 2200μgm(-3) for propylene glycol, 136μgm(-3) for glycerol and 0.6μgm(-3) for nicotine were reached. Carbonyls were not detected above the detection limits in chamber studies. Particles in the size range of 20nm to 300nm constantly increased during vaping activity and reached final peak concentrations of 7×10(6)particlesL(-1). Moreover, the tested products showed design flaws such as leakages from the cartridge reservoirs. Possible long term effects of e-cigarettes on health are not yet known. E-cigarettes, the impact of vaping on health and the composition of refill liquids require therefore further research into the product characteristics. The consumers would benefit from harmonised quality and safety improvements of e-cigarettes and refill liquids. PMID:25455424 DOI: 10.1016/j.ijheh.2014.10.001

Tob Control. 2017 Mar;26(e1):e16-e18. doi: 10.1136/tobaccocontrol-2016-053074. Epub 2016 Sep 5.

Should electronic cigarette use be covered by clean indoor air laws?

Yingst JM[1], Veldheer S[1], Hammett E[1], Hrabovsky S[1], Foulds J[1].

Abstract

BACKGROUND:

Some jurisdictions have passed legislation that bans electronic cigarette (e-cig) use (vaping) in public places similarly to smoking. Many other jurisdictions have not yet determined how to regulate vaping in public places. This study examined the proportion of current e-cig users who find their vaping restricted in public places and further evaluated factors associated with the differences between restricted and unrestricted vapers.

METHODS:

3960 experienced exclusive e-cig users completed an online survey from December 2012 to May 2014 about their e-cig use. Restricted vapers were defined as those who reported not being able to vape in places where smoking is typically banned. Unrestricted vapers were defined as those who reported being able vape in places where smoking is typically banned. χ^2 and two-sided t-tests were used as appropriate to determine differences between variables of interest.

RESULTS:

Participants were a mean age of 40.3 years, 72.0% male, 91.8% white and 85.1% were from the USA. 26.1% (n=1034) of users reported restricted vaping, while 73.9% (n=2926) reported unrestricted vaping. Restricted vapers used less frequently (p<0.001) and were less dependent compared with unrestricted vapers (p=0.001). Of the restricted vapers, only 12% (n=124) reported finding it difficult to refrain from vaping in places where they were not supposed to. These users were more dependent (p<0.001) and more likely to experience strong cravings (p<0.001), compared with users who did not find it difficult to refrain from vaping.

CONCLUSIONS:

This study found that most vapers report unrestricted use of their e-cig. **Of the restricted vapers, the majority (88%) do not find it difficult to refrain from vaping in places where they are not supposed to vape.**

PMID: 27596227 PMCID: PMC5536097 DOI: 10.1136/tobaccocontrol-2016-053074

EXHIBIT

9

9. https://www.ncbi.nlm.nih.gov/pubmed/?term=Main+and+side+stream+effects+of+electronic+cigarettes

J Environ Manage. **2019 May** 15;238:10-17. doi: 10.1016/j.jenvman.2019.01.030. Epub 2019 Mar 2.

Main and side stream effects of electronic cigarettes.

Papaefstathiou E[1], Stylianou M[2], Agapiou A[3].

Abstract

Over the last decade there has been a significant boost towards the use of electronic cigarettes (e-cigarettes), especially among youth. Different concentrations of propylene glycol (PG) or vegetable glycerin (VG), flavors and nicotine are mixed in plastic cartridges and commercially offered or privately produced by the vapers. During vaping, a mixture of air and vapors is inhaled to the lungs. Since the ingredients of the e-cigarettes are not burned but vaporized (heated), fewer chemicals are emitted. The levels of potentially toxic compounds (e.g. volatile organic compounds (VOCs), particulate matter (PM), metals, radicals, nitrosamines, etc.) emitted from vaping appear to be lower compared to that of tobacco smoking (from combustible cigarettes). Nevertheless, measurable toxic elements and VOCs are still released (e.g. acetaldehyde, formaldehyde, acrolein, benzene, etc.) along with other volatiles associated with e-liquid flavoring and device variability with PG and VG. The wide range of available flavors at various purities along with the heating temperature are important parameters affecting the evolution of VOCs and aerosols. There is lack of standardized short- and long-term epidemiological medical data (chronic exposure) on e-cigarettes effects to users, non-users and the human micro-environment (second- or third-hand exposure). Therefore, the potential health, safety and environmental effects of vaping are reviewed, examined and discussed.

KEYWORDS:

E-cigarette; Environmental impact assessment; GC-MS; VOCs; Vaping

PMID: 30836280 DOI: 10.1016/j.jenvman.2019.01.030

10. https://www.ncbi.nlm.nih.gov/pubmed/?term=Formaldehyde+in+electronic+cigarettes+and+in+heat-not-burn+products

Epidemiol Prev. 2018 Sep-Dec;42(5-6):351-355. doi: 10.19191/EP18.5-6.P351.104.

[Formaldehyde in electronic cigarettes and in heat-not-burn products: let's make the point].

[Article in Italian]

De Marco C[1], Borgini A[2,3], Ruprecht AA[4,3], Veronese C[5], Mazza R[4,6], Bertoldi M[2], Tittarelli A[7], Scaburri A[2], Ogliari AC[5], Zagà V[8], Contiero P[2], Tagliabue G[7], Boffi R[5].

The spread of electronic cigarettes (e-cigs) and of the so-called heat-not-burn (HnB), also known as heated tobacco products, presented as a less harmful alternative to traditional cigarettes, required further in-depth studies to demonstrate the real benefits or possible risks linked to this type of habit among smokers and possible new smokers. **There are numerous harmful substances produced by these devices, such as metals, organic compounds, and aldehydes. The presence of formaldehyde is particularly worrying: its indoor concentration is 2.7, 1.2, and 40 µg/m3 for HnB, e-cigs, and traditional cigarettes, respectively**. **The evidence of this substance, which numerous epidemiological studies have already shown to be harmful to health (in particular, the International Agency for Research on Cancer classified it as a group 1 carcinogen), would lead to the need to modify the legislation with more restrictive rules on the use of these devices in public environment** and in particular in the presence of more susceptible subjects, such as minors and pregnant women.

PMID: 30370737 DOI: 10.19191/EP18.5-6.P351.104

11. https://www.ncbi.nlm.nih.gov/pubmed/?term=Use+of+electronic+cigarettes+(e-cigarettes)+impairs+indoor+air+quality+and+increases+FeNO+levels+of+e-cigarette+consumers

International Journal of Hygiene and Environmental Health
journal homepage: www.elsevier.com/locate/ijheh

Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers

Wolfgang Schober[a,*], Katalin Szendrei[a], Wolfgang Matzen[a], Helga Osiander-Fuchs[b], Dieter Heitmann[c], Thomas Schettgen[d], Rudolf A. Jörres[e], Hermann Fromme[a]

Abstract

Despite the recent popularity of e-cigarettes, to date only limited data is available on their safety for both users and secondhand smokers. The present study reports a comprehensive inner and outer exposure assessment of e-cigarette emissions in terms of particulate matter (PM), particle number concentra- tions (PNC), volatile organic compounds (VOC), polycyclic aromatic hydrocarbons (PAH), carbonyls, and metals. In six vaping sessions nine volunteers consumed e-cigarettes with and without nicotine in a thor- oughly ventilated room for two hours. We analyzed the levels of e-cigarette pollutants in indoor air and monitored effects on FeNO release and urinary metabolite profile of the subjects. For comparison, the components of the e-cigarette solutions (liquids) were additionally analyzed.

During the vaping sessions substantial amounts of 1,2-propanediol, glycerine and nicotine were found in the gas-phase, as well as high concentrations of PM (mean 197 □g/m^3). The concentration of putative carcinogenic PAH in indoor air increased by 20% to 147 ng/m^3 , and aluminum showed a 2.4-fold increase. PNC ranged from 48,620 to 88,386 particles/cm^3 (median), with peaks at diameters 24–36 nm. FeNO increased in 7 of 9 individuals. The nicotine content of the liquids varied and was 1.2-fold higher than claimed by the manufacturer.

Our data confirm that e-cigarettes are not emission-free and their pollutants could be of health concern for users and secondhand smokers. In particular, **ultrafine particles formed from supersaturated 1,2- propanediol vapor can be deposited in the lung, and aerosolized nicotine seems capable of increasing the release of the inflammatory signaling molecule NO upon inhalation.** In view of consumer safety, e- cigarettes and nicotine liquids should be officially regulated and labeled with appropriate warnings of potential health effects, particularly of toxicity risk in children.

EXHIBIT

12

12. https://www.ncbi.nlm.nih.gov/pubmed/?term=Systemic+absorption+of+nicotine+following+acute+secondhand+exposure+to+electronic+cigarette+aerosol

International Journal of Hygiene and Environmental HealthVolume 221, Issue 5, June 2018, Pages 816-822

Systemic absorption of nicotine following acute secondhand exposure to electronic cigarette aerosol in a realistic social setting

https://doi.org/10.1016/j.ijheh.2018.05.003

Abstract

Evidence suggests exposure of nicotine-containing e-cigarette aerosol to nonusers leads to systemic absorption of nicotine. However, no studies have examined acute secondhand exposures that occur in public settings. Here, we measured the serum, saliva and urine of nonusers pre- and post-exposure to nicotine via e-cigarette aerosol. Secondarily, we recorded factors affecting the exposure.

Six nonusers of nicotine-containing products were exposed to secondhand aerosol from ad libitum e-cigarette use by three e-cigarette users for 2 h during two separate sessions (disposables, tank-style). Pre-exposure (baseline) and post-exposure peak levels (Cmax) of cotinine were measured in nonusers' serum, saliva, and urine over a 6-hour follow-up, plus a saliva sample the following morning. We also measured solution consumption, nicotine concentration, and pH, along with use behavior.

Baseline cotinine levels were higher than typical for the US population (median serum session one = 0.089 ng/ml; session two = 0.052 ng/ml). Systemic absorption of nicotine occurred in nonusers with baselines indicative of no/low tobacco exposure, but not in nonusers with elevated baselines. Median changes in cotinine for disposable exposure were 0.007 ng/ml serum, 0.033 ng/ml saliva, and 0.316 ng/mg creatinine in urine. For tank-style exposure they were 0.041 ng/ml serum, 0.060 ng/ml saliva, and 0.948 ng/mg creatinine in urine. Finally, we measured substantial differences in solution nicotine concentrations, pH, use behavior and consumption.

Our data show that although exposures may vary considerably, nonusers can systemically absorb nicotine following acute exposure to secondhand e-cigarette aerosol. This can particularly affect sensitive subpopulations, such as children and women of reproductive age.

Keywords

NicotineE-cigaretteSecondhandAerosolCotinine

1. Introduction

Studies show a dramatic increase in experimentation and use of electronic cigarettes among US adults and youth (Arrazola et al., 2014; Giovenco et al., 2014; King et al., 2015). One area of particular concern to the public health community is nonusers' exposure to the contents of e-cigarette aerosol, particularly sensitive subpopulations such as children, the developing fetus and pregnant women. In addition to nicotine, e-cigarettes' aerosols can contain heavy metals, ultrafine particles, and cancer-causing agents like acrolein (Goniewicz et al., 2013a; McAuley et al., 2012; Pellegrino et al., 2012; Schober et al., 2013; Schripp et al., 2013). The aerosol of e-cigarettes can also contain propylene glycol (PG) or vegetable glycerin (VG) and flavorings. The health effects of chronic inhalation of these substances are currently unknown. Moreover, fundamental questions remain about what compounds to measure, how best to measure them, and how best to describe the variable effects of e-cigarette solutions, uses, and devices when assessing health threats from e-cigarettes.

Most e-cigarettes deliver aerosolized nicotine, which raises concerns for nonusers about the potential for acute poisonings, developmental and reproductive toxicity, and addiction (Chatham-Stephens et al., 2014; England et al., 2015; U.S. Department of Health and Human Services, Printed with corrections, January 2014). Studies have measured nicotine in air following e-cigarette aerosol generation (Czogala et al., 2013; Schripp et al., 2013), and Flouris and colleagues exposed never-smokers to machine-generated e-cigarette aerosol in an exposure chamber for a single hour and measured serum cotinine concentrations immediately after the exposure and an hour later (Flouris et al., 2013). Although the values were not published, cotinine concentrations in the never-smokers passively exposed to e-cigarette aerosol were significantly higher than in a control group. Similarly, Ballbe and colleagues measured urine and salivary cotinine in nonusers who lived with exclusive e-cigarette users (n = 5) and found significantly higher levels of cotinine in these nonusers compared to nonusers living in homes where no smoker or e-cigarette user was living (n = 24), both in urine and saliva (p-values 0.008 and 0.003, respectively) (Ballbe et al., 2014).

However, these studies did not simulate realistic short-term exposures that occur in social or public settings, nor did they describe the factors affecting the exposures. To address this gap in the scientific literature, we examined acute secondhand nicotine exposure to nonusers by using three habitual e-cigarette users (active users) vaping ad libitum in a room co-occupied by six nonusers for two hours. The number of e-cigarette users for each exposure represented a plausible number of users in a physical space comparable to public spaces such as bars or restaurants, or to a private space such as a household room. We also accounted for other sources of nicotine exposure and the extent to which certain factors, such as solution and device characteristics, as well as how the e-cigarette users used their device (use behavior) might affect exposure.

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4. Discussion

Our findings suggest that nonusers of e-cigarettes can experience systemic absorption of nicotine from acute exposure to secondhand e-cigarette aerosol. However, the exposure may vary considerably depending upon solution, device, baseline cotinine levels, and use behavior of e-cigarette users. We recorded large variability among the measured nicotine concentrations and pH of e-cigarette solutions used, and there were also large differences in e-cigarette use behavior and solution consumption among the active users.

6. Conclusion

Nonusers of e-cigarettes can experience systemic absorption of nicotine from acute exposure to secondhand e-cigarette aerosol. Although less than levels produced by conventional cigarettes, the exposure is greater than in clean indoor air – the standard. Also, the exposure may vary considerably depending upon solution, device, baseline nicotine levels and the use behavior of e-cigarette users. In addition, aerosols produced from the use of e-cigarettes may contain other harmful constituents that were not measured in this study.

These findings could have important implications for public health policy, planning, and practice. **Since allowing e-cigarette use in public settings can result in systemic absorption of nicotine in nonusers, extending clean indoor air policies to include e-cigarettes would be expected to reduce nicotine exposure and absorption among nonusers, which is particularly important for subpopulations who are sensitive to nicotine's effects, including children and women of reproductive age.**

13. https://jamanetwork-com.proxy.library.umkc.edu/journals/jamapediatrics/fullarticle/2611944

jamapediatrics.com

Secondhand Exposure to Electronic Cigarette Aerosol Among US Youths

Electronic cigarette (e-cigarette) use has increased consider- ably since these products were introduced into the US mar- ketplace in 2007,[1] and e-cigarettes are the most commonly used tobacco product among US youths.[2] In contrast to combus- tible tobacco products, e-cigarettes do not produce side-stream emissions from the device itself. However, **aerosol is produced during activation of the device, some of which is ex- haled into the environment where nonusers can be exposed through inhalation, ingestion, or dermal contact.[3]**

Secondhand aerosol (SHA) from e-cigarettes can contain harmful and potentially harmful substances including nico- tine, heavy metals, ultrafine particulate, volatile organic com- pounds such as formaldehyde and acetaldehyde, and other toxicants.[3,4] However, to our knowledge, the extent to which US youths are exposed to SHA is unknown. This study as- sessed self-reported SHA exposure among US students.

Methods | Data came from the 2015 National Youth Tobacco Sur- vey, a cross-sectional survey of US middle school and high school students (n = 17 711). National Youth Tobacco Survey uses a 3-stage sampling design (counties, schools, and classes) to yield nationally representative estimates.[2] Written ap- proval to participate in the survey was obtained from parents

or legal guardians. This secondary analysis of deidentified pub- lic use data was exempt from human participants review.

Self-reported SHA exposure was assessed by asking, "dur- ing the past 30 days, on how many days did you breathe the vapor from someone who was using an electronic cigarette or e-cigarette in an indoor or outdoor public library?" Seven re- sponse options ranged from "0 days" to "all 30 days." Respon- dents who indicated any response other than "0 days" were considered exposed to SHA.

Point estimates and 95% CIs were reported overall and by school level, sex, race/ethnicity, current (past 30-day) e-cigarette use, current (past 30-day) other tobacco product use (cigars, cigarillos, or little cigars; chewing tobacco, snuff, or dip; pipe tobacco; bidis; snus; dissolvable tobacco; and hoo-kah or waterpipe used with tobacco), and past 30-day second-

[e] Past 30-day use and ever-use were determined separately for each of the following other tobacco products: cigarettes; cigars, cigarillos, or little cigars; chewing tobacco, snuff, or dip; pipe filled with tobacco; bidis; snus; dissolvable tobacco; hookah or waterpipe used with tobacco. Responses were used to categorize respondents into 3 mutually exclusive categories of other tobacco product use. Current users included respondents who reported yes to ever use and at least 1 day to past 30-day use for any of the listed tobacco products. Former users included respondents who reported yes to ever use but 0 days to past 30-day use for any of the listed tobacco products. Never-users included respondents who reported no to ever-use and 0 days to past 30-day use for all of the listed tobacco products.

[f] RespondentswereaskedʺDuringthepast30days,onhowmanydaysdidyou breathe the smoke from someone who was smoking tobacco products in an indoor or outdoor public place?" Response options included 0 days, 1 or 2

days,3to5days,6to9days,10to19days,20to29days,orall30days. Respondents who indicated any response other than 0 days were considered exposed to secondhand smoke.

hand smoke (SHS) exposure from combustible tobacco prod- ucts. Population counts were extrapolated from probability weights. Data were analyzed using R 3.2.3 (R Programming).

Results | Overall, 24.2% of students (6.5 million) reported SHA exposure (Table). Exposure was 21.9% among boys and 26.7% among girls and ranged from 15.3% among non-Hispanic Afri- can American individuals to 27.0% among non-Hispanic white individuals. By e-cigarette use, exposure was 66.8% among cur- rent users, 28.9% among former users, and 16.4% among never- users. By other tobacco product use, exposure was 51.5% among current users, 32.3% among former users, and 16.8% among never-users. Secondhand aerosol exposure was reported among 40.0% of students exposed to SHS and among 8.5% of students not exposed to SHS.

Discussion | **One in 4 US youths are exposed to SHA from e-cigarettes including 4.4 million who are not current e-cigarette users** and 1 million not exposed to SHS from com- bustible tobacco. These findings underscore the importance of tobacco prevention strategies, including comprehensive poli- cies that address both SHS and SHA, to prevent youth expo- sure to this public health threat.

To protect the public from both SHS and SHA, it is critical to modernize clean indoor air policies to include e-cigarettes. Such policies **can maintain standards for clean indoor air, reduce the potential for renormalization of tobacco use, and prevent in- voluntary exposure to nicotine and other e-cigarette emissions.**[1] As of January **2017, 8 states and more than 500 communities have comprehensive indoor air laws that prohibit e-cigarettes.**[5]

Efforts are also warranted to educate youths and youth in- fluencers about the potential dangers of SHA exposure.[1] Specifi- cally, pediatricians can incorporate screening for e-cigarette use and SHA exposure into clinical practice, and counsel parents, youths, and caregivers about the potential harms of SHA and the importance of avoiding exposure.[6] Further research on SHA con- stituents as well as prevalence, correlates, and locations of ex- posure, could help inform public health policy and practice.

Teresa W. Wang, PhD, MS Kristy L. Marynak, MPP Israel T. Agaku, DMD, MPH Brian A. King, PhD, MPH

Author Affiliations: Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia (Wang, Marynak, Agaku, King); Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia (Wang). **Corresponding Author:** Teresa W. Wang, PhD, MS, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Hwy, MS F-79, Atlanta, GA 30341 (yxn7@cdc.gov).

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Tob Control. 2017 Jan;26(1):109-112. doi: 10.1136/tobaccocontrol-2015-052772. Epub 2016 Feb 15.

Electronic cigarette use and indoor air quality in a natural setting.

Soule EK[1], Maloney SF[1], Spindle TR[1], Rudy AK[1], Hiler MM[1], Cobb CO[1].

Author information

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Department of Psychology, Virginia Commonwealth University, Center for the Study of Tobacco Products, Richmond, Virginia, USA.

Abstract

INTRODUCTION:

Secondhand smoke (SHS) from combustible cigarettes causes numerous diseases. Policies have been developed to prevent SHS exposure from indoor cigarette use to reduce health risks to non-smokers. However, fewer policies have been implemented to deter electronic cigarette (ECIG) use indoors, and limited research has examined the impact of secondhand exposure to ECIG aerosol.

METHODS:

Indoor air quality was measured at a 2-day ECIG event held in a large room at a hotel. Fine particulate matter (PM) was measured using 2 devices that measured concentrations of PM 2.5 μm aerodynamic diameter or smaller ($PM_{2.5}$). Measurements were taken before the event, over 2 days when the event was ongoing, and the day after the event. $PM_{2.5}$ measurements were also taken from the restaurant at the hotel hosting the event and a restaurant at a nearby hotel.

RESULTS:

During 6 time points when the event was ongoing, between 59 and 86 active ECIG users were present in the event room (room volume=4023 m^3). While the event was ongoing, median $PM_{2.5}$ concentrations in the event room increased from a baseline of 1.92-3.20 $\mu g/m^3$ to concentrations that ranged from 311.68 $\mu g/m^3$ (IQR 253.44-411.84 $\mu g/m^3$) to 818.88 $\mu g/m^3$ (IQR 760.64-975.04 $\mu g/m^3$).

CONCLUSIONS:

$PM_{2.5}$ concentrations observed at the ECIG event were higher than concentrations reported previously in hookah cafés and bars that allow cigarette smoking. This study indicates that indoor ECIG use exposes non-users to secondhand ECIG aerosol. Regulatory bodies should consider establishing policies that prohibit ECIG use anywhere combustible cigarette use is prohibited.

KEYWORDS:

Electronic nicotine delivery devices; Public policy; Secondhand smoke

EXHIBIT

15

15.

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E-Cigarettes: A Review of New Trends in Cannabis Use.

Giroud C[1,2,3], de Cesare M[4], Berthet A[5,6,7], Varlet V[8,9,10], Concha-Lozano N[11,12,13], Favrat B[14,15,16,17].

Abstract

The emergence of electronic cigarettes (e-cigs) has given cannabis smokers a new method of inhaling cannabinoids. E-cigs differ from traditional marijuana cigarettes in several respects. First, it is assumed that vaporizing cannabinoids at lower temperatures is safer because it produces smaller amounts of toxic substances than the hot combustion of a marijuana cigarette. **Recreational cannabis users can discretely "vape" deodorized cannabis extracts with minimal annoyance to the people around them and less chance of detection.** There are nevertheless several drawbacks worth mentioning: although manufacturing commercial (or homemade) cannabinoid-enriched electronic liquids (e-liquids) requires lengthy, complex processing, some are readily on the Internet despite their lack of quality control, expiry date, and conditions of preservation and, above all, any toxicological and clinical assessment. Besides these safety problems, the regulatory situation surrounding e-liquids is often unclear. More simply ground cannabis flowering heads or concentrated, oily THC extracts (such as butane honey oil or BHO) can be vaped in specially designed, pen-sized marijuana vaporizers. Analysis of a commercial e-liquid rich in cannabidiol showed that it contained a smaller dose of active ingredient than advertised; testing our laboratory-made, purified BHO, however, confirmed that it could be vaped in an e-cig to deliver a psychoactive dose of THC. The health consequences specific to vaping these cannabis preparations remain largely unknown and speculative due to the absence of comprehensive, robust scientific studies. **The most significant health concerns involve the vaping of cannabinoids by children and teenagers. E-cigs could provide an alternative gateway to cannabis use for young people. Furthermore, vaping cannabinoids could lead to environmental and passive contamination.**

KEYWORDS: adolescence; cannabis; electronic cigarette; vaping

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16. Should e-cigarette use be permitted in smoke-free public places? No

Chapman, Simon; Daube, Mike; Maziak, Wasim.**Tobacco Control; London** Vol. 26, Iss. e1, (Mar 2017): e3.DOI:10.1136/tobaccocontrol-2016-053359

Abstract
Translate

Correspondence to Professor Simon Chapman, School of Public Health, University of Sydney, Edward Ford Building A27, Sydney, NSW 2006, Australia; simon.chapman@sydney.edu.au Introduction While some early examples of smoke-free policy were introduced because of community preferences for clean indoor air and fire safety, smoke-free policy today is predicated on a large body of evidence that has accumulated since the early 1970s about harm to others from secondhand smoke.1 2 In contrast, those advocating for vaping to be allowed in smoke-free public places centre their case on gossamer-thin evidence that vaping emissions are all but benign and therefore pose negligible risks to others akin to inhaling steam from showers, kettles or saunas.3 Not just water vapour This is likely to be baseless. Unlike vapourised water, electronic nicotine delivery system **(ENDS) emissions comprise nicotine, carbonyls, metals, organic volatile compounds, besides particulate matter,4 and putative carcinogenic polycyclic aromatic hydrocarbon.**5 6 Moreover, the **high concentrations of nanoparticles in vape, despite their small mass, may have significant toxicological impact.7 This is likely due to their increased ability for deep penetration into the pulmonary and cardiovascular systems.**5 Importantly, the short time span since the advent of ENDS and the latency of candidate respiratory and cardiovascular diseases that may be caused or exacerbated by ambient exposure to ENDS emissions preclude definitive risk inference.7 Taking the current immature evidence as a proof of safety and using it to advocate for policy that allows ENDS indoors could prove reckless. [...]with delightful irony, the 2016 Global Forum on Nicotine, (focused on ENDS and including leading ENDS advocates) banned ENDS use by delegates in conference areas. Indoor Air 2010; 20: 52–60. doi:10.1111/j.1600-0668.2009.00625.x 16 Chapman S. "Half-pregnant" occupational health policy on environmental tobacco smoke.

More

Full Text

Translate

Correspondence to Professor Simon Chapman, School of Public Health, University of Sydney, Edward Ford Building A27, Sydney, NSW 2006, Australia; simon.chapman@sydney.edu.au

Introduction

While some early examples of smoke-free policy were introduced because of community preferences for clean indoor air and fire safety, smoke-free policy today is predicated on a large body of evidence that has accumulated since the early 1970s about harm to others from secondhand smoke.[1 2] In contrast, those advocating for vaping to be allowed in smoke-free public places centre their case on gossamer-thin evidence that vaping emissions are all but benign and therefore pose negligible risks to others akin to inhaling steam from showers, kettles or saunas.[3]

Not just water vapour

This is likely to be baseless. Unlike vapourised water, electronic nicotine delivery system (ENDS) emissions comprise nicotine, carbonyls, metals, organic volatile compounds, besides particulate matter,[4] and putative carcinogenic polycyclic aromatic hydrocarbon.[5 6] Moreover, the high concentrations of nanoparticles in vape, despite their small mass, may have significant toxicological impact.[7] This is likely due to their increased ability for deep penetration into the pulmonary and cardiovascular systems.[5]

Importantly, the short time span since the advent of ENDS and the latency of candidate respiratory and cardiovascular diseases that may be caused or exacerbated by ambient exposure to ENDS emissions preclude definitive risk inference.[7] Taking the current immature evidence as a proof of safety and using it to advocate for policy that allows ENDS indoors could prove reckless.

Recent reports of rapid-onset changes in aortic stiffness after exposure to vape,[8] of mice exposed to vape with nicotine developing features of chronic obstructive pulmonary disease[9] and a 2014 report of increases in fractional exhaled nitric monoxide (FeNo),[5] a marker of eosinophilic airway inflammation, following vaping are examples of possibly vanguard research findings that may prove important.

Vaping on aircraft presents catastrophic risk because of the risk of explosions and fires.[10] The unregulated vaping gear industry, with amateurs also modifying equipment, remains an ongoing risk in this respect. Many combustible products have long been prohibited on aircraft in carry-on and checked baggage.

Real world exposures

While documented indoor concentrations of exhaled vape constituents are often lower than those arising from cigarettes,[9] real world scenarios can involve significant exposure. Scenes from 'vapecons' abound on YouTube,[11] where large numbers of ENDS users participate in 'clouding' contests, show worst case scenarios (eg, http://www.youtube.com/watch?v=4NPe3rAYG_Q&t=0m46s). The air in such settings is visibly and constantly thick with vape. In a recent study,[12] $PM_{2.5}$ counts were measured in a 4023 m^3 room at a vapecon over six occasions when between 59 and 86 active ENDS users were present. Median $PM_{2.5}$ concentrations in the room increased from a baseline of 1.92–3.20 $\mu g/m^3$ to concentrations ranging from 311.68 to 818.88 μg/m^3; 125–330 times higher than in the same room when empty and higher than $PM_{2.5}$ concentrations recorded in bars where cigarette or waterpipe smoking were allowed.[13]

Vaping advocates acknowledge wide variations in public vaping practices, asserting that while some 'take joy in producing huge clouds of vapour' others 'wish to produce as little fog as possible' and 'produce so little visible fog that they vape freely in public–at work, in meetings, in restaurants, and in planes, trains and buses.' And it is even seriously claimed that 'nobody even notices'.[14]

Public policy needs to deal with this diversity and assume more than the most discreet, low-key scenarios. If vaping were allowed indoors, would any restrictions apply? Would bar staff be required to limit the number of people vaping, or request or order them to be discreet or 'considerate' with their exhalations as with the ineffective approaches that were once made for smokers?[15] Will arguments occur about whether a plume is excessive? Should and how might 'clouding' be forbidden? Will airlines allow a maximum of five passengers to vape but not 50? How will those charged with enforcing smoke-free measures, whether in public places or locations such as cars and buses where children can be heavily exposed, distinguish between smokers and vapers? Good luck with all of that.

The history of smoke-free policy saw early ludicrously ineffective and discredited efforts to accommodate continuing smoking indoors such as 'magic line' divisions between smoking and non-smoking sections;[16] courtesy campaigns[17] and ventilation.[18] The folly of these efforts should not be repeated with exposure to vaping.

Helping smokers quit versus triggering relapse in former smokers?

By allowing vaping in all currently smoke-free indoor public and workplace areas, it is also asserted that many smokers not yet vaping may see this as an attractive benefit and take it up. This is a factor cited by some youth for trying ENDS.[19] **While some smokers would quit smoking with ENDS, many more would engage in dual use.[20] Given that smoke-free policies have been important drivers of smoking reduction and cessation,[21] it is plausible that being able to vape in public places may in fact dampen decisions to quit or lead to relapse for many. Indeed, experimental evidence suggests that exposure to ENDS advertising[22] [23]and imagery[24] may stimulate smokers and ex-smokers to try ENDS, smoke more cigarettes or relapse to smoking.[16] [17]**

Another argument used by indoor vaping advocates is that indoor vaping bans will cause former smokers who now vape to go outside, where exposure to sensory cues from exiled cigarette smokers will trigger their relapse back to smoking. This would be all the fault of non-smokers selfishly putting their own health and comfort ahead of vapers and contributing to their stigmatisation.[25] By this argument non-smokers should be happy to be exposed to ambient vape in aircraft, workplaces, restaurants and bars (or even sustained clouding sessions) to make ENDS users feel more 'included' and in the hope that they might quit smoking.

Renormalisation of the smoking performance

The ENDS industry's business model involves promoting vaping as an alternative to smoking. But only the most disingenuous or naïve could deny that the prospect of attracting the far more numerous non-smokers, particularly youth, to vaping would be their only long-term sustainable business model.[26] Policies which maximise public exposure to vaping will likely be essential to recruiting new consumers of various tobacco/nicotine products.

A collateral beneficial effect of smoke-free policy has been the denormalisation of smoking. This has seriously eroded the tobacco industry goal of allowing smoking to occur without restriction, and portraying smoking as a normal, highly desirable behaviour. All major tobacco companies have invested heavily in ENDS but have not desisted from aggressive tobacco marketing, targeting disadvantaged groups or opposing effective tobacco control measures. They want people to smoke or smoke *and* vape, not vape *instead* of smoke. With the vaping performance or 'act' sharing much with the smoking act, the tobacco industry would hold high hopes of renormalising the use of its traditional and immensely profitable products. This is likely to cue interest in vaping in non-smokers and ex-smokers, an outcome far removed from the ostensible putative benefits of having only smokers switch.[27] It will also erode the benefits achieved by non-smoking policies over many years in ensuring that children do not see smoking behaviour as normal and acceptable.

If ENDS emissions were really benign, indoor vaping advocates should take courage and call for it to be allowed in classrooms, crèches, hospitals and neonatal wards. That they do not rather suggests that they know well that such a position would be irresponsible.

Finally, and with delightful irony, the 2016 Global Forum on Nicotine, (focused on ENDS and including leading ENDS advocates) banned ENDS use by delegates in conference areas. The organisers' plea that delegates in public areas "please be discreet and considerate. Use low powered devices as it helps to keep the amount of vapour created to a minimum" could not be more revealing.[28]

Footnote

Contributors All three authors contributed to writing the paper.

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