HHS Public Access

Author manuscript

Annu Rev Public Health. Author manuscript; available in PMC 2020 July 09.

Published in final edited form as:

Annu Rev Public Health. 2020 April 02; 41: 363–380. doi:10.1146/annurev-publhealth-040119-094043.

Effects of Electronic Cigarettes on Indoor Air Quality and Health

Liqiao Li[1], **Yan Lin**[1], **Tian Xia**[2], **Yifang Zhu**[1]

[1]Department of Environmental Health Sciences, Jonathan and Karin Fielding School of Public Health, University of California, Los Angeles, California 90095-1772, USA

[2]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, California 90095-1772, USA

Abstract

With the rapid increase in electronic cigarette (e-cig) users worldwide, secondhand exposure to e-cig aerosols has become a serious public health concern. We summarize the evidence on the effects of e-cigs on indoor air quality, chemical compositions of mainstream and secondhand e-cig aerosols, and associated respiratory and cardiovascular effects. The use of e-cigs in indoor environments leads to high levels of fine and ultrafine particles similar to tobacco cigarettes (t-cigs). Concentrations of chemical compounds in e-cig aerosols are generally lower than those in t-cig smoke, but a substantial amount of vaporized propylene glycol, vegetable glycerin, nicotine, and toxic substances, such as aldehydes and heavy metals, has been reported. Exposures to mainstream e-cig aerosols have biologic effects but only limited evidence shows adverse respiratory and cardiovascular effects in humans. Long-term studies are needed to better understand the dosimetry and health effects of exposures to secondhand e-cig aerosols.

Keywords

particulate matter; $PM_{2.5}$; ultrafine particles; nicotine; respiratory and cardiovascular effects

INTRODUCTION

An electronic cigarette (e-cig) is a battery-powered nicotine delivery system widely used as an alternative to tobacco cigarettes (t-cigs). Since 2011, the global e-cig market has grown rapidly and is projected to reach $48.9 billion by 2025, more than 70% of the market being in North America and Europe (2). The number of e-cig users has also increased markedly, especially among adolescents, despite the US Food and Drug Administration (FDA)'s prohibition of sales to persons under the age of 18 (136). In the United States, the total number of current e-cig users in middle schools and high schools increased from 0.3 million

yifang@ucla.edu.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

in 2011 to 3.6 million in 2018 (23). Similar increases among adolescents have been observed in other countries, such as the United Kingdom, Canada, South Korea, New Zealand, Finland, and Poland (9, 12).

For t-cigs, the combustion of tobacco leaves releases nicotine and substantial amounts of toxic by-products. In comparison, e-cigs deliver nicotine by vaporizing e-liquids, which typically use propylene glycol (PG) and vegetable glycerin (VG) as the suspension media for nicotine and various flavorings. E-cigs are marketed as a safer alternative to t-cigs because they are combustion-free, yet their use has also increased greatly among nonsmokers (88). Because e-cigs are easy to use, have appealing flavors, and are perceived risk-free (12, 20), they are becoming the most popular tobacco product among adolescents. The newly introduced pod-based e-cigs (e.g., JUUL), which use nicotine salts, offer a wide range of flavors, and have a sleek design, are even more attractive to adolescents than are regular tank-based e-cigs (20, 48, 57, 87). The impacts of e-cigs on population health remain largely unknown; however, with increasing evidence on their biological effects from in vitro and in vivo studies (107), the safety of e-cigs has become a serious public health concern.

Not only active users but also bystanders may be exposed to e-cig aerosols. Estimates indicate that more than 70% of inhaled e-cig aerosols are eventually exhaled (143), which may cause secondhand exposures. E-cigs are commonly used in many places, such as homes, cars, restaurants, bars, and workplaces (46), where vulnerable populations, such as children, adolescents, and pregnant women, might be exposed (27, 139). Secondhand exposure in indoor environments is of particular concern because people typically spend more than 80% of their time indoors (64), where emitted pollutants are not diluted as quickly or as extensively as outdoors. Yet, to what extent such secondhand exposures affect human health is unclear. While a large number of health studies on t-cig secondhand smoke exist (55), data from these studies cannot be extrapolated to e-cigs because the emission characteristics are different.

To provide a better understanding of the public health risks associated with secondhand exposures to e-cig aerosols, we summarize here the evidence for the impacts of e-cigs on indoor air quality and human health. The schematic process from e-cig emissions, to secondhand exposures, and to potential health effects is summarized in Figure 1.

THE LITERATURE SEARCH

We reviewed articles published in English and listed on PubMed and the Web of Science before April 2019 that investigated either particulate matter (PM) or chemical compositions in e-cig aerosols, as well as associated health effects. Inclusion criteria include (*a*) e-cig aerosol studies on fine particulate matter ($PM_{2.5}$, particles with aerodynamic diameters ≤2.5 μm) or ultrafine particles (UFPs; particles with a diameter ≤100 nm), (*b*) both mainstream and secondhand exposure studies on chemical compositions in e-cig aerosols, and (*c*) active and passive human exposure studies on e-cig health effects. Key search terms included “electronic cigarette” OR “e-cigarette” OR “e-cig” OR “vaping” in combination with “aerosol” OR “particle” OR “particulate matter (PM),” “chemical composition” OR “chemical emission” OR “exposure,” “mainstream” OR “secondhand” OR “indoor air

quality," and "health." We extracted data on particle and chemical concentrations from the text, tables, or supporting information in the identified articles. To compare the results across different studies, we report chemical compositions in mass per puff for mainstream and mass per cubic meter (m^3) for secondhand studies, respectively.

IMPACTS OF E-CIGS ON INDOOR AIR QUALITY

Studies evaluating the effects of e-cigs on particulate matter (PM) were typically conducted either in a room (>30 m^3) or in a chamber (<1 m^3). Studies conducted in rooms represent real-world exposures but were often affected by various environmental factors, such as relative humidity, air exchange rate, and temperature, which are difficult to fully control. On the other hand, chamber studies usually have sufficient control over environmental factors and thus can systematically isolate and investigate the effects of e-cig devices and e-liquid compositions. However, the concentrations of pollutants reported in chamber studies are often orders of magnitude higher than in real-world indoor environments. In the following sections, we focus on studies conducted in real-world indoor environments.

Indoor Particle Concentrations

Exposure to outdoor $PM_{2.5}$ is a well-established risk factor for respiratory and cardiovascular diseases (14). Several indoor studies have reported high concentrations of $PM_{2.5}$ resulting from e-cigs (Figure 2a), which could reach up to 1,121 μg/m^3, or ~45 times as high as the World Health Organization's recommended 25 μg/m^3 limit for 24-h outdoor concentrations (140). In most cases, the reported indoor $PM_{2.5}$ levels during e-cig use are above 150 μg/m^3, which are similar to those produced by t-cigs. The impacts of e-cigs on indoor air quality are also similar to, if not greater than, other combustion-free nicotine delivery systems, such as waterpipe and "heat-not-burn" products (40, 41, 113). The $PM_{2.5}$ concentrations of 600 to 800 μg/m^3, as reported in vape shops and vaping conventions (97, 125), are about twice as high as those in hookah bars (148). In comparison, the $PM_{2.5}$ concentrations observed across a wide range of common indoor environments without e-cigs, such as homes, offices, schools, and daycare, are from 8 to 52 μg/m^3 (95).

In addition to $PM_{2.5}$, UFPs are also of great health concern (42) because they have a greater surface area per unit mass than do larger particles, so they can bind to more toxic chemicals (132). The indoor UFPs during e-cig use can increase up to 20 times over the baseline concentration (7.2×10^3 to 6.2×10^4 particles/cm^3; Figure 2b) (52) but are still lower than those from t-cigs (7×10^4 to 2.1×10^5 particles/cm^3) (40, 74, 113, 117) and other combustion-free nicotine delivery systems (7.7×10^3 to 3.2×10^5 particles/cm^3) (40, 41, 113). Similar to $PM_{2.5}$, indoor UFP concentrations during e-cig use are also higher than those across the wide range of common indoor environments without e-cigs (95).

As shown in Figure 2, studies on t-cig secondhand smoke have been conducted worldwide, but studies on e-cigs are mainly from North America and Europe. The current prevalence of e-cigs in other countries and regions is relatively low, but the e-cig market in many populous countries (e.g., China) is expanding rapidly (109). Thus, secondhand exposures to e-cig aerosols will likely become a potential public health problem in those countries soon. Detailed information on $PM_{2.5}$ and UFP levels, background concentrations, emission

protocol, room size, and air exchange rate for both e-cig and t-cig room studies is summarized in Supplemental Table 1.

Factors Affecting Indoor Particle Concentrations

In addition to particle concentrations, particle size distribution is also important to respiratory health because smaller particles (especially UFPs) generally penetrate deeper into the lung (54). E-cig particles are primarily in the submicron size range (42, 62), exhibiting a bimodal size distribution; one mode is located ~15–30 nm and the other is ~85–100 nm (119, 120, 146). Both particle concentration and particle size distribution are affected by emissions from the e-cig device, exhalation by the e-cig user, and indoor environmental factors, as illustrated in Figure 1 and discussed below.

E-cig emissions are affected by various intrinsic factors, including the e-cig device type, heating coil temperature, power voltage, and e-liquid compositions (7, 39, 42, 45, 68, 105, 122, 123, 147). E-cigs have evolved quickly over time from the cigalike, to the more advanced tank style with customizable voltage and e-liquids, to the recent pod-based vaping systems (47, 57, 87). The power voltage that determines the heating coil temperature has been associated with particle emissions (39, 45). The tank style, which allows a higher voltage, can produce more particles than the cigalike type (89). In addition, particle emissions from e-cigs are also influenced by the e-liquid compositions. The presence of nicotine (42) and higher PG/VG ratios tend to produce more particles (7). The recently introduced pod-based JUUL has not been well studied and raises even more health concerns owing to its high nicotine content in protonated salt and its popularity among adolescents (48, 87).

Variables related to the e-cig user, such as the puffing topography (i.e., flow rate, puff duration, and interpuff interval) and the process of inhalation and exhalation, also affect particle concentrations. In general, the particle concentration increases with higher puffing flow rates, longer puff durations, and shorter interpuff intervals (19, 45, 97, 147). E-cig particles tend to grow in human lungs under high humidity owing to the hygroscopic effect (106, 124). Other physiological factors in the respiratory system, such as lung capacity, air flow, and breath pattern, might also affect e-cig aerosol dynamics. Unfortunately, none of these factors have been studied, and the differences between the inhaled mainstream and the exhaled secondhand e-cig aerosols remain unknown.

Once released into the room air, e-cig particles are subject to aerosol dynamics under certain environmental conditions. In contrast to t-cig smoke, e-cig particles mainly consist of droplets that are more volatile because the e-liquid main ingredient, PG, has a relatively high saturation vapor pressure. E-cig particles have been observed to evaporate within seconds (146). At high particle number concentrations, coagulation is also an important particle-removal mechanism that reduces the number of particles but increases particle size (39, 91). In addition, e-cig particles can be removed from the room air by gravitational settling and surface deposition, leading to potential third-hand exposures, a concern that also warrants future study (51). Increasing dilution or air exchange rate may enhance particle evaporation and reduce particle concentrations and particle sizes (39, 62, 90, 97, 144). Similarly, increasing temperature or decreasing relative humidity may also enhance evaporation and

reduce particle size (119, 142). Because e-cig particles are markedly dynamic, their concentrations decay rapidly over distances (>1.5 m) from the source (i.e., e-cig users), especially for $PM_{2.5}$ mass concentration (97, 146). Understanding the dynamics of e-cig particles in an indoor environment is important because it can guide exposure assessment and mitigation strategies.

CHEMICAL COMPOSITIONS OF E-CIG AEROSOLS

The effects of e-cig aerosols on health are determined largely by their chemical compositions. The most commonly reported chemicals in both mainstream and secondhand e-cig aerosols are PG, VG, nicotine, carbonyls, aromatic volatile organic compounds (VOCs), trace metals, and tobacco-specific nitrosamines (TSNAs) (Figure 3; Supplemental Table 2). Many chemicals are present in both gas and particulate phases (119). The partition between gas and particulate phases affects the concentration and fate of e-cig-emitted chemicals and warrants future study.

As shown in Figure 3, the chemical profiles of the mainstream and secondhand e-cig aerosols are similar, but as expected, the concentrations of most chemicals in the secondhand aerosols are much lower than in the mainstream. Overall, the most abundant chemicals detected in the e-cig mainstream are PG and VG, followed by nicotine, carbonyls, aromatic VOCs, and trace metals. Most of the chemicals in the mainstream come from the major components of e-liquids: PG, VG, and nicotine. Although the FDA states that ingesting PG and VG in consumer and household products is safe, inhaling vaporized PG and VG at high concentrations may irritate the lungs (69), which is a unique health risk for e-cig aerosols (81, 84). The significant amount of nicotine reported in the e-cig aerosols also poses several health risks. Adolescents are particularly susceptible to nicotine's addictive effects (135). Existing evidence indicates that never-smoking youth who are exposed to nicotine through e-cigs are more likely to start smoking compared with naïve e-cig users (47). In addition, nicotine contributes to adverse health effects on the cardiocirculatory, respiratory, and gastrointestinal systems (11, 92).

Other observed chemicals such as formaldehyde, acetaldehyde, propanol, acrolein, acetone, and benzene are likely produced either by dehydration of PG/VG or by the reactions between PG and VG at high heating coil temperatures (99, 105, 112, 122). E-cig-related aldehydes might also come from flavoring additives in the e-liquid (68). Aldehydes are cytotoxic and can produce adverse respiratory effects (58). In addition, formaldehyde and acetaldehyde are classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1) and possibly carcinogenic to humans (Group 2B), respectively (58). Among the aromatic VOCs, the IARC lists benzene as a human carcinogen and toluene may be neurotoxic (58).

The likely sources of trace metals, especially those with relatively higher concentrations (i.e., chromium, aluminum, and copper), are the metal-coated wires of the heating coils (114, 141). Inhaling trace metals may irritate the respiratory system and impair respiration (141). Cadmium, lead, chromium, arsenic, and nickel are also classified as human carcinogens (61). Two studies found nicotine-derived nitrosamines in e-cig aerosols, such as

N′-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (49, 84), which are strong carcinogens that may cause lung and oral cancers (53). Whether these compounds are products of chemical reactions of nicotine or impurities in the e-liquid is not clear (29).

The concentrations of most chemicals in the e-cig mainstream aerosols are lower than those of t-cigs (Figure 3). The only exceptions are PG and VG, which are major components of e-liquid but are not used in t-cigs. Concentrations of trace metals in mainstream aerosols are similar in e-cigs and t-cigs. However, chromium, a carcinogenic and respiratory toxicant, is at higher concentrations in e-cigs, suggesting potential risks from chromium-coated wire in heating coils (141). The concentration of nicotine in e-cig mainstream aerosol is similar to or slightly lower than that in t-cig smoke. Of note, the nicotine content in a single JUUL pod is higher than that in 20 t-cigs and may lead to potential cytotoxicity and more significant addiction effects (102). The concentrations of carbonyls and aromatic VOCs are 10–1,000 times higher in the mainstream emissions of t-cigs than in e-cigs. Because these compounds are highly toxic, the observed lower concentrations indicate that e-cig aerosols are likely less toxic than t-cig smoke (16, 100).

In addition to the chemicals described above, e-cig aerosols contain a wide variety of VOCs at a much lower level, such as acetonitrile, isoprene, ethanol, diacetyl, and acetoin, which likely originate from the flavoring additives (3, 73, 79, 81). Even weaker evidence exists in the literature on the presence of polycyclic aromatic hydrocarbons, crotonaldehyde, acetol, glyoxal, glycidol, and benzaldehyde in e-cig aerosols.

HEALTH EFFECTS OF E-CIG AEROSOLS

The chemical profiles of mainstream and secondhand e-cig aerosols are similar (Figure 3), suggesting that the results of the studies on active e-cig use and secondhand exposures likely reflect the health effects of similar chemical mixtures at different doses. As previously reviewed, many studies have shown that e-cig aerosols are safer than t-cig smoke (100). However, substantial evidence indicates that e-cig aerosols are not safe to cells in vitro or animals in vivo. Results from in vitro studies have identified the biologic effects on various cell types, including airway epithelium and vascular endothelium (107, 130). Similarly, e-cig aerosols also impair lung functions in animals, with inflammation and immune abnormalities as the likely underlying mechanisms (107), and perturb the cardiovascular system (101, 110). E-cig aerosols also present marked carcinogenicity (78) and neurological toxicity (98) in animals, in addition to the observed respiratory and cardiovascular effects (22, 98). However, it remains controversial whether the dosages used in animal studies are relevant to human exposures and whether the results are consistent across different species.

The respiratory and cardiovascular effects of e-cig aerosols were also examined in human studies; most of these focused on the effects of active e-cig use, with only a few studies on secondhand exposures. As indicated by circulating concentrations of cotinine, doses in e-cig active exposure studies are usually higher than those in secondhand studies (Table 1). The results of these studies suggest likely short-term effects (≤2 h exposure) of e-cig aerosols on preclinical end points (Figure 1).

Respiratory Effects

Most human studies on the respiratory system examine the effects of short-term (≤1 h) exposure among a small number of healthy subjects (Table 1). Lung function is one of the most commonly studied end points, but the results of different studies are inconsistent. Active e-cig use by healthy t-cig smokers over 5 min slightly but significantly reduced lung function measures [i.e., forced expiratory volume in 1 s (FEV1) and forced expiratory flow (FEF) 25%] in a randomized crossover trial (34). However, similar effects were not observed in two crossover trials (one randomized and one nonrandomized), in which active e-cig use over 5 min or 30 min did not change any lung function measure among healthy t-cig smokers (37, 137). In another two crossover trials on secondhand e-cig aerosols (one randomized and one nonrandomized), neither 30-min nor 1-h exposures altered the lung function measures among healthy nonsmokers (37, 133). In contrast, more consistent results are reported for airway resistance, which was significantly increased after active e-cig use or passive exposure in two clinical trials, as determined by impulse oscillometry (133, 137). In addition, a case-control study found substantially altered respiratory proteomic profiles among e-cig users, indicative of impending airway obstruction (44). Nevertheless, the clinical importance of these early changes is not clear. Also unclear is whether increased airway resistance induced by e-cig exposures will worsen over time and eventually contribute to decreased lung function.

Studies have also assessed the short-term effects (≤2 h) of e-cig aerosols on exhaled nitric oxide, a biomarker of airway inflammation associated with increased risk of asthma and bronchitis (129). Three studies report no effect (6, 34, 37), and four studies show either increased (85, 118) or decreased exhaled nitric oxide concentrations after the exposures (133, 137). In two cross-sectional studies of adolescents, e-cig use was significantly associated with greater odds of asthma attacks [odds ratio (OR) = 1.12; 95% confidence interval (CI) (1.01–1.26)] (72) and chronic bronchitis symptoms [OR = 1.70; 95% CI (1.11–2.59)] (86). Likewise, passive exposures to e-cig aerosols were associated with asthma attacks in cross-sectional studies of adolescents with a history of asthma [OR = 1.27; 95% CI (1.11–1.47)] (10), suggesting potential adverse respiratory effects of secondhand exposures, at least among susceptible populations.

Cardiovascular Effects

Evidence of secondhand exposures to e-cig aerosols on cardiovascular effects in humans is limited. Nevertheless, the effects of active e-cig use on cardiovascular biomarkers have been frequently documented (Table 1). Both habitual and short-term e-cig use can cause a cardiac-autonomic imbalance, as indicated by heart rate variability. Nicotine has been suggested as a likely cause (93, 94). The existing evidence also suggests that active e-cig use induces systemic oxidative stress and inflammation and impairs endothelial function (6, 15, 17, 94). Although oxidative stress and inflammation are important in the pathogenesis of cardiovascular diseases, to what extent the observed cardiovascular effects of e-cigs are clinically relevant is unclear. The cross-sectional National Health Interview Surveys of 2014 (n = 37,000) and 2016 (n = 33,000) found that daily e-cig use was associated with myocardial infarction [OR = 1.79; 95% CI (1.20 to 2.66)] (4), but more evidence is needed,

especially from long-term, large-cohort studies, before e-cigs can be causally linked with confidence to cardiovascular diseases.

CONCLUSIONS AND FUTURE PERSPECTIVES

The evidence in the literature confirms that e-cigs degrade indoor air quality and that bystanders are at risk of secondhand exposure. Indoor particle concentrations attributed to e-cigs are similar to those attributed to t-cigs. Although studies of secondhand e-cig aerosols are limited, their chemical composition profiles are similar to those of mainstream e-cig aerosols but have much lower concentrations. E-cigs generate fewer carcinogenic and toxic compounds than do t-cigs, but they still produce substantial amounts of PG, VG, and nicotine, as well as some toxic compounds such as aldehydes and heavy metals. Current health effect studies in humans focus on the acute effects and early biomarkers. These studies have suggested potential respiratory and cardiovascular effects from e-cig aerosols. However, results from these studies are inconsistent, leading to a call for large-cohort and long-term exposure studies that examine the linkage between e-cigs and clinical end points.

Although the effects of e-cigs on human health are not yet fully understood, the high levels of indoor air pollutants produced by e-cigs call for precautionary measures to protect public health. As of October 2016, 32 countries had banned e-cigs from public spaces (67). In the United States, as of July 1, 2019, 18 states and 861 municipalities have already expanded smoke-free laws to include e-cigs and have prohibited their use in smoke-free places (5). In certain places, such as casinos, bars, and other gaming venues where t-cigs are allowed, e-cig use can even worsen indoor air quality. Until the long-term health effects are fully established, we recommend restricting the use of e-cigs in public indoor spaces to protect bystanders from secondhand exposures.

Given the uncertainties of the chemical products of the heating process and the complexity of flavoring additives, the e-cig design features and e-liquid compositions should be further studied to better understand their effects on e-cig aerosol toxicity as the scientific basis for future regulations. Indoor air pollution due to e-cigs could potentially be reduced by enhancing ventilation and air filtration. Unfortunately, studies on mitigation measures that may inform policy are still limited. Future studies also need to focus on identifying vulnerable populations and monitoring places that may contribute to high levels of secondhand exposures, such as vape shops (102), vaping conventions (125), and other indoor environments with no restrictions on e-cig use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This work was supported by the Tobacco-Related Disease Research Program (TRDRP) (26IR-0002 and 23XT-0001) and the National Heart, Lung, and Blood Institute (1R01HL139379-01A1).

LITERATURE CITED

1. Acevedo-Bolton V, Ott WR, Cheng KC, Jiang RT, Klepeis NE, Hildemann LM. 2014 Controlled experiments measuring personal exposure to PM2.5 in close proximity to cigarette smoking. Indoor Air 24:199–212 [PubMed: 23808850]
2. Adroit Mark. Res. 2018 Global e-cigarette market size 2017 by type (disposable, rechargeable, modular), by region and forecast 2018 to 2025 Rep., AdroitMark. Res., Dallas, TX https://www.adroitmarketresearch.com/industry-reports/e-cigarette-market
3. Allen JG, Flanigan SS, LeBlanc M, Vallarino J, MacNaughton P, et al. 2016 Flavoring chemicals in e-cigarettes: diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. Environ. Health Perspect 124:733–39 [PubMed: 26642857]
4. Alzahrani T, Pena I, Temesgen N, Glantz SA. 2018 Association between electronic cigarette use and myocardial infarction. Am. J. Prev. Med 55:455–61 [PubMed: 30166079]
5. ANRF (Am. Nonsmok. Rights Found.). 2019 Electronic smoking devices and secondhand aerosol Rep. 1810 [FS-39], ANRF, Berkeley, CA https://no-smoke.org/wp-content/uploads/pdf/electronic-smoking-devices-secondhand-aerosol.pdf
6. Antoniewicz L, Bosson JA, Kuhl J, Abdel-Halim SM, Kiessling A, et al. 2016 Electronic cigarettes increase endothelial progenitor cells in the blood of healthy volunteers. Atherosclerosis 255:179–85 [PubMed: 27693003]
7. Baassiri M, Talih S, Salman R, Karaoghlanian N, Saleh R, et al. 2017 Clouds and “throat hit”: effects of liquid composition on nicotine emissions and physical characteristics of electronic cigarette aerosols. Aerosol Sci. Technol 51:1231–39
8. Ballbè M, Martinez-Sánchez JM, Sureda X, Fu M, Perez-Ortuno R, et al. 2014 Cigarettes versus e-cigarettes: passive exposure at home measured by means of airborne marker and biomarkers. Environ. Res 135:76–80 [PubMed: 25262078]
9. Bauld L, MacKintosh AM, Eastwood B, Ford A,Moore G, et al. 2017 Young people’s use of e-cigarettes across the United Kingdom: findings from five surveys 2015–2017. Int. J. Environ. Res. Public Health 14:E973 [PubMed: 28850065]
10. Bayly JE, Bernat D, Porter L, Choi K. 2019 Secondhand exposure to aerosols from electronic nicotine delivery systems and asthma exacerbations among youth with asthma. Chest 155:88–93 [PubMed: 30359612]
11. Benowitz NL, Burbank AD. 2016 Cardiovascular toxicity of nicotine: implications for electronic cigarette use. Trends Cardiovasc. Med 26:515–23 [PubMed: 27079891]
12. Breland A, Soule E, Lopez A, Ramôa C, El-Hellani A, Eissenberg T. 2017 Electronic cigarettes: What are they and what do they do? Ann. N. Y. Acad. Sci 1394:5–30 [PubMed: 26774031]
13. Buettner-Schmidt K, Lobo ML, Travers MJ, Boursaw B. 2015 Tobacco smoke exposure and impact of smoking legislation on rural and non-rural hospitality venues in North Dakota. Res. Nurs. Health 38:268–77 [PubMed: 25962373]
14. Burnett RT, Pope CA 3rd, Ezzati M, Olives C, Lim SS, et al. 2014 An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. Environ. Health Perspect 122:397–403 [PubMed: 24518036]
15. Carnevale R, Sciarretta S, Violi F, Nocella C, Loffredo L, et al. 2016 Acute impact of tobacco versus electronic cigarette smoking on oxidative stress and vascular function. Chest 150:606–12 [PubMed: 27108682]
16. Cervellati F, Muresan XM, Sticozzi C, Gambari R, Montagner G, et al. 2014 Comparative effects between electronic and cigarette smoke in human keratinocytes and epithelial lung cells. Toxicol. In Vitro 28:999–1005 [PubMed: 24809892]
17. Chatterjee S, Tao J-Q,Johncola A, Guo W, Caporale A, et al. 2019 Acute exposure to e-cigarettes causes inflammation and pulmonary endothelial oxidative stress in nonsmoking, healthy young subjects. Am. J. Physiol. Lung Cell. Mol. Physiol 317:L155–66 [PubMed: 31042077]
18. Chen R, Aherrera A, Isichei C, Olmedo P, Jarmul S, et al. 2017 Assessment of indoor air quality at an electronic cigarette (vaping) convention. J. Expo. Sci. Environ. Epidemiol 28:522–29 [PubMed: 29288255]

19. Chen WH, Wang P, Ito K, Fowles J, Shusterman D,et al. 2018Measurement of heating coil temperature for e-cigarettes with a “top-coil” clearomizer. PLOS ONE 13:e0195925 [PubMed: 29672571]
20. Chen-Sankey JC, Kong G, Choi K. 2019 Perceived ease of flavored e-cigarette use and e-cigarette use progression among youth never tobacco users. PLOS ONE 14:e0212353 [PubMed: 30811486]
21. Counts ME, Morton MJ, Laffoon SW, Cox RH, Lipowicz PJ. 2005 Smoke composition and predicting relationships for international commercial cigarettes smoked with three machine-smoking conditions. Regul. Toxicol. Pharmacol 41:185–227 [PubMed: 15748796]
22. Crotty Alexander LE, Drummond CA, Hepokoski M, Mathew D, Moshensky A, et al. 2018 Chronic inhalation of e-cigarette vapor containing nicotine disrupts airway barrier function and induces systemic inflammation and multiorgan fibrosis in mice. Am. J. Physiol. Regul. Integr. Comp. Physiol 314:R834–47 [PubMed: 29384700]
23. Cullen KA,Ambrose BK, Gentzke AS,Apelberg BJ,Jamal A,King BA. 2018 Use of electronic cigarettes and any tobacco product among middle and high school students—United States, 2011–2018. MMWR 67:1276–77 [PubMed: 30439875]
24. Czogala J, Goniewicz ML, Fidelus B, Zielinska-Danch W, Travers MJ, Sobczak A. 2014 Secondhand exposure to vapors from electronic cigarettes. Nicotine Tob. Res 16:655–62 [PubMed: 24336346]
25. Dai J, Kim K-H, Szulejko JE,Jo S-H. 2017A simple method for the parallel quantification of nicotine and major solvent components in electronic cigarette liquids andvaped aerosols. Microchem. J 133:237–45
26. Dicpinigaitis PV, Chang AL, Dicpinigaitis AJ, Negassa A. 2016 Effect of e-cigarette use on cough reflex sensitivity. Chest 149:161–65 [PubMed: 26291648]
27. Drehmer JE, Nabi-Burza E, Walters BH, Ossip DJ, Levy DE, et al. 2019 Parental smoking and e-cigarette use in homes and cars. Pediatrics 143:e20183249 [PubMed: 30858346]
28. El-Hellani A, Salman R, El-Hage R, Talih S, Malek N, et al. 2018 Nicotine and carbonyl emissions from popular electronic cigarette products: correlation to liquid composition and design characteristics. Nicotine Tob. Res 20:215–23 [PubMed: 27798087]
29. Farsalinos KE, Gillman G, Poulas K, Voudris V. 2015 Tobacco-specific nitrosamines in electronic cigarettes: comparison between liquid and aerosol levels. Int. J. Environ. Res. Public Health 12:9046–53 [PubMed: 26264016]
30. Farsalinos KE, Kistler KA, Pennington A, Spyrou A, Kouretas D, Gillman G. 2018 Aldehyde levels in e-cigarette aerosol: findings from a replication study and from use of a new-generation device. Food Chem. Toxicol 111:64–70 [PubMed: 29109042]
31. Farsalinos KE, Voudris V, Spyrou A, Poulas K. 2017 E-cigarettes emit very high formaldehyde levels only in conditions that are aversive to users: a replication study under verified realistic use conditions. Food Chem. Toxicol 109:90–94 [PubMed: 28864295]
32. Farsalinos KE, Yannovits N, Sarri T, Voudris V, Poulas K. 2018 Nicotine delivery to the aerosol of a heat-not-burn tobacco product: comparison with a tobacco cigarette and e-cigarettes. Nicotine Tob. Res 20:1004–9 [PubMed: 28637344]
33. Farsalinos KE, Yannovits N, Sarri T, Voudris V, Poulas K, Leischow SJ. 2018 Carbonyl emissions from a novel heated tobacco product (IQOS): comparison with an e-cigarette and a tobacco cigarette. Addiction 113:2099–106 [PubMed: 29920842]
34. Ferrari M, Zanasi A, Nardi E, Morselli Labate AM, Ceriana P, et al. 2015 Short-term effects of a nicotine-free e-cigarette compared to a traditional cigarette in smokers and non-smokers. BMC Pulm. Med 15:120 [PubMed: 26459355]
35. Flora JW,Meruva N,Huang CB,Wilkinson CT, Ballentine R, et al.2016 Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. Regul. Toxicol. Pharmacol 74:1–11 [PubMed: 26617410]
36. Flora JW, Wilkinson CT, Wilkinson JW, Lipowicz PJ, Skapars JA, et al. 2017 Method for the determination of carbonyl compounds in e-cigarette aerosols. J. Chromatogr. Sci 55:142–48 [PubMed: 28087758]

37. Flouris AD, Chorti MS, Poulianiti KP,Jamurtas AZ, Kostikas K, et al. 2013Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. Inhal. Toxicol 25:91–101 [PubMed: 23363041]
38. Flouris AD, Poulianiti KP, Chorti MS,Jamurtas AZ, Kouretas D, et al. 2012 Acute effects of electronic and tobacco cigarette smoking on complete blood count. Food Chem. Toxicol 50:3600–3 [PubMed: 22858449]
39. Floyd EL, Queimado L, Wang J, Regens JL, Johnson DL. 2018 Electronic cigarette power affects count concentration and particle size distribution of vaping aerosol. PLOS ONE 13:e0210147 [PubMed: 30596800]
40. Forster M, McAughey J, Prasad K, Mavropoulou E, Proctor C. 2018 Assessment of tobacco heating product THP1.0. Part 4: characterisation of indoor air quality and odour. Regul. Toxicol. Pharmacol 93:34–51 [PubMed: 28989082]
41. Fromme H, Dietrich S, Heitmann D, Dressel H, DiemerJ, et al. 2009 Indoor air contamination during a waterpipe (narghile) smoking session. Food Chem. Toxicol 47:1636–41 [PubMed: 19394392]
42. Fuoco FC, Buonanno G, Stabile L, Vigo P. 2014 Influential parameters on particle concentration and size distribution in the mainstream of e-cigarettes. Environ. Pollut 184:523–29 [PubMed: 24172659]
43. Geiss O, Bianchi I, Barahona F, Barrero-Moreno J. 2015 Characterisation of mainstream and passive vapours emitted by selected electronic cigarettes. Int. J. Hyg. Environ. Health 218:169–80 [PubMed: 25455424]
44. Ghosh A, Coakley RC, Mascenik T, Rowell TR, Davis ES, et al. 2018 Chronic e-cigarette exposure alters the human bronchial epithelial proteome. Am. J. Respir. Crit. Care Med 198:67–76 [PubMed: 29481290]
45. Gillman IG, Kistler KA, Stewart EW, Paolantonio AR. 2016 Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. Regul. Toxicol. Pharmacol 75:58–65 [PubMed: 26743740]
46. Giovenco DP, Lewis MJ, Delnevo CD. 2014 Factors associated with e-cigarette use: a national population survey of current and former smokers. Am. J. Prev. Med 47:476–80 [PubMed: 24880986]
47. Glantz SA, Bareham DW. 2018 E-cigarettes: use, effects on smoking, risks, and policy implications. Annu. Rev. Public Health 39:215–35 [PubMed: 29323609]
48. Goniewicz ML, Boykan R, Messina CR, Eliscu A, Tolentino J. 2018 High exposure to nicotine among adolescents who use Juul and other vape pod systems (‘pods’). Tob. Control 10.1136/tobaccocontrol-2018-054565
49. Goniewicz ML, Knysak J, Gawron M, Kosmider L, Sobczak A, et al. 2014 Levels ofselected carcinogens and toxicants in vapour from electronic cigarettes. Tob. Control 23:133–39 [PubMed: 23467656]
50. Goniewicz ML, Kuma T, Gawron M, Knysak J, Kosmider L. 2013 Nicotine levels in electronic cigarettes. Nicotine Tob. Res 15:158–66 [PubMed: 22529223]
51. Goniewicz ML, Lee L. 2015 Electronic cigarettes are a source of thirdhand exposure to nicotine. Nicotine Tob. Res 17:256–58 [PubMed: 25173774]
52. Guo H,Morawska L, He CR, Zhang YLL, Ayoko G, Cao M. 2010 Characterization ofparticle number concentrations and PM2.5 in a school: influence of outdoor air pollution on indoor air. Environ. Sci. Pollut. Res. Int 17:1268–78 [PubMed: 20195908]
53. Hecht SS, Stepanov I, Carmella SG. 2016 Exposure and metabolic activationbiomarkers ofcarcinogenic tobacco-specific nitrosamines. Acc. Chem. Res 49:106–14 [PubMed: 26678241]
54. Hinds WC. 1999 Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles. Hoboken, NJ: Wiley
55. Holcomb LC. 1993 Indoor air quality and environmental tobacco smoke: concentration and exposure. Environ. Int 19:9–40
56. Höllbacher E, Ters T, Rieder-Gradinger C, Srebotnik E. 2017 Emissions of indoor air pollutants from six user scenarios in a model room. Atmos. Environ 150:389–94

57. Huang J, Duan Z, Kwok J, Binns S, Vera L, et al. 2019 Vaping versus JUULing: how the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market. Tob. Control 28:146–51 [PubMed: 29853561]
58. Huang SJ, Xu YM, Lau ATY. 2018 Electronic cigarette: a recent update of its toxic effects on humans. J. Cell. Physiol 233:4466–78 [PubMed: 29215738]
59. IARC (Int. Agency Res. Cancer). 1986 Tobacco Smoking IARC Monogr. Eval. Carcinog. Risks Hum Lyon, Fr.: IARC
60. IARC (Int. Agency Res. Cancer). 2004 Tobacco Smoke and Involuntary Smoking IARC Monogr. Eval. Carcinog. Risks Hum Lyon, Fr.: IARC
61. IARC (Int. Agency Res. Cancer). 2019 Agents classified by the IARC monographs, volumes 1–123 IARC Monographs on the Identification of Carcinogenic Hazards to Humans, World Health Organization, Geneva, updated July 8 https://monographs.iarc.fr/agents-classified-by-the-iarc/
62. Ingebrethsen BJ, Cole SK, Alderman SL. 2012 Electronic cigarette aerosol particle size distribution measurements. Inhal. Toxicol 24:976–84 [PubMed: 23216158]
63. IOM (Inst. Med.). 2010 Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence. Washington, DC: Natl. Acad. Press
64. Jenkins PL, Phillips TJ, Mulberg EJ, Hui SP. 1992 Activity patterns of Californians—use of and proximity to indoor pollutant sources. Atmos. Environ. Part A 26:2141–48
65. Jensen RP, Luo WT, Pankow JF, Strongin RM, Peyton DH. 2015 Hidden formaldehyde in e-cigarette aerosols. N. Engl. J. Med 372:392–94 [PubMed: 25607446]
66. Johnson JM, Naeher LP, Yu XZ, Rathbun SL, Muilenburg JL, Wang JS. 2018 Air monitoring at large public electronic cigarette events. Int. J. Hyg. Environ. Health 221:541–47 [PubMed: 29477829]
67. Kennedy RD, Awopegba A, De León E, Cohen JE. 2017 Global approaches to regulating electronic cigarettes. Tob. Control 26:440–45 [PubMed: 27903958]
68. Khlystov A, Samburova V. 2016 Flavoring compounds dominate toxic aldehyde production during e-cigarette vaping. Environ. Sci. Technol 50:13080–85 [PubMed: 27934275]
69. Kienhuis AS, Soeteman-Hernandez LG, Bos PMJ, Cremers H, Klerx WN, Talhout R. 2015 Potential harmful health effects of inhaling nicotine-free shisha-pen vapor: a chemical risk assessment of the main components propylene glycol and glycerol. Tob. Induc. Dis 13:15 [PubMed: 26120296]
70. Kim J, Ban H, Hwang Y, Ha K, Lee K. 2016b Impact of partial and comprehensive smoke-free regulations on indoor air quality in bars. Int. J. Environ. Res. Public Health 13:E754 [PubMed: 27472349]
71. Kim J, Lee K, Kwon HJ, Lee DH, Kim K. 2016a Association between secondhand smoke in hospitality venues and urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol concentrations in non-smoking staff. Int. J. Environ. Res. Public Health 13:E1101 [PubMed: 27834821]
72. Kim SY, Sim S, Choi HG. 2017 Active, passive, and electronic cigarette smoking is associated with asthma in adolescents. Sci. Rep 7:17789 [PubMed: 29259221]
73. Klager S, Vallarino J, MacNaughton P, Christian DC, Lu Q, Allen JG. 2017 Flavoring chemicals and aldehydes in e-cigarette emissions. Environ. Sci. Technol 51:10806–13 [PubMed: 28817267]
74. Konstantopoulou SS, Behrakis PK, Lazaris AC, Nicolopoulou-Stamati P. 2014 Indoor air quality in a bar/restaurant before and after the smoking ban in Athens, Greece. Sci. Total Environ 476:136–43 [PubMed: 24463032]
75. Kosmider L, Kimber CF, Kurek J, Corcoran O, Dawkins LE. 2018 Compensatory puffing with lower nicotine concentration e-liquids increases carbonyl exposure in e-cigarette aerosols. Nicotine Tob. Res. 20:998–1003 [PubMed: 29065196]
76. Kosmider L, Sobczak A, Fik M, Knysak J, Zaciera M, et al. 2014 Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. Nicotine Tob. Res 16:1319–26 [PubMed: 24832759]
77. Kungskulniti N, Charoenca N, Peesing J,Trangwatana S, Hamann S, et al. 2015 Assessment of secondhand smoke in international airports in Thailand, 2013. Tob. Control 24:532–35 [PubMed: 24638967]

78. Lee H-W, Park S-H, Weng M-W, Wang H-T, Huang WC, et al. 2018 E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells. PNAS 115:E1560–69 [PubMed: 29378943]

79. Lee MS, LeBouf RF, Son YS, Koutrakis P, Christiani DC. 2017 Nicotine, aerosol particles, carbonyls and volatile organic compounds in tobacco- and menthol-flavored e-cigarettes. Environ. Health 16:42 [PubMed: 28449666]

80. Lerner CA, Sundar IK, Watson RM, Elder A, Jones R, et al. 2015 Environmental health hazards of e-cigarettes and their components: oxidants and copper in e-cigarette aerosols. Environ. Pollut 198:100–7 [PubMed: 25577651]

81. Liu JM, Liang QW, Oldham MJ, Rostami AA, Wagner KA, et al. 2017 Determination of selected chemical levels in room air and on surfaces after the use of cartridge- and tank-based e-vapor products or conventional cigarettes. Int. J. Environ. Res. Public Health 14:E969 [PubMed: 28846634]

82. Liu R,Jiang Y, Li Q, Hammond SK. 2014 Assessing exposure to secondhand smoke in restaurants and bars 2 years after the smoking regulations in Beijing China., Indoor Air 24:339–49 [PubMed: 24387295]

83. Loffredo CA,Tang Y,Momen M,Makambi K, Radwan GN,About-Foutoh A. 2016 PM2.5 as a marker of exposure to tobacco smoke and other sources ofparticulate matter in Cairo, Egypt. Int. J. Tuberc. Lung Dis 20:417–22 [PubMed: 27046726]

84. Margham J,McAdam K, Forster M,Liu C,Wright C, et al. 2016 Chemical composition of aerosol from an e-cigarette: a quantitative comparison with cigarette smoke. Chem. Res. Toxicol 29:1662–78 [PubMed: 27641760]

85. Marini S, Buonanno G, Stabile L, Ficco G. 2014 Short-term effects of electronic and tobacco cigarettes on exhaled nitric oxide. Toxicol. Appl. Pharmacol 278:9–15 [PubMed: 24732441]

86. McConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, et al. 2017 Electronic cigarette use and respiratory symptoms in adolescents. Am. J. Respir. Crit. Care Med 195:1043–49 [PubMed: 27806211]

87. McKelvey K, Baiocchi M, Halpern-Felsher B.2018 Adolescents' and young adults' use and perceptions of pod-based electronic cigarettes. JAMA Netw. Open 1:e183535 [PubMed: 30646249]

88. McMillen RC, Gottlieb MA, Shaefer RMW,Winickoff JP, Klein JD. 2015 Trends in electronic cigarette use among U.S. adults: Use is increasing in both smokers and nonsmokers. Nicotine Tob. Res 17:1195–202 [PubMed: 25381306]

89. Melstrom P, Koszowski B,Thanner MH, Hoh E, King B, et al. 2017Measuring PM2.5, ultrafine particles, nicotine air and wipe samples following the use of electronic cigarettes. Nicotine Tob. Res 19:1055–61 [PubMed: 28340080]

90. Meng Q, Son Y, Kipen H, Laskin D, Schwander S, Delnevo C. 2017 Particles released from primary e-cigarette vaping: particle size distribution and particle deposition in the human respiratory tract. Am. J. Respir. Crit. Care Med 195:A1023

91. Mikheev VB, Brinkman MC, Granville CA, Gordon SM, Clark PI. 2016 Real-time measurement of electronic cigarette aerosol size distribution and metals content analysis. Nicotine Tob. Res 18:1895–902 [PubMed: 27146638]

92. Mishra A, Chaturvedi P, Datta S, Sinukumar S,Joshi P, Garg A. 2015 Harmful effects of nicotine. Indian J. Med. Paediatr. Oncol 36:24–31 [PubMed: 25810571]

93. Moheimani RS, Bhetraratana M, Peters KM, Yang BK, Yin F, et al. 2017 Sympathomimetic effects of acute e-cigarette use: role of nicotine and non-nicotine constituents. J. Am. Heart Assoc 6:e006579 [PubMed: 28931527]

94. Moheimani RS, Bhetraratana M, Yin F, Peters KM, Gornbein J, et al. 2017 Increased cardiac sympathetic activity and oxidative stress in habitual electronic cigarette users: implications for cardiovascular risk. JAMA Cardiol. 2:278–84 [PubMed: 28146259]

95. Morawska L, Ayoko GA, Bae GN, Buonanno G, Chao CYH, et al. 2017 Airborne particles in indoor environment of homes, schools, offices and aged care facilities: the main routes of exposure. Environ. Int 108:75–83 [PubMed: 28802170]

96. Movsisyan NK, Petrosyan V,Harutyunyan A, Petrosyan D, Stillman F. 2014 Clearingthe air: improving smoke-free policy compliance at the national oncology hospital in Armenia. BMC Cancer 14:943 [PubMed: 25495431]

97. Nguyen C, Li L, Sen CA, Ronquillo E, Zhu Y. 2019 Fine and ultrafine particles concentrations in vape shops. Atmos. Environ 211:159–69

98. Nguyen T, Li GE, Chen H, Cranfield CG, McGrath KC, Gorrie CA. 2018 Maternal e-cigarette exposure results in cognitive and epigenetic alterations in offspring in a mouse model. Chem. Res. Toxicol 31:601–11 [PubMed: 29863869]

99. Ogunwale MA, Li MX, Raju MVR, Chen YZ, Nantz MH, et al. 2017 Aldehyde detection in electronic cigarette aerosols. ACS Omega 2:1207–14 [PubMed: 28393137]

100. Oh AY, Kacker A. 2014 Do electronic cigarettes impart a lower potential disease burden than conventional tobacco cigarettes?: Review on e-cigarette vapor versus tobacco smoke. Laryngoscope 124:2702–6 [PubMed: 25302452]

101. Olfert IM, DeVallance E, Hoskinson H, Branyan KW, Clayton S, et al. 2018 Chronic exposure to electronic cigarettes results in impaired cardiovascular function in mice. J. Appl. Physiol 124:573–82 [PubMed: 29097631]

102. Omaiye EE, McWhirter KJ, Luo W, Pankow JF, Talbot P. 2019 High-nicotine electronic cigarette products: toxicity ofJUUL fluids and aerosols correlates strongly with nicotine and some flavor chemical concentrations. Chem. Res. Toxicol 32:1058–69 [PubMed: 30896936]

103. Pagano T, DiFrancesco AG, Smith SB, George J,Wink G, et al.2016 Determination ofnicotine content and delivery in disposable electronic cigarettes available in the United States by gas chromatography-mass spectrometry. Nicotine Tob. Res 18:700–7 [PubMed: 26045251]

104. Palazzolo DL, Crow AP, Nelson JM,Johnson RA. 2017 Trace metals derived from electronic cigarette (ECIG) generated aerosol: potential problem of ECIG devices that contain nickel. Front. Physiol 7:663 [PubMed: 28119618]

105. Pankow JF, Kim K, McWhirter KJ, Luo W, Escobedo JO, et al. 2017 Benzene formation in electronic cigarettes. PLOS ONE 12:e0173055 [PubMed: 28273096]

106. Pichelstorfer L, Hofmann W, Winkler-Heil R, Yurteri CU, McAughey J. 2016 Simulation of aerosol dynamics and deposition of combustible and electronic cigarette aerosols in the human respiratory tract. J. Aerosol Sci 99:125–32

107. Dinakar C, O'Connor GT. 2016 The health effects of electronic cigarettes. N. Engl. J. Med 375:2608

108. Poulianiti K, Karatzaferi C, Flouris AD,Fatouros IG, Koutedakis Y,Jamurtas AZ. 2016 Antioxidant responses following active and passive smoking of tobacco and electronic cigarettes. Toxicol. Mech. Methods 26:455–61 [PubMed: 27464467]

109. Prescient Strateg. Intell. 2018 E-cigarette market by product—global size, share, development, growth, and demand forecast, 2013–2023. Rep. 4655423, Prescient Strateg. Intell., East Delhi, India

110. Qasim H, Karim ZA, Silva-Espinoza JC, Khasawneh FT, Rivera JO, et al. 2018 Short-term e-cigarette exposure increases the risk of thrombogenesis and enhances platelet function in mice. J. Am. Heart Assoc 7:e009264 [PubMed: 30021806]

111. Qu Y, Kim KH, Szulejko JE. 2018 The effect of flavor content in e-liquids on e-cigarette emissions of carbonyl compounds. Environ. Res 166:324–33 [PubMed: 29909173]

112. Qu Y, Szulejko JE, Kim K-H,Jo S-H. 2019 The effect of varying battery voltage output on the emission rate of carbonyls released from e-cigarette smoke. Microchem. J 145:47–54

113. Ruprecht AA, DeMarco C, Saffari A, Pozzi P,Mazza R, et al. 2017 Environmental pollution and emission factors of electronic cigarettes, heat-not-burn tobacco products, and conventional cigarettes. Aerosol Sci. Technol 51:674–84

114. Saffari A, Daher N, Ruprecht A, De Marco C, Pozzi P, et al. 2014 Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: comparison of emission rates and secondhand exposure. Environ. Sci. Process. Impacts 16:2259–67 [PubMed: 25180481]

115. Salamanca JC,Meehan-Atrash J,Vreeke S, Escobedo JO, Peyton DH, Strongin RM. 2018 E-cigarettes can emit formaldehyde at high levels under conditions that have been reported to be non-averse to users. Sci. Rep 8:7559 [PubMed: 29765089]

116. Samburova V, Bhattarai C, Strickland M, Darrow L, Angermann J, et al. 2018 Aldehydes in exhaled breath during e-cigarette vaping: pilot study results. Toxics 6:E46 [PubMed: 30087275]
117. Scheitel M, Stanic M, Neuberger M. 2016 PM_{10}, $PM_{2.5}$, PM_1, number and surface of particles at the child's seat when smoking a cigarette in a car. AIMS Environ. Sci 3:582–91
118. Schober W, Szendrei K, Matzen W, Osiander-Fuchs H, Heitmann D, et al. 2014 Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers. Int. J. Hyg. Environ. Health 217:628–37 [PubMed: 24373737]
119. Schripp T, Markewitz D, Uhde E, Salthammer T. 2013 Does e-cigarette consumption cause passive vaping? Indoor Air 23:25–31 [PubMed: 22672560]
120. Scungio M, Stabile L, Buonanno G. 2018 Measurements of electronic cigarette-generated particles for the evaluation of lung cancer risk of active and passive users. J. Aerosol Sci 115:1–11
121. Shamo F, Wilson T, Kiley J, Repace J. 2015 Assessing the effect of Michigan's smoke-free law on air quality inside restaurants and casinos: a before-and-after observational study. BMJ Open 5:e007530
122. Sleiman M, Logue JM, Montesinos VN, Russell ML, Litter MI, et al. 2016 Emissions from electronic cigarettes: key parameters affecting the release of harmful chemicals. Environ. Sci. Technol 50:9644–51 [PubMed: 27461870]
123. Son Y,Wackowski O,Weisel C, Schwander S,Mainelis G, et al. 2018 Evaluation of e-vapor nicotine and nicotyrine concentrations under various e-liquid compositions, device settings, and vaping topographies. Chem. Res. Toxicol 31:861–68 [PubMed: 30080399]
124. Sosnowski TR, Kramek-Romanowska K. 2016 Predicted deposition of e-cigarette aerosol in the human lungs. J. Aerosol Med. Pulm. Drug Deliv 29:299–309 [PubMed: 26907696]
125. Soule EK,Maloney SF, Spindle TR, Rudy AK,Hiler MM, Cobb CO. 2017 Electronic cigarette use and indoor air quality in a natural setting. Tob. Control 26:109–12 [PubMed: 26880745]
126. Stohs SJ, Bagchi D, Bagchi M. 1997 Toxicityoftrace elements in tobacco smoke. Inhal. Toxicol 9:867–90
127. Talih S, Balhas Z, Salman R, El-Hage R, Karaoghlanian N, et al. 2017 Transport phenomena governing nicotine emissions from electronic cigarettes: model formulation and experimental investigation. Aerosol Sci. Technol 51:1–11 [PubMed: 28706340]
128. Talih S, Balhas Z, Salman R, Karaoghlanian N, Shihadeh A.2016 "Direct dripping": a high-temperature, high-formaldehyde emission electronic cigarette use method. Nicotine Tob. Res 18:453–59 [PubMed: 25863521]
129. Taylor DR, Pijnenburg MW, Smith AD, DeJongste JC. 2006 Exhalednitric oxide measurements: clinical application and interpretation. Thorax 61:817–27 [PubMed: 16936238]
130. Taylor M,Jaunky T, Hewitt K, Breheny D, Lowe F,et al.2017A comparative assessment of e-cigarette aerosols and cigarette smoke on in vitro endothelial cell migration. Toxicol. Lett 277:123–28 [PubMed: 28658606]
131. Tayyarah R,Long GA. 2014 Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air. Regul. Toxicol. Pharmacol 70:704–10 [PubMed: 25444997]
132. Terzano C, Di Stefano F, Conti V, Graziani E, Petroianni A. 2010 Air pollution ultrafine particles: toxicity beyond the lung. Eur. Rev. Med. Pharmacol. Sci 14:809–21 [PubMed: 21222367]
133. Tzortzi A, Teloniatis S, Matiampa G, Bakellas G, Vyzikidou VK, et al. 2018 Passive exposure to e-cigarette emissions: minor respiratory effects. Tob. Prev. Cessation 4:A78
134. US DHHS (Dep. Health Hum. Serv.). 2006 The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report to the Surgeon General Atlanta, GA: U.S. Dep. Health Hum. Serv., Cent. Dis. Control Prev., Coord. Cent. Health Promot., Natl. Cent. Chronic Dis. Prev. Health Promot., Off. Smok. Health
135. US DHHS (Dep. Health Hum. Serv.). 2014 The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General Atlanta, GA: U.S. Dep. Health Hum. Serv., Cent. Dis. Control Prev., Coord. Cent. Health Promot., Natl. Cent. Chronic Dis. Prev. Health Promot., Off. Smok. Health

136. US DHHS (Dep. Health Hum. Serv.), FDA (Food Drug Adm.). 2016 Deeming tobacco products to be subject to the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act; restrictions on the sale and distribution of tobacco products and required warning statements for tobacco products. Fed. Regist 81(90):28973–9106 [PubMed: 27192730]

137. Vardavas CI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PK. 2012 Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. Chest 141:1400–6 [PubMed: 22194587]

138. Volesky KD, Maki A, Scherf C, Watson L, Van Ryswyk K, et al. 2018 The influence of three e-cigarette models on indoor fine and ultrafine particulate matter concentrations under real-world conditions. Environ. Pollut 243:882–89 [PubMed: 30245450]

139. Wang TW,Marynak KL,Agaku IT, King BA. 2017 Secondhand exposure to electronic cigarette aerosol among US youths. JAMA Pediatr. 171:490–92 [PubMed: 28319226]

140. WHO (World Health Organ.). 2006 Air Quality Guidelines for Particulate Matter, Ozone, Nitrogen Dioxide and Sulfur Dioxide: Global Update for 2005. Geneva: WHO

141. Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P. 2013 Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. PLOS ONE 8:e57987 [PubMed: 23526962]

142. Wright TP, Song C, Sears S, Petters MD. 2016 Thermodynamic and kinetic behavior of glycerol aerosol. Aerosol Sci. Technol 50:1385–96

143. Zhang YP, Sumner W, Chen DR. 2013Invitro particle size distributions in electronic and conventional cigarette aerosols suggest comparable deposition patterns. Nicotine Tob. Res 15:501–8 [PubMed: 23042984]

144. Zhao J, Pyrgiotakis G, Demokritou P. 2016 Development and characterization of electronic-cigarette exposure generation system (Ecig-EGS) for the physico-chemical and toxicological assessment of electronic cigarette emissions. Inhal. Toxicol 28:658–69 [PubMed: 27829296]

145. Zhao JY, Nelson J, Dada O, Pyrgiotakis G, Kavouras IG, Demokritou P. 2018 Assessing electronic cigarette emissions: linking physico-chemical properties to product brand, e-liquid flavoring additives, operational voltage and user puffing patterns. Inhal. Toxicol 30:78–88 [PubMed: 29564955]

146. Zhao TK, Nguyen C, Lin C-H, Middlekauff HR, Peters K, et al. 2017 Characteristics of secondhand electronic cigarette aerosols from active human use. Aerosol Sci. Technol 51:1368–76

147. Zhao TK, Shu S, Guo QJ, Zhu YF. 2016 Effects of design parameters and puff topography on heating coil temperature and mainstream aerosols in electronic cigarettes. Atmos. Environ 134:61–69

148. Zhou S, Behrooz L, Weitzman M, Pan G, Vilcassim R, et al. 2017 Secondhand hookah smoke: an occupational hazard for hookah bar employees. Tob. Control 26:40–45 [PubMed: 26811352]

149. Zhou Z, Bohac D, Boyle RG. 2016 Continuous weeklong measurements of indoor particle levels in a Minnesota Tribal Casino Resort. BMC Public Health 16:870 [PubMed: 27557528]

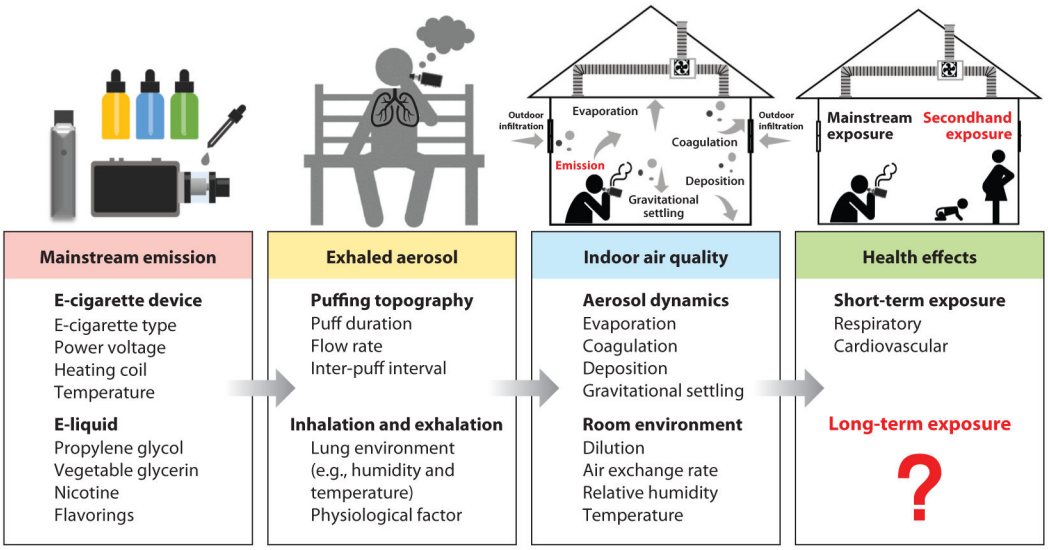

Figure 1.
Schematic process from electronic cigarette emissions, to secondhand exposures, and to potential health effects.

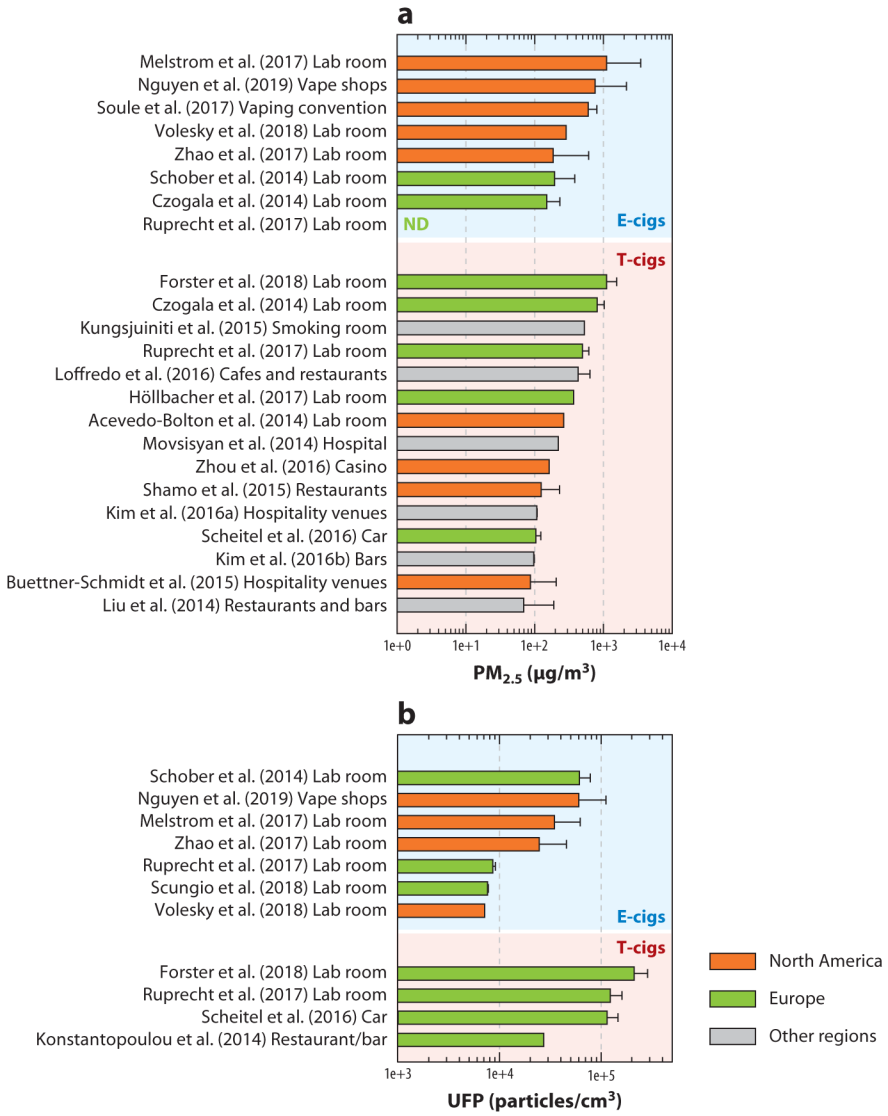

Figure 2.

Average concentration of (*a*) $PM_{2.5}$ and (*b*) ultrafine particles (UFPs) in secondhand electronic cigarette (e-cig) aerosols reported for various indoor environments (i.e., laboratory settings and real-world public indoor spaces), by region. Data are from 11 studies on e-cigs and 16 studies on tobacco cigarettes (t-cigs) that reported mean $PM_{2.5}$ and UFP in a laboratory or public indoor environment (1, 13, 24, 40, 56, 70, 71, 74, 77, 82, 83, 89, 96, 97, 113, 117, 118, 120, 121, 125, 138, 146, 149). Abbreviation: ND, not detected.

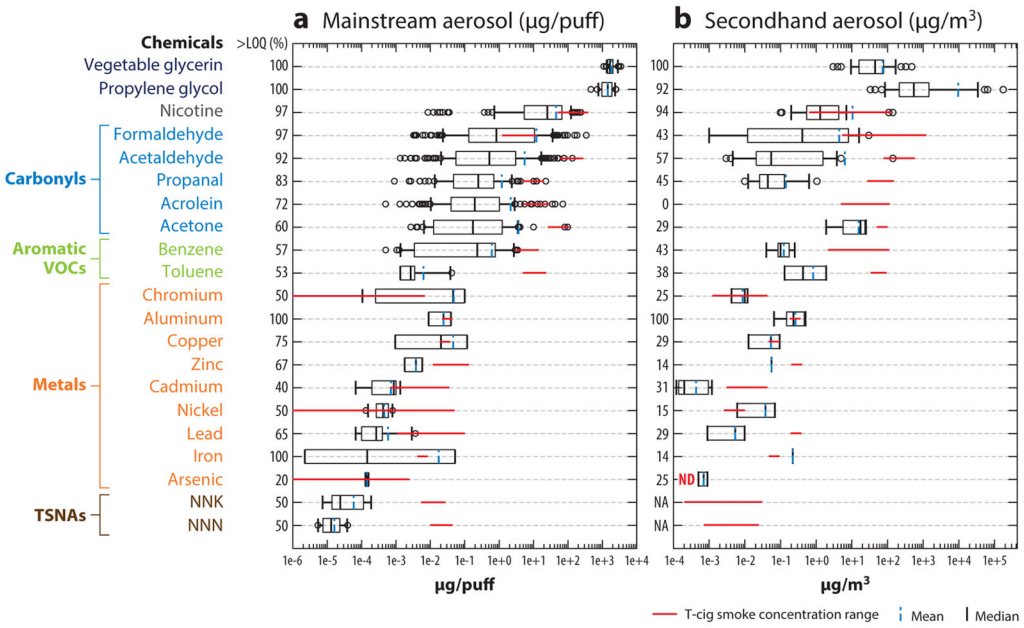

Figure 3.

Chemical compositions of (*a*) mainstream electronic cigarette aerosols (μg/puff) from 37 studies and (*b*) secondhand electronic cigarette aerosols (μg/m^3) from 11 studies. Concentrations of tobacco cig (t-cig)-emitted chemicals are presented as ranges (*red line*) as a reference group. All the data included are background-subtracted values when applicable (8, 18, 21, 24, 25, 28-33, 35, 36, 43, 45, 48-50, 59, 60, 63, 65, 66, 68, 75, 76, 80, 81, 84, 89, 91, 99, 103-105, 111-116, 118, 119, 122, 123, 126-128, 131, 134, 141, 145). Abbreviations: > LOQ%, the percentage of available data points above the limit of quantification (LOQ); ND, not detected; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN, N′-nitrosonornicotine; TSNAs, tobacco-specific nitrosamines; VOCs, volatile organic compounds.

Table 1

Summary of studies on the health effects in humans of active electronic cigarette use and passive exposure to secondhand electronic cigarette aerosols

Study[a]	Design	Study subjects (sample size)	Exposure concentrations	Exposure duration	Health effect assessment	Findings
Respiratory effects: active e-cig use						
Flouris et al. 2013 (37)	Randomized crossover trial	Healthy t-cig smokers (n = 15)	10.4 puffs, serum cotinine: 60.6 ng/ml	30 min	Lung function, eCO, and eNO	No differences before and after e-cig use
Ferrari et al. 2015 (34)	Randomized crossover trial	Healthy t-cig smokers (n = 10) and nonsmokers (n = 10)	NA	5 min	Lung function, eCO, and eNO	Reduction in lung function after e-cig use only among smokers
Antoniewicz et al. 2016 (6)	Randomized crossover trial	Healthy seldom smokers (n = 16)	10 puffs, plasma cotinine: 4.1 ng/ml	10 min	eNO	No differences before and after e-cig use
Vardavas et al. 2012 (137)	Nonrandomized crossover trial	Healthy t-cig smokers (n = 30)	NA		Lung function, eNO, and airway resistance	Increased airway resistance and decreased eNO after e-cig use
Marini et al. 2014 (85)	Nonrandomized crossover trial	Healthy t-cig smokers (n = 25)	NA	5 min	eNO	Increased eNO after e-cig use
Schober et al. 2014 (118)	Controlled exposure study	Healthy t-cig smokers (n = 9)	132 puffs	2 h	eCO and eNO	Increased eNO after the use of e-cig with nicotine
Dicpinigaitis et al. 2016 (26)	Controlled exposure study	Healthy nonsmokers (n = 30)	30 puffs	15 min	Cough reflex sensitivity	Inhibited cough reflex sensitivity after the use of e-cig with nicotine
Ghosh et al. 2018 (44)	Case-control	Healthy nonsmokers (n = 18) and e-cig users (n = 10)	1.8 puffs/h, serum cotinine: 97.2 ng/ml	NA	Airway proteome	Markedly changed protein profiles in lungs among e-cig users that may have clinical implications for the development of chronic lung diseases
Kim et al. 2017 (72)	Cross-sectional study	Adolescents (ages 12–18 years) (n = 216,056)	Self-reported e-cig use in past 30 days: 8% of the total population	NA	Asthma attack in the past 12 months	Higher odds of asthma attack [OR = 1.12; 95% CI (1.01–1.26)] associated with the e-cig use
McConnell et al. 2017 (86)	Cross-sectional study	Adolescents (age ~17 years) (n = 2,086)	Self-reported past (24.0%) and current (9.6%) e-cig users	NA	Self-reported chronic bronchitis symptoms and wheeze	Higher odds of chronic bronchitis symptoms [OR = 1.70; 95% CI (1.11–2.59)] associated with past e-cig use
Respiratory effects: passive exposure						
Flouris et al. 2013 (37)	Randomized crossover trial	Healthy nonsmokers (n = 15)	Serum cotinine: 2.4 ng/ml	1 h	Lung function, eCO, and eNO	No differences before and after the exposures
Tzortzi et al. 2018 (133)	Nonrandomized crossover trial	Healthy nonsmokers (n = 40)	120 puffs/h in a 35-m^3 room	30 min	Lung function, eCO, eNO, and airway resistance	Increased air resistance and decreased eNO after the exposures
Bayly et al. 2019 (10)	Cross-sectional study	Adolescents (ages 11–17 years) with self-reported	Self-reported exposure in past 30	NA	Asthma attack in the past 12 months	Higher odds of asthma attack [OR = 1.27; 95% CI (1.11–

Study[a]	Design	Study subjects (sample size)	Exposure concentrations	Exposure duration	Health effect assessment	Findings
		asthma (n = 11,830)	days: 33% of the total population			1.47)] associated with the exposures
Cardiovascular effects: active e-cig use						
Flouris et al. 2012 (38)	Randomized crossover trial	Healthy t-cig smokers (n = 15)	10.4 puffs, serum cotinine: 60.6 ng/ml	30 min	Complete blood count	No differences before and after e-cig use
Antoniewicz et al. 2016 (6)	Randomized crossover trial	Healthy seldom smokers (n = 16)	10 puffs, plasma cotinine: 4.1 ng/ml	10 min	Endothelial function biomarkers	Increased endothelial progenitor cell counts after e-cig use
Poulianiti et al. 2016 (108)	Randomized crossover trial	Healthy t-cig smokers (n = 15)	10.4 puffs, serum cotinine: 60.6 ng/ml	30 min	Oxidative stress biomarkers	No differences before and after e-cig use
Moheimani et al. 2017 (93)	Randomized crossover trial	Healthy nonsmokers (n = 33)	60 puffs, plasma nicotine: 4.1 ng/ml	30 min	Heart rate variability, blood pressure, and biomarkers of oxidative stress and inflammation	A shift in cardiac autonomic balance after the use of e-cig with nicotine
Carnevale et al. 2016 (15)	Nonrandomized crossover trial	Healthy t-cig smokers (n = 20) and nonsmokers (n = 20)	9 puffs	NA	Biomarkers of endothelial function and oxidative stress	Changes in biomarkers indicative of increased oxidative stress and decreased endothelia function after e-cig use
Chatterjee et al. 2019 (17)	Controlled exposure study	Healthy nonsmokers (n = 10)	16–17 puffs	3 min	Biomarkers of oxidative stress and inflammation	Changes in biomarkers indicative of increased oxidative stress and inflammation after e-cig use
Moheimani et al. 2017 (94)	Case-control study	Healthy nonsmokers (n = 23) and e-cig users (n = 19)	Plasma cotinine: 3.8–139 ng/ml	1.6 years	Heart rate variability, blood pressure, and biomarkers of oxidative stress and inflammation	A shift in cardiac autonomic balance and an increase in oxidative stress among e-cig users
Alzahrani et al. 2018 (4)	Cross-sectional study	Adults (ages >18 years) (n = 69,725)	Self-reported daily e-cig users: 1.1% of the total population	NA	Self-reported history of myocardial infarction	Higher odds of myocardial infarction [OR = 1.79; 95% CI (1.20–2.66)] associated with daily e-cig use
Cardiovascular effects: passive exposures						
Flouris et al. 2012 (38)	Randomized crossover trial	Healthy nonsmokers (n = 15)	Serum cotinine: 2.4 ng/ml	1 h	Complete blood count	No differences before and after the exposures
Poulianiti et al. 2016 (108)	Randomized crossover trial	Healthy nonsmokers (n = 15)	Serum cotinine: 2.4 ng/ml	1 h	Oxidative stress biomarkers	No differences before and after the exposures

Abbreviations: CI, confidence interval; e-cig, electronic cigarette; eCO, exhaled carbon monoxide; eNO, exhaled nitric oxide; NA, not applicable; OR, odds ratio; t-cig, tobacco cigarette.

[a]Studies with the same design are shown in chronological order based on publication date.