



Volatile organic compounds in regular and organic vaping liquids: a public health concern

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Received: 7 March 2024 / Accepted: 8 September 2024 / Published online: 19 September 2024
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Abstract

Electronic cigarettes (e-cigarettes) are a growing public health concern. Vaping liquids used in e-cigarettes emit a range of chemicals, including potentially hazardous volatile organic compounds (VOCs). Exposure to VOCs is associated with adverse effects including asthma attacks, neurological disorders, and increased risk of cancer. This study investigated the VOCs emitted into the headspace of a gas chromatograph/mass spectrometer from e-cigarette vaping liquids, identified potentially hazardous compounds, and compared emissions between regular and organic versions. Vaping liquids ($n=25$) were randomly selected from the market and analysed for their volatile emissions using headspace gas chromatography/mass spectrometry. The products were available for sale in the US, Australia, and New Zealand, and included regular (flavoured and flavourless) and organic (flavoured) versions. Results revealed that the vaping liquids collectively emitted 162 VOCs with 47 classified as potentially hazardous. Notably, all of the flavoured vaping liquids (regular and organic) emitted one or more VOCs classified as potentially hazardous. Further, among the 47 VOC occurrences classified as potentially hazardous, none were listed on any vaping liquid label or related product website. We found no significant difference in VOCs emitted between the regular (flavoured) and organic (flavoured) vaping liquids, and 40% of the hazardous VOCs detected were the same among these regular and organic versions. This study adds to the growing body of evidence that vaping liquids are a source of exposure to numerous volatile compounds, including potentially hazardous VOCs such as benzene, toluene and xylene. Moreover, the long-term health effects of vaping liquids are not well understood, highlighting the need for improved information on ingredients and health risks.

Keywords Vaping liquid · E-cigarette · E-liquid · Flavour · Volatile organic compounds · Emissions · Public health

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Introduction

E-cigarettes or vapes are associated with adverse effects on human health (Banks et al. 2022; Harris et al. 2022). Vaping liquids used in e-cigarette devices contain volatile organic compounds (VOCs), including hazardous compounds such as benzene, toluene and xylene (Chivers et al. 2019; LeBouf et al. 2018). Exposure to VOCs is associated with adverse health effects including respiratory disease, neurological disorders, and increased risk of cancer (Alford and Kumar 2021; Halios et al. 2022; Maung et al. 2022). Active vaping also generates numerous secondary pollutants including fine particulate matter (i.e., PM_{2.5}), carbon monoxide, acetaldehyde, acetone, acrolein, and formaldehyde (Australian Government 2019). Exposure to PM_{2.5} is hazardous even at very low levels, and increasing evidence suggests there is no safe level of exposure (WHO 2021).

Globally, the consumption of e-cigarette vaping liquids has grown considerably over the past five years (Banks et al. 2022; Tehrani et al. 2022). Younger people are the largest cohort of regular users of vaping liquids, and are also among the largest group of new vapers (Banks et al. 2022). For tobacco smokers, e-cigarettes are promoted as a smoking cessation tool. However, evidence of this is limited, and smokers who have tried e-cigarettes with the intention of quitting tobacco smoking often end up as “dual users” (i.e., smoking tobacco and vaping), thus compounding associated health problems (Bozier et al. 2020). Also concerning is that people who have not previously smoked (“never smokers”) are starting to use e-cigarettes, and that young people are particularly attracted to them (Bozier et al. 2020). Although the long-term health consequences of vaping are still being investigated, short-term health effects include nausea, vomiting, mouth and airway irritation, asthma exacerbations, and palpitations (National Lung Foundation 2021). In some cases, the acute health effects can be catastrophic. In the US, a sudden spike in the number of lung related illnesses occurred in 2019 (Guo et al. 2021). The e-cigarette or vaping use-associated lung injury (EVALI) outbreak was caused by the use of e-cigarette or vaping products (primarily containing cannabis) and resulted in more than 2,807 hospitalisations and 68 deaths (CDC 2021).

Several studies have examined VOC emissions from flavoured and flavourless vaping liquids. A US Study of 145 vaping liquids revealed that ethanol was the most frequently detected compound (in 95% of the liquids analysed), followed by acetaldehyde (61%) and d-limonene (54%) (Lebouf et al., 2018), all of which are potentially hazardous to health. In the same study, the hazardous compounds of benzene, xylene(s), and toluene were detected in 20%, 16%, and 13% of the vaping liquids, respectively (Lebouf et al., 2018). Derivatives of benzene were also found in the

extract of 10 different flavoured vaping liquids evaluated by Ween et al. (2021). Another study analysed the volatile components from 10 “nicotine-free” vaping liquids on the Australian market and found that all the products contained the acutely toxic compound 2-chlorophenol (Chivers et al. 2019; SWA 2020). It also revealed that nicotine was present in six of the “nicotine-free” products—in some instances at concentrations similar to those of low-dose nicotine-containing vaping liquids (Chivers et al. 2019). Further, an international review examined the volatile emissions from vaping liquids and identified 243 unique chemicals, including 38 compounds that were known poisons (Australian Government 2019). However, to the best of our knowledge, no study has explored emissions from regular and organic versions of e-cigarette vaping liquids, the similarities and differences among them, the prevalence of hazardous compounds, or the ingredients disclosed.

This present study investigated VOCs emission into the headspace of a gas chromatograph/mass spectrometer from 25 vaping liquids of different types and brands commercially available in Australia (AU), the United States (US) and New Zealand (NZ). Vaping liquids categories include regular (flavoured and flavourless) and organic (flavoured) versions. The study aimed to (1) determine the most prevalent compounds among different vaping liquid types and categories, (2) identify VOCs classified as potentially hazardous, (3) compare emissions between organic and regular vaping liquids, and (4) assess differences between the VOCs emitted from vaping liquids and the ingredients listed on vaping liquids labels or websites.

Materials and methods

Sampling and analysis

For this study, a set of 25 vaping liquids, representing different brands and types, were randomly selected, taking into account different flavours, regular or organic claims, and store locations. The vaping liquids included 10 flavoured regular vaping liquids, 10 flavoured organic vaping liquids, and 5 flavourless regular vaping liquids. Vaping liquids for this study were purchased from vape shops or online vape stores in Australia, the United States, and New Zealand.

In this study, “flavoured vaping liquids” are identified as vaping liquids that contain flavours, “flavourless vaping liquids” are identified as vaping liquids with the claim of flavourless or unflavoured, “organic vaping liquids” are identified as vaping liquids with the claim of organic, and “regular vaping liquids” are identified as vaping liquids that are not in the organic category.

For this study, a Shimadzu Headspace Gas Chromatography/Mass Spectrometry (GC/MS) QP2010 equipped with a BPX-VOL capillary column and a Shimadzu AOC-500 automated injection system was used to analyze VOC emissions from vaping liquids. For each experiment, approximately 2 g of vaping liquid was placed into a 10 ml amber vial and then tightly sealed with a screw cap with PTFE/silicone septum. After incubation at 40°C for 1 h, 2.5 mL of the headspace was injected into the heated injection port (240 °C, split ratio 25) of the GC/MS column (30 m × 0.25 mm, 1.4 µm film thickness) with helium as the carrier gas. The oven temperature ranged from 35°C to 220°C, and the total run time was 45 min. Mass spectrometry operated in full scan mode (m/z 25–400), with ion source and interface temperatures at 200°C and 240°C. Periodic blank analyses were conducted daily to correct for any background impurities. The experiments were repeated twice for each sample to confirm the precision of the measurements. Then, the emitted compounds were identified using the mass spectral library of the National Institute of Standards and Technology NIST Version 2.0 (Stein 2008). In this paper, we use the terms “emissions” and “emitted” to refer to the evaporation of volatile compounds from the vaping liquids into the headspace of the gas chromatograph/mass spectrometer used in their identification.

Hazard identification

The VOCs emitted into the headspace from the vaping liquids were classified as: (i) potentially hazardous under Globally Harmonized System of Classification and Labeling of Chemicals (GHS) (UNECE 2023), (ii) potentially hazardous under California Proposition 65 (OEHHA 2023), (iii) potentially hazardous under Hazardous Air Pollutants (HAPs), United States Environmental Protection Agency (EPA 2023), or (iv) possibly carcinogenic under World Health Organization (WHO 2023).

Results

VOCs emitted

A summary of VOCs from the vaping liquids studied in the headspace of the gas chromatograph/mass spectrometer is provided in Table 1. The term “VOC occurrences” refers to the number of individual VOCs identified in each vaping liquid. The term “VOC identities” refers to the number of unique VOCs identified among vaping liquids, where each VOC may be present in one or more of the vaping liquids. Complete data on VOC identities and VOC occurrences for all vaping liquid types and categories, are presented in Supplementary Tables 1–8.

Most prevalent VOCs

The most prevalent (frequently detected) VOCs were provided for different vaping liquid types and categories in Table 2 and Supplementary Tables 1–5. Among all 20 flavoured vaping liquids the most prevalent VOCs (in at least 30% of products) were propylene glycol, ethanol, limonene, alpha-pinene, ethyl butyrate, beta-pinene, and eucalyptol. Among the 10 flavoured regular vaping liquids the most prevalent VOCs (in at least 40% of products) were propylene glycol, limonene, ethyl butyrate, alpha-pinene, ethanol, and ethyl propionate. Among the 10 flavoured organic vaping liquids the most prevalent VOCs (in at least 40% of products) were propylene glycol, ethanol, limonene, alpha-pinene, beta-pinene, and eucalyptol.

Potentially hazardous VOCs

Among the 25 vaping liquids, the analysis found the following potentially hazardous VOC occurrences and identities for each product type: for all 25 vaping liquids, 47 potentially hazardous VOC occurrences representing 11 potentially hazardous VOC identities; for 10 flavoured regular

Table 1 VOCs emitted from the vaping liquids studied*

Type	Number of vaping liquids	Emitted		Listed (on product label or safety data sheet)	
		All emitted VOCs	Potentially hazardous VOCs	All listed VOCs	Potentially hazardous VOCs
Regular (flavoured)	10	92 occurrences 52 identities	29 occurrences 9 identities	11 occurrences 2 identities	0 occurrences 0 identities
Organic (flavoured)	10	69 occurrences 43 identities	17 occurrences 5 identities	10 occurrences 1 identity	0 occurrences 0 identities
Regular (flavourless)	5	6 occurrences 2 identities	1 occurrence 1 identity	5 occurrences 1 identity	0 occurrences 0 identities
Total	25	162 occurrences 73 identities	47 occurrences 11 identities	26 occurrences 2 identities	0 occurrences 0 identities

*“VOC occurrences” refers to the number of individual VOCs emitted from each vaping liquid

“VOC identities” refers to the number of unique VOCs emitted from one or more of the vaping liquid

Table 2 Most prevalent VOCs emitted from the vaping liquids studied

Compound	CAS #	Prevalence (# of vaping liquids)		
		Total	Regular (n = 10)	Organic (n = 10)
<i>All flavoured vaping liquids (n = 20)</i>				
Propylene glycol	106-27-4	20	10	10
Ethanol*	64-17-5	13	4	9
Limonene*	138-86-3	12	7	5
alpha-Pinene	80-56-8	9	4	5
Ethyl butyrate	105-54-4	7	6	1
beta-Pinene	127-91-3	6	2	4
Eucalyptol	470-82-6	6	2	4
2-Heptyl-4-methyl-1,3-dioxolane	74094-61-4	4	3	1
Camphene	79-92-5	4	2	2
Ethyl acetate*	141-78-6	4	3	1
Ethyl propionate*	105-37-3	4	4	0
Hexyl acetate	142-92-7	4	1	3
Isoamyl acetate*	123-92-2	4	3	1
Isocaryophyllene	118-65-0	4	1	3
<i>Regular (flavoured) vaping liquids (n = 10)</i>				
Propylene glycol	4254-15-3	10		
Limonene*	138-86-3	7		
Ethyl butyrate	105-54-4	6		
alpha-Pinene	80-56-8	4		
Ethanol*	64-17-5	4		
Ethyl propionate*	105-37-3	4		
2-Heptyl-4-methyl-1,3-dioxolane	74094-61-4	3		
2-Methylbutyl acetate*	624-41-9	3		
Ethyl acetate*	141-78-6	3		
Isoamyl acetate*	123-92-2	3		
Isoamyl isovalerate	659-70-1	3		
<i>Organic (flavoured) vaping liquids (n = 10)</i>				
Propylene glycol	4254-15-3	10		
Ethanol*	64-17-5	9		
Limonene*	138-86-3	5		
alpha-Pinene	80-56-8	5		
beta-Pinene	127-91-3	4		
Eucalyptol	470-82-6	4		
Hexyl acetate	142-92-7	3		
Isocaryophyllene	118-65-0	3		
<i>Regular (flavourless) vaping liquids (n = 5)</i>				
Propylene glycol	4254-15-3	5		
Methanol*	67-56-1	1		

*Classified as potentially hazardous

vaping liquids, 29 potentially hazardous VOC occurrences representing 9 potentially hazardous VOC identities; for 10 flavoured organic vaping liquids, 17 potentially hazardous VOC occurrences representing 5 potentially hazardous VOC identities; and for 5 flavourless regular vaping liquids, 1 potentially hazardous VOC occurrence representing 1 potentially hazardous VOC identity (Table 1).

Most prevalent potentially hazardous VOCs

Prevalent potentially hazardous VOCs for different vaping liquid types and categories are presented in Tables 3 and 4. Among all 20 flavoured vaping liquids the most prevalent potentially hazardous VOCs (in at least 20% of products) were ethanol, limonene, ethyl acetate, ethyl propionate, and isoamyl acetate. Among the 10 flavoured regular vaping liquids the most prevalent potentially hazardous VOCs (in at least 40% of products) were limonene, ethanol, and ethyl propionate. Among the 10 flavoured organic vaping liquids

Table 3 Potentially hazardous* VOCs emitted from the vaping liquids studied

Compound	CAS #	Prevalence (# of vaping liquids)		
		Total	Regular (n = 10)	Organic (n = 10)
<i>All flavoured vaping liquids (n = 20)</i>				
Ethanol	64-17-5	13	4	9
Limonene	138-86-3	12	7	5
Ethyl acetate	141-78-6	4	3	1
Ethyl propionate	105-37-3	4	4	0
Isoamyl acetate	123-92-2	4	3	1
2-Methylbutyl acetate	624-41-9	3	3	0
Butyl butyrate	109-21-7	2	2	0
beta-Myrcene	123-35-3	2	2	0
(S)-p-mentha-1,8-diene	5989-54-8	1	0	1
Amyl acetate	628-63-7	1	1	0
<i>Regular (flavoured) vaping liquids (n = 10)</i>				
Limonene	138-86-3	7		
Ethanol	64-17-5	4		
Ethyl propionate	105-37-3	4		
2-Methylbutyl acetate	624-41-9	3		
Ethyl acetate	141-78-6	3		
Isoamyl acetate	123-92-2	3		
Butyl butyrate	109-21-7	2		
beta-Myrcene	123-35-3	2		
Amyl acetate	628-63-7	1		
<i>Organic (flavoured) vaping liquids (n = 10)</i>				
Ethanol	64-17-5	9		
Limonene	138-86-3	5		
(S)-p-mentha-1,8-diene	5989-54-8	1		
Ethyl acetate	141-78-6	1		
Isoamyl acetate	123-92-2	1		
<i>Regular (flavourless) vaping liquids (n = 5)</i>				
Methanol	67-56-1	1		

*Classified as hazardous

Table 4 Classification of potentially hazardous VOCs according to standards or regulations

Compound	CAS #	Prevalence (# of Products)	GHS	HAPs	Prop65
Ethanol	64-17-5	13	✓		
Limonene	138-86-3	12	✓		
Ethyl acetate	141-78-6	4	✓		
Ethyl propionate	105-37-3	4	✓		
Isoamyl acetate	123-92-2	4	✓		
2-Methylbutyl acetate	624-41-9	3	✓		
beta-Myrcene ^c	123-35-3	2			✓
Butyl butyrate	109-21-7	2	✓		
(S)-p-mentha-1,8-diene	5989-54-8	1	✓		
Amyl acetate	628-63-7	1	✓		
Methanol	67-56-1	1	✓	✓	✓

GHS: Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2023)

HAPs: United States Environmental Protection Agency (EPA) - Hazardous Air Pollutants (EPA 2023)

Prop65: California Proposition 65 (OEHHA 2023)

^cClassified as possibly carcinogenic (2B: Possibly carcinogenic to humans) (WHO 2023)

the most prevalent potentially hazardous VOCs (in at least 50% of products) were ethanol and limonene.

The regulatory assessment also investigated VOCs with classifications of potential carcinogenic risk according to the World Health Organization (WHO 2023). Among VOCs emitted, beta-myrcene emitted from flavoured regular vaping liquids, representing 2 identities, is classified as possibly carcinogenic to humans (2B) (Table 4).

Comparison of VOCs emitted from regular (flavoured) and organic (flavoured) vaping liquids

Among the prevalent VOCs in flavoured vaping liquids (Table 2), no significant difference was found in VOC occurrences between regular and organic vaping liquids ($p=0.65$, Mann-Whitney U Test). In addition, among the most prevalent potentially hazardous VOCs in flavoured vaping liquids (Table 3), no significant difference was found in the most prevalent potentially hazardous VOC occurrences between regular (flavoured) and organic (flavoured) vaping liquids ($p=0.07$, Mann-Whitney U Test). Further, among the most prevalent VOCs classified as potentially hazardous in all vaping liquids (Table 3), approximately 40% of VOC identities were the same among these regular and organic vaping liquids.

VOCs emitted from flavourless vaping liquids

Among the 5 flavourless regular vaping liquids, 6 VOC occurrences representing 2 VOC identities, and 1 VOC occurrence representing 1 potentially hazardous VOC identity were emitted from products (Table 1). For all 5 flavourless regular vaping liquids, the only two emitted compounds were propylene glycol (in 100% of products) and methanol (in 20% of products) (Table 2), of which methanol is classified as a potentially hazardous VOC.

Listing of ingredients

Among all the 162 VOC occurrences emitted from all 25 vaping liquids, only 26 VOC occurrences, representing 2 VOC identities (i.e., propylene glycol and menthol) were listed on any product label. Thus, fewer than 3% of all VOC identities were listed on vaping liquid labels or related product websites. Further, among the 47 VOC occurrences classified as potentially hazardous, none of them were listed on any vaping liquid label or website.

Discussion

This study found that vaping liquids of all types, including both regular and organic versions, emit numerous VOCs, some of which are classified as hazardous to humans. All of the flavoured vaping liquids, both regular and organic, emitted one or more VOCs classified as potentially hazardous, with no significant difference between the regular and organic versions. In addition, 40% of the hazardous VOCs detected were the same among regular and organic vaping liquids. Notably, fewer than 3% of the VOCs detected, and none of the potentially hazardous VOCs, were disclosed on any product labels or related publicly available resources.

Several international sources have revealed that flavours play a vital role in vaping initiation (FDA 2023; Havermans, 2021; Gendall and Hoek 2021). Fruit, candy, dessert, and coffee flavours were reported to be the most popular (Havermans, 2021). In the US, nearly 85% of young users chose e-cigarettes that were flavoured (e.g., fruit, candy, dessert) (FDA 2023), and among New Zealanders (aged between 18 and 70 years) “flavour” was one of the main reasons for vaping (Gendall and Hoek 2021). For current smokers, tobacco flavoured vapes were preferred, while former smokers favoured mint or menthol flavoured vapes, and never smokers preferred confectionery, sweets, or lolly flavours (Gendall and Hoek 2021). Flavoured vaping products with names such as “Cotton Candy” and “Toffee Apple” obscure the wide range of hazardous compounds contained within the product. In addition to flavours, vaping devices with bright colours, toy like appearance, easy concealment and other factors are known to attract users (especially young people) to e-cigarettes (National Lung Foundation 2021). An ongoing challenge is the lack of labelling and disclosure of product ingredients, either on the packet or elsewhere. Therefore, measures to convey the risk of volatile ingredients in e-cigarettes are vital, such as plain packaging with clear health warnings akin to Australian tobacco labelling (Australian and Government 2023).

Vaping emissions are of particular concern as vaping liquids are largely regulated for their nicotine content, but not for the presence of other hazardous compounds, including those identified in this study: ethanol, limonene, ethyl acetate, ethyl propionate, isoamyl acetate, 2-methylbutyl acetate, beta-myrcene, butyl butyrate, (S)-p-mentha-1,8-diene, amyl acetate, methanol, and others (e.g., Chivers et al. 2019). Flavouring compounds have been found to influence the formation of toxic and carcinogenic secondary reaction products (i.e., aldehydes) during active vaping. In one study, the production of aldehydes from e-cigarette use was found to be exponentially dependent on the concentration of flavouring compounds (Khlystov and Samburova 2016). Although it is well established the thermal degradation (i.e.,

from heating) of propylene glycol or glycerol can lead to formation of secondary reaction products, the concentration and number of different flavouring compounds used in a vaping liquid has important implications for secondary reaction product formation.

Another health critical aspect of e-cigarette use is exposure of other people to “second hand” vaping emissions (e.g., aldehydes, $\text{PM}_{2.5}$). Potentially hazardous chemicals released during use of e-cigarettes included diacetyl, propionaldehyde, acetaldehyde and formaldehyde (Klager et al. 2017). In an outdoor setting, e-cigarette use resulted in average $\text{PM}_{2.5}$ concentrations of $5 \mu\text{g}/\text{m}^3$ and $50 \mu\text{g}/\text{m}^3$ at distances of 3 meters and 1 m from the source, respectively (Cheng et al. 2022). Further, $\text{PM}_{2.5}$ measurements conducted at the front of vaping stores in the USA revealed concentrations of $27 \mu\text{g}/\text{m}^3$ at approximately 3 meters from the shop door and $5 \mu\text{g}/\text{m}^3$ at approximately 8 m from the door, respectively (Li et al. 2021). Comparison of these levels to the recently revised WHO annual exposure guideline of $5 \mu\text{g}/\text{m}^3$, and 24-hour exposure guideline of $15 \mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$ suggest that exposure to secondary particulates from active vaping can be substantial (WHO 2021).

To protect public health, some government jurisdictions are restricting the sale and use of e-cigarettes. For instance, in California, a new law went into effect on December 21, 2022 that completely prohibits the sale of menthol cigarettes and nearly all other flavoured tobacco products, including flavoured e-cigarettes, as well as tobacco product flavour enhancers (CA Health & Safety Code § 104559.5, 2022). Tobacco products include any electronic device that delivers nicotine or other vaporized liquids to the person inhaling from the device. Notably, even flavoured vaping liquids and flavoured e-cigarette products that do not contain nicotine are prohibited. (CA Health & Safety Code § 104559.5, 2022). Californian regulations can serve as a model for other countries to protect public health by reducing exposure to hazardous emissions from vaping products. To support the development of legislation, future research is needed, including a greater understanding of the long-term health impacts of exposure to primary and secondary emissions from e-cigarettes.

This study has several limitations. First, this study has a relatively small sample size of 25 e-cigarette vaping liquids. Nevertheless, we randomly selected these products from market in three countries (US, AU, NZ), and they therefore represent typical products available to consumers. Second, the GC/MS headspace analysis did not evaluate VOCs that may have formed through interactions with external constituents (or active vaping) such as secondary reaction products (e.g., aldehydes, $\text{PM}_{2.5}$) (Cheng et al. 2022; Li et al., 2021). Instead, the analysis focused on primary emissions and identified compounds that were individual ingredients

in each product. Third, the overall risk of exposure to hazardous air pollutants may therefore be greater than the risk posed from the VOCs discussed in our analysis. The classifications used in this study are not intended as an assessment of safety or hazard, and do not imply that these VOCs, either individually or in mixtures, are the only potentially hazardous compounds contained in the vaping liquids. Fourth, of the 25 vaping liquids, 23 were labelled as nicotine free. We did not focus on nicotine detection in the analysis and cannot confirm that these products contained nicotine. However, previous evidence suggest that this is highly likely (Chivers et al. 2019). These results nonetheless are an important foundation that can support additional research to evaluate secondary pollutant emissions and exposures from e-cigarettes and associated health risks.

Conclusions

Our study found that vaping liquids emit numerous volatile chemicals, including potentially hazardous VOCs. The vaping liquids collectively emitted 162 VOCs with 47 classified as potentially hazardous. None of these chemicals were included on the vaping liquid labels or related online product information. The study’s findings underscore the need to raise awareness of the potentially hazardous chemical compounds in vaping liquids, and that there no significant difference in ingredients between regular and organic versions of vaping liquids. Clear labelling is needed that provides information on ingredients and possible health effects. More research is warranted to further explore the emissions and exposures associated with vaping, including primary and secondary emissions from vaping activities and second hand vaping exposure.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11869-024-01645-9>.

Acknowledgements We gratefully acknowledge support from RMIT Urban Futures Enabling Impact Platform, the Commonwealth Scientific and Industrial Research Organisation (CSIRO) and the Healthy Environments And Lives (HEAL) National Research Network. The views expressed are those of the authors and do not represent those of institutions.

Author contributions The study conception and design was led by Nigel Goodman, Anne Steinemann, and Neda Nematollahi. Material preparation, data collection and analysis were performed by Neda Nematollahi, Spas Kolev, and Nigel Goodman. The first draft of the manuscript was written by Nigel Goodman, Neda Nematollahi, Anne Steinemann, Justine Lew Weinberg, and Jennifer Flattery. Subsequent drafts of the manuscript were written by Nigel Goodman, Neda Nematollahi, Anne Steinemann, Justine Lew Weinberg, Jennifer Flattery, Sotiris Vardoulakis, Michael Tong, and Spas Kolev. All authors contributed to writing of the final manuscript. All authors read and approved the final manuscript.

Funding This study was funded by RMIT University through the Urban Futures Enabling Impact Platform, The University of Melbourne, and the Healthy Environments And Lives (HEAL) National Research Network from the National Health and Medical Research Council Special Initiative in Human Health and Environmental Change (NHMRC Grant No. 2008937). SDK is grateful for the financial support provided by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project No BG-RRP-2.004-0008.

Open Access funding enabled and organized by CAUL and its Member Institutions

Data availability All data from this project is available in the manuscript tables or as electronic supplementary information.

Declarations

Conflict of interest The authors declare no conflict of interest.

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