

- 1 Electronic cigarettes for smoking cessation..... PG 2
- 2 Chemical Composition of Aerosol from an E-Cigarette:  
A Quantitative Comparison with Cigarette Smoke..... PG 4
- 3 Trendy e-cigarettes enter Europe:  
Chemical characterization of JUUL pods and its aerosols..... PG 8
- 4 Selected Harmful and Potentially Harmful Constituents  
Levels in Commercial e-Cigarettes..... PG 10
- 5 The Evolving E-cigarette: Comparative Chemical  
Analyses of E-cigarette Vapour and Cigarette Smoke..... PG 11
- 6 Electronic cigarettes for smoking cessation (Review)..... PG 12
- 7 Levels of Selected Carcinogens and Toxicants in  
Vapour from Electronic Cigarettes..... PG 13
- 8 Chemical Composition and *in vitro* Toxicity Profile of a  
Pod-Based E-Cigarette Aerosol Compared to Cigarette  
Smoke..... PG 14
- 9 Metal concentrations in electronic cigarette aerosol:  
effect of open-system and closed-system devices and power  
settings..... PG 15
- 10 Tobacco smoking in Sub-Saharan Africa:  
A systematic review and meta-analysis..... PG 17

# The Science of Less Harm

Evidence-based insights



# 1 Electronic cigarettes for smoking cessation

Hartmann-Boyce J, et al. Electronic cigarettes for smoking cessation. CDSR. 2022;(11).



## BACKGROUND



Since smoking offers a sensory, behavioural, and social experience, current treatments are limited in that ex-smokers crave the need to hold a cigarette and enjoy the company of other smokers. The introduction of **electronic cigarettes (EC)** may help overcome these limitations.



ECs are hand-held devices that have disposable or refillable cartridges/reservoirs/pods that store e-liquids made up of propylene glycol, glycerol, with or without nicotine and flavours. A battery-powered heating coil then heats the e-liquid and an aerosol is then formed for inhalation. The common term used for aerosol is 'vaper' and EC use is referred to as 'vaping'.



Studies have reported that users, "share a sense of shared identity with other users, similar to tobacco-smoking identity, and also report pleasure and enjoyment of use, suggesting that ECs may be viewed less as medical cessation aids but rather as acceptable alternatives to tobacco smoking".

There are many positive health benefits associated with smoking cessation. However, it remains a **challenge** for smokers to maintain **cessation long-term**. **As few as 5% of smokers remain abstinent** a year later. There are various products on the market to aid in the quitting process by providing nicotine at a lower and slower rate, i.e., nicotine patches and nicotine gum. However, the **long-term quit rates remain low** with these **nicotine-replacement therapy (NRT)** options.



## STUDY OBJECTIVES

To examine the **safety, tolerability and effectiveness of using ECs** to assist smokers who use tobacco to achieve **long-term smoking abstinence**.

## STUDY OUTCOMES

1

### Primary Outcomes

#### Cessation at the longest follow-up point

(at least six months from the start of the intervention)

**Number of participants reporting adverse events (AEs) or serious adverse events (SAEs) at one week or longer**

2

### Secondary Outcomes

**Number of people still using study product** (EC or pharmacotherapy) **at longest follow-up** (at least six months)

**Changes in the following health-related measures at the longest follow-up** (one week or longer):

- Carbon monoxide (CO) - measured through breath or blood
- Blood pressure (BP)
- Heart rate (HR)
- Blood oxygen saturation
- Lung function measures
- Known toxins/carcinogens - measured through blood or urine

## METHODS

An electronic search for studies was performed from 2004 to July 2022 using the following databases: The Cochrane Tobacco Addiction Group's Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, PsycINFO, ClinicalTrials.gov and the World Health Organisation (WHO) International Clinical Trials Registry Platform.

A total of 78 studies were included representing 22 052 participants overall. Included studies were characterised by the following trial types:

**40** randomised controlled trials (RCTs)

**7** randomised cross-over trials

**31** uncontrolled cohort intervention studies



## RESULTS



### Smoking Cessation

- Participants were more **likely to stop smoking** for at least six months **using nicotine e-cigarettes** than using NRT or e-cigarettes without nicotine.
- **Nicotine e-cigarettes may assist more people** to stop smoking as opposed to no support or behavioural support only.
- **For every 100 people using nicotine e-cigarettes** as a measure to stop smoking, **8 to 12 may successfully stop, compared with only 6 of 100 people using NRT**, 7 of 100 using e-cigarettes without nicotine, or 4 of 100 people with no support or behavioural support only.



### Adverse events or serious adverse events

- **Moderate certainty was noted for AEs** that occurred in nicotine EC compared to non-nicotine EC, and NRT.
- Across comparisons, there was **low to very low certainty regarding AEs and SAEs** due to a lack of data.
- Studies that did measure SAEs reported **no events in either study arm**.
- There was **no difference** in the number of people experiencing AEs or SAEs in the nicotine EC compared to non-nicotine EC groups.
- For nicotine EC compared to behavioural support alone or no support suggest that an additional **14 people per 100 assigned to nicotine EC may experience AEs**, but with no difference in SAEs.
- AEs that did occur were typically related to **irritation at the site of use** i.e. dry mouth and cough, which resolved over time.
- There were **no SAEs related to EC use**.



### Health-related outcomes

- **Data was significantly limited on the range of health-related outcomes** (CO, toxins, lung function, BP, pulse, oxygen) with only one to two studies contributing this type of data.

## CONCLUSION

**Nicotine EC** can aid in smoking cessation for at least **six months**. Across comparisons, the rate of smoking **cessation at six months or longer**, showed **high probability in EC with nicotine compared to NRT**, moderate certainty compared to non-nicotine EC and low-certainty (limited by risk of bias and inaccuracy) compared to behavioural support alone or to no support. **No studies showed serious adverse events related to EC use** and the most common adverse events were throat or mouth irritation, headache, cough and nausea, all of which resolved with continued use.

## 2 Chemical Composition of Aerosol from an E-Cigarette: A Quantitative Comparison with Cigarette Smoke

Margham J, et al. Chemical Composition of Aerosol from an E-Cigarette: A Quantitative Comparison with Cigarette Smoke. *Chem. Res. Toxicol*; 2016; 29:1662–1678.



Over the past ten years, electronic nicotine delivery systems (ENDS), especially electronic cigarettes (e-cigarettes), have become increasingly popular as alternatives to traditional tobacco cigarettes. Worldwide, there are over **10 million e-cigarette users**, with significant numbers in the United States (US), United Kingdom (UK), France and other European countries.



There has been rapid innovation in product design, resulting in a **wide variety of e-cigarette designs** worldwide, primarily powered by a battery unit heating a liquid (e-liquid) to produce an aerosol.



Most e-cigarettes consist of a battery unit and an atomiser, with e-liquids containing **ingredients like propylene glycol (PG), vegetable glycerol (VG), water, nicotine and various flavours**.



E-cigarette designs can be grouped into four categories:

- 1 **Disposable and rechargeable designs** (resembling cigarettes)
- 2 **Closed-system modular designs** (separate battery units and e-liquid cartridges)
- 3 **Open-system modular designs** (atomiser refills with separately sold e-liquids)
- 4 **Tank or box-mod systems** (customisation of components and operating conditions)



The **rise in e-cigarette popularity** is largely attributed to **consumer preference**, with many tobacco smokers transitioning to e-cigarettes either partially or completely. The majority of e-cigarette users are either former smokers or use both traditional and electronic cigarettes, while the **proportion of non-smokers using e-cigarettes remains relatively low**.



Some scientists believe that the use of e-cigarettes carries lower risks compared to smoking tobacco cigarettes due to the lower levels of toxicants found in comparison to tobacco cigarettes. Over 50 years, more than 100 harmful and potentially harmful **constituents (HPHCs) have been identified in tobacco and cigarette smoke** posing significant health risks and death among users.



Despite generally lower levels of toxicants in e-cigarette aerosols compared to tobacco cigarettes, the presence of these substances, even at low levels, indicates that **e-cigarette use is not entirely risk-free**. Certain toxicants, such as formaldehyde, acetaldehyde and acrolein, can reach levels similar to those found in traditional tobacco cigarettes, especially when e-liquid transport to the atomiser is inadequate for the electrical power setting, leading to dry-puff conditions. Studies using very high e-cigarette power settings have highlighted this concern.

### AIM

To date, **no single study has comprehensively characterised the chemical composition of e-cigarettes by comparing emissions** of all known compounds with those from tobacco cigarettes. Although three studies (Flora et al; Tayyarah and Long; Lauterbach and Laugesen) did attempt to examine the broad range of compounds to some extent but provided an incomplete picture.



**This current study aimed to fill the gap by reporting emission levels of 142 chemicals and 8 collated measures, covering a wide range of cigarette smoke constituents and key e-cigarette constituents of concern.**

## METHODS

In the experimental procedures, two types of smoking devices were tested:

- 1 **A Ky3R4F Kentucky Reference Tobacco Cigarette**, a standardised product commonly used in scientific studies. The detailed characteristics and smoke yields of HPHC have been previously documented in this reference cigarette.
- 2 **The e-cigarette, known as the Vype ePen**. It is a closed-modular system, manufactured by Nicoventures Trading Ltd. The 'blended tobacco' flavour was used as it was the most commonly sold flavour.



The Health Canada Intense (HCI) smoking regime was used for generating cigarette smoke emissions for toxicant measurement, featuring a 55 cm<sup>3</sup> puff volume, a 2-second puff duration, with a bell-shaped puff profile, taken twice per minute, with all filter ventilation holes blocked. E-cigarette puffing was measured using method 81, published by The Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA). This method featured a rectangular flow puff with a puff volume of 55 cm<sup>3</sup> and a duration of 3 seconds, taken twice per minute.



Twenty-seven different analytical methods were utilised by the analysis laboratory to quantify emissions from various sources, including mainstream emissions from the e-cigarette, Ky3R4F cigarette, and air/method blanks. These methods measured a total of 150 measurands, comprising 142 analytes and 8 collated values. The majority of these methods were based on Health Canada protocols for cigarette smoke analysis, with additional methods developed by Labstat for HPHCs and e-cigarette compounds. Adaptations were made to these methods for use with e-cigarettes where necessary.



Due to the varying consumption patterns of tobacco cigarettes (10-15 puffs) and e-cigarettes (> 200 puffs) the data was presented per stick for the Ky3R4F cigarette or per 100 puff block for the e-cigarette and on a per-puff basis.



For numerous measured substances, emissions fell below the limit of detection (LOD) and/or the limit of quantification (LOQ). When both the emissions from the e-cigarette and the Ky3R4F reference cigarette were below the LOD or LOQ for a particular substance, that substance was excluded from the percentage difference calculation.



The study primarily focused on measuring the smoke yields of the Ky3R4F cigarette under the HCI smoking regime. However, to provide a lower comparative set of toxicant levels for comparing e-cigarette aerosol emissions, comparisons were also made with the mainstream smoke emissions of Ky3R4F conducted under the International Organisation for Standardisation (ISO) conditions. This comparison was facilitated using data from Roemer *et al.*, who reported emissions of various cigarette smoke toxicants from Ky3R4F under both ISO and HCI smoking regimes and provided ratios for the yields measured under the two methods.



In addition, air/method background measurements were performed as certain HPHCs in e-cigarette emissions can approach background air levels. To assess this, measurements of 142 target constituents were conducted simultaneously in the laboratory background and during e-cigarette emissions testing. This enabled an evaluation of potential background contamination within the air, analytical equipment, and reagents used for e-cigarette emission analysis, thereby distinguishing between background contaminants and actual e-cigarette emissions.



This involved collecting blocks of 100 puffs of laboratory air without any e-cigarette present on the puffing machine, followed by analysis using the same equipment and reagents used for e-cigarette emission analysis. However, a comparable control step was not feasible for tobacco cigarette measurements due to the release of relatively high emissions of toxicants into room air while burning. Regardless, this is less concerning for tobacco cigarettes due to their significantly higher toxicant levels and lower puff count, potentially reducing contamination.

## RESULTS

Tables 1 and 2 summarise the 25 compounds detected at some level in the emissions from the e-cigarette as follows:

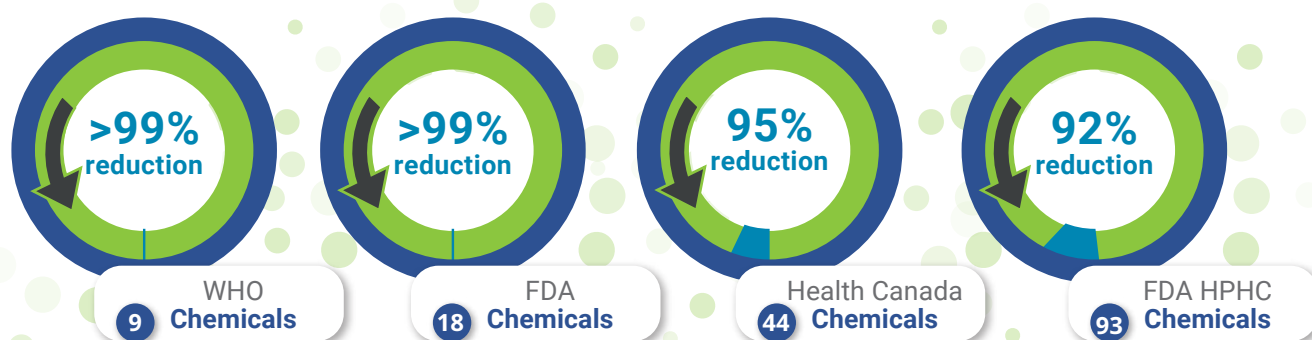
**Table 1. Emissions Measured from ePen at Quantifiable Levels <sup>a</sup>**

|                                                                                                                                            |                     | ePen and air/<br>method blank<br>LOD and LOQ<br>per collection |       | ePen        |      |               |       |               | air/method blank |      |               |      |                | Kentucky reference 3R4F smoke measurements |       |                    |                           |       |                         |  |
|--------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------|-------|-------------|------|---------------|-------|---------------|------------------|------|---------------|------|----------------|--------------------------------------------|-------|--------------------|---------------------------|-------|-------------------------|--|
|                                                                                                                                            |                     |                                                                |       | puffs 1-100 |      | puffs 101-200 |       |               | puffs 1-100      |      | puffs 101-200 |      |                | LOD and LOQ<br>per collection              |       |                    | per cigarette<br>emission |       |                         |  |
| smoke<br>constituent                                                                                                                       | toxicant<br>list    | LOD                                                            | LOQ   | mean        | SD   | mean          | SD    | ePen/<br>puff | mean             | SD   | mean          | SD   | blank/<br>puff | LOD                                        | LOQ   | number<br>of puffs | mean                      | SD    | 3R4F<br>p/puff          |  |
| formaldehyde,<br>μg                                                                                                                        | T, F18,<br>BCV, FEL | 0.722                                                          | 2.41  | 12.1        | 4.8  | 12.3          | 4.9   | 0.122         | 6.59             | 0.31 | 6.79          | 0.4  | 0.067          | 0.4                                        | 1.2   | 10.8               | 94.9                      | 6.2   | 8.79                    |  |
| acetaldehyde,<br>μg                                                                                                                        | T, F18,<br>BCV, FEL | 1.95                                                           | 6.49  | 10.4        | 2.7  | 10.7          | 2.9   | 0.106         | NQ               | NQ   | NQ            | NQ   | 0.042          | 0.97                                       | 3.24  | 10.8               | 1732                      | 43    | 160.4                   |  |
| acrolein, μg                                                                                                                               | T, F18,<br>BCV, FEL | 1.43                                                           | 4.75  | 6.11        | 4.94 | 7.9           | 5.56  | 0.070         | BDL              | BDL  | BDL           | BDL  | 0.007          | 0.71                                       | 2.38  | 10.8               | 172                       | 3     | 15.94                   |  |
| allyl alcohol,<br>ng                                                                                                                       | ECIG                | 67.65                                                          | 226.5 | 464         | 134  | 609           | 282   | 5.365         | BDL              | BDL  | BDL           | BDL  | 0.338          | 67.65                                      | 2265  | 10.4               | 16978                     | 644   | 1.63 X 10 <sup>3</sup>  |  |
| glyoxal, μg                                                                                                                                | ECIG                | 0.126                                                          | 0.42  | 4.81        | 10.1 | 6.45          | 7.6   | 0.056         | NQ               | NQ   | 0.44          | 0.17 | 0.004          | 0.63                                       | 2.1   | 10.6               | 20.44                     | 2.66  | 1.93                    |  |
| methyl,<br>glyoxal, μg                                                                                                                     | ECIG                | 0.077                                                          | 0.256 | 4.59        | 2.7  | 4.62          | 1.92  | 0.046         | 0.29             | 0.12 | NQ            | NQ   | 0.002          | 0.38                                       | 1.28  | 10.6               | 18.2                      | 0.68  | 1.72                    |  |
| glycerol, mg                                                                                                                               | ECIG                | 0.072                                                          | 0.24  | 153         | 18.3 | 162.7         | 13    | 1.579         | NQ               | NQ   | NQ            | NQ   | 0.002          | 0.02                                       | 0.08  | 10.5               | 2.05                      | 0.12  | 1.95 X 10 <sup>-1</sup> |  |
| propylene,<br>glycol, mg                                                                                                                   | ECIG                | 0.012                                                          | 0.04  | 66.7        | 8.61 | 75.06         | 6.22  | 0.709         | NQ               | NQ   | NQ            | NQ   | 0.000          | 0                                          | 0.01  | 10.5               | 0.03                      | 0     | 2.92 X 10 <sup>-3</sup> |  |
| chrysene, ng                                                                                                                               | FEL                 | 0.23                                                           | 0.78  | 0.88        | 0.35 | 1.23          | 0.33  | 0.011         | NQ               | NQ   | BDL           | BDL  | 0.003          | 0.08                                       | 0.26  | 10.3               | 36.79                     | 3.59  | 3.57                    |  |
| nicotine, mg                                                                                                                               | F18, FEL            | 0.007                                                          | 0.022 | 3.57        | 1.10 | 2.75          | 0.981 | 0.032         | BDL              | BDL  | BDL           | BDL  | 0.00004        | 0.002                                      | 0.007 | 10.8               | 1.84                      | 0.077 | 0.170                   |  |
| myosmine, ng                                                                                                                               | ECIG                | 318                                                            | 1060  | 2664        | 526  | 2810          | 455   | 27.37         | BDL              | BDL  | BDL           | BDL  | 1.590          | 64                                         | 212   | 11.1               | 9809                      | 701   | 883.7                   |  |
| cotinine, ng                                                                                                                               | ECIG                | 76.3                                                           | 254   | 1123        | 145  | 1044          | 148   | 10.835        | BDL              | BDL  | BDL           | BDL  | 0.382          | 15                                         | 51    | 11.1               | 50861                     | 1912  | 4582                    |  |
| NNN, ng                                                                                                                                    | T, F18,<br>BCV      | 0.492                                                          | 1.641 | 5.16        | 0.56 | 5.61          | 1.03  | 0.054         | NQ               | NQ   | 1.83          | 0.51 | 0.014          | 0.2                                        | 0.66  | 10.6               | 264.67                    | 22.2  | 24.97                   |  |
| chromium, ng                                                                                                                               | BCV, FEL            | 13.54                                                          | 45.13 | 50.4        | 13.9 | NQ            | NQ    | 0.399         | NQ               | NQ   | NQ            | NQ   | 0.293          | 1.35                                       | 4.51  | 10.9               | NQ                        | NQ    | 0.27                    |  |
| Compounds not higher than Air/Method Blank in original study, but measured higher from ePen than Air/Method Blank during Puff Volume Study |                     |                                                                |       |             |      |               |       |               |                  |      |               |      |                |                                            |       |                    |                           |       |                         |  |
| acetone, μg                                                                                                                                | BCV, FEL            | 1.69                                                           | 5.64  | 5.95        | 3.29 | 8.56          | 2.98  | 0.073         | 10               | 0.7  | 11.1          | 0.9  | 0.106          | 0.8                                        | 2.8   | 10.8               | 726                       | 16    | 67.21                   |  |
| butyraldehyde                                                                                                                              | BCV                 | 1.62                                                           | 5.41  | BDL         | BDL  | BDL           | BDL   | 0.008         | BDL              | BDL  | BDL           | BDL  | 0.008          | 0.812                                      | 2.71  | 10.8               | 92.5                      | 4.80  | 8.56                    |  |

**Table 2. Emissions Identified from ePen at Levels Too Low to Quantify <sup>a</sup>**

|                                                                                                                                                            |                  | ePen and air/<br>method blank<br>LOD and LOQ<br>per collection |       | ePen        |     |               |     |                         | air/method blank |     |               |     |                         | Kentucky reference 3R4F smoke measurements |       |                    |                           |      |                         |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|----------------------------------------------------------------|-------|-------------|-----|---------------|-----|-------------------------|------------------|-----|---------------|-----|-------------------------|--------------------------------------------|-------|--------------------|---------------------------|------|-------------------------|--|
|                                                                                                                                                            |                  |                                                                |       | puffs 1-100 |     | puffs 101-200 |     |                         | puffs 1-100      |     | puffs 101-200 |     |                         | LOD and LOQ<br>per collection              |       |                    | per cigarette<br>emission |      |                         |  |
| smoke<br>constituent                                                                                                                                       | toxicant<br>list | LOD                                                            | LOQ   | mean        | SD  | mean          | SD  | ePen/<br>puff           | mean             | SD  | mean          | SD  | air blank/<br>puff      | LOD                                        | LOQ   | number<br>of puffs | mean                      | SD   | 3R4F<br>p/puff          |  |
| propionalde-<br>hyde, $\mu\text{g}$                                                                                                                        | BCV, FEL         | 2                                                              | 6.67  | BDL         | BDL | NQ            | NQ  | 2.67 X 10 <sup>-2</sup> | BDL              | BDL | BDL           | BDL | 100 X 10 <sup>-2</sup>  | 1                                          | 3.34  | 10.8               | 133                       | 5    | 123                     |  |
| menthol, mg                                                                                                                                                | ECIG             | 0.012                                                          | 0.041 | NQ          | NQ  | NQ            | NQ  | 2.65 X 10 <sup>-4</sup> | NQ               | NQ  | BDL           | BDL | 1.63 X 10 <sup>-4</sup> | 0                                          | 0.001 | 10.5               | BDL                       | BDL  | 1.94 X 10 <sup>-4</sup> |  |
| diacetyl, $\mu\text{g}$                                                                                                                                    | ECIG             | 0.087                                                          | 0.29  | NQ          | NQ  | NQ            | NQ  | 1.89 X 10 <sup>-3</sup> | BDL              | BDL | BDL           | BDL | 4.35 X 10 <sup>-4</sup> | 0.44                                       | 1.45  | 10.6               | 266.52                    | 279  | 2.51 X 10 <sup>-3</sup> |  |
| anatabine,<br>ng                                                                                                                                           | ECIG             | 252                                                            | 841   | NQ          | NQ  | NQ            | NQ  | 5.47                    | BDL              | BDL | BDL           | BDL | 1.26                    | 50.4                                       | 168   | 11.1               | 30071                     | 1131 | 2709.07                 |  |
| anabasine, ng                                                                                                                                              | FEL              | 431                                                            | 1440  | NQ          | NQ  | NQ            | NQ  | 9.36                    | BDL              | BDL | BDL           | BDL | 2.16                    | 8.62                                       | 288   | 11.1               | 9364                      | 4.50 | 843.56                  |  |
| $\beta$ -nicotyrine,<br>ng                                                                                                                                 | ECIG             | 234                                                            | 779   | NQ          | NQ  | NQ            | NQ  | 5.07                    | BDL              | BDL | BDL           | BDL | 1.17                    | 47                                         | 156   | 11.1               | 9790                      | 149  | 882.01                  |  |
| NDMA, ng                                                                                                                                                   | FEL              | 1.78                                                           | 5.93  | BDL         | BDL | NQ            | NQ  | 2.37 X 10 <sup>-2</sup> | BDL              | BDL | BDL           | BDL | 8.89 X 10 <sup>-3</sup> | 0.59                                       | 1.98  | 10.5               | 8.46                      | 2.58 | 0.81                    |  |
| nickel, ng                                                                                                                                                 | BCV, FEL         | 28.48                                                          | 94.92 | NQ          | NQ  | NQ            | NQ  | 6.17 X 10 <sup>-1</sup> | NQ               | NQ  | BDL           | BDL | 3.80 X 10 <sup>-1</sup> | 285                                        | 9.49  | 10.9               | NQ                        | NQ   | 0.57                    |  |
| Compounds not higher than Air/Method Blank in original study, but measured higher from ePen than Air/Method Blank in Some Experiments of Puff Volume Study |                  |                                                                |       |             |     |               |     |                         |                  |     |               |     |                         |                                            |       |                    |                           |      |                         |  |
| propylene<br>oxide, ng                                                                                                                                     | FEL              | 156                                                            | 520   | BDL         | BDL | BDL           | BDL | 0.78                    | BDL              | BDL | BDL           | BDL | 0.78                    | 15.6                                       | 52    | 10.5               | 1.1 X 10 <sup>-3</sup>    | 90.7 | 103                     |  |

<sup>a</sup> Abbreviations: BCV, British Columbia List; BDL, below detection limit; ECIG, chemicals reported in e-cigarette emissions; F18, FDA current reporting list; FEL, full FDA established lists of HPHCs; LOD, Limit of detection; LOQ, limit of quantification; NNN, *N*-nitrosornicotine; NQ, not quantifiable; p/puff, per puff.



**Figure 1. Comparison of percent reduction in e-cigarette emissions in comparison to those from Ky3R4F under HCl puffing conditions.**

Figure 1 illustrates the substantial differences in emissions between e-cigarettes (Vype ePen) and conventional cigarettes (Ky3R4F), indicating that across all toxicant lists, Vype ePen consistently exhibited substantially lower exposure to toxicants compared to Ky3R4F, with reductions ranging between 92% and >99%, depending on the specific toxicant list. The comparison was conducted by analysing the percentage differences in per-puff emissions between Vype ePen and Ky3R4F, categorised according to four toxicant lists: the nine World Health Organisation (WHO) TobReg constituents, the 18 constituents on the Food and Drug Administration (FDA) abbreviated HPHC reporting list, the Health Canada list of 44 tobacco smoke toxicants, and the full FDA list of 96 HPHCs. Without subtracting air/method blank values, Vype ePen emissions were directly compared to Ky3R4F.

## DISCUSSION



The complexity of e-cigarette aerosol was compared to mainstream cigarette smoke by combining emissions data and findings from a puff volume study. **Results showed that 104 chemical measurands were not detected in the Vype ePen emissions, while 21 were present due to laboratory background.**



Among the remaining compounds, nine were too low to be quantified, leaving 16 compounds generated by the e-cigarette at quantifiable levels. **Eight of these compounds were carbonyls or alcohols linked to thermal decomposition, three were major e-liquid ingredients, three were impurities in pharmaceutical-grade nicotine, one was a metallic element from the e-cigarette coil, and one (chrysene) had an unknown origin.**



In contrast, **mainstream cigarette smoke contained approximately 100 compounds at quantifiable levels.** These findings highlight the comparative simplicity of e-cigarette aerosol compared to tobacco cigarette smoke.



In addition, the study demonstrated that the comparison of **HCl data with those reported by Roemer *et al.* were generally in good agreement, with most analytes within 30% of each other.**



Qualitative comparisons suggested consistency with previous findings regarding **low levels of tobacco-specific nitrosamines (TSNAs) and nicotine-related compounds.** Some differences were noted, such as the absence of toluene emissions in this study. Nevertheless, the main conclusion remained consistent in that e-cigarette emissions of many toxicants are significantly lower than those from tobacco cigarettes.



Overall, the data indicate that **e-cigarette aerosol contains substantially lower levels of toxicants of regulatory interest compared to tobacco cigarette smoke.** However, it must be emphasised that while significantly lower, **e-cigarette emissions may still pose a toxicologically significant dose,** highlighting the need for further quantitative risk assessment and clinical studies to better understand the health implications.

## CONCLUSIONS

The study highlights the relative **chemical simplicity of e-cigarette aerosols compared to tobacco cigarette smoke, with emissions of cigarette smoke harmful and HPHCs being significantly lower (82 to >99% lower) per-puff from e-cigarettes.**

These findings underscore the potential of **meticulous product design to minimise toxicant generation in e-cigarette devices.** While suggesting that e-cigarettes may offer a less harmful alternative to tobacco smoking, the study emphasises that the **presence of toxicants in e-cigarette aerosols indicates they are not risk-free.** Further research, including *in vitro* preclinical studies, biomarker analyses, and population studies, is necessary to confirm this hypothesis.

Additionally, this study **emphasises the significance of conducting air/method blank measurements and controlling chemical background to reduce contamination and errors in analytical data.** These measures are crucial for ensuring the accuracy and reliability of research in this field and provide valuable guidance for future studies.

### 3 Trendy e-cigarettes enter Europe: Chemical characterization of JUUL pods and its aerosols

Mallock N, *et al.* Trendy e-cigarettes enter Europe: chemical characterization of JUUL pods and its aerosols. *Arch Toxicol*; 2020;94:1985–1994.

**Electronic cigarettes have sparked debates among researchers and policymakers due to their potential benefits and risks.** While they offer a significant reduction in exposure to carcinogens and toxicants compared to traditional tobacco cigarettes, concerns persist regarding their impact on health.



**Studies suggest possible adverse effects on brain development and cardiovascular health from the nicotine in e-cigarettes.** Further investigation and assessment of these health implications are necessary. Critics also argue that smokers who transition to e-cigarettes may not fully quit nicotine consumption, thus using e-cigarettes as a long-term alternative instead.



The landscape of e-cigarettes is rapidly evolving, with two significant developments emerging: **"open systems"** allowing users to customise vapourisation settings and nicotine levels, and **"pod systems"** offering pre-filled, user-friendly devices. These innovations have contributed to a public health crisis in the United States.



**Pod systems often feature high nicotine salt formulations,** delivering nicotine efficiency comparable to that of traditional cigarettes. Despite the high nicotine content (up to 5%) additives like benzoic or salicylic acid are used to mitigate potential airway irritation by adjusting pH levels and free-base nicotine amounts, enhancing consumer tolerance. JUUL, the popular brand of e-liquids among adolescents, contains benzoic acid and up to 5% nicotine.



The **JUUL device** is flat with an elongated battery and a compartment where specific pods connect into. Its **discreet design** and low vapour production enables "stealth" vaping. The pods, are sold in four-packs, and are prefilled and disposable, containing a tank with a coil and wick, and a rectangular mouthpiece. Initially containing **20 mg/mL nicotine**, the **modified versions now offer 18 mg/mL and 9 mg/mL of nicotine**. Other ingredients include vegetable glycerol, propylene glycol, benzoic acid and flavourings.

#### AIM

The aim of this study by Mallock N, *et al.* (2020) was to establish a **baseline for nicotine and toxicant levels in the aerosol of both the original and modified versions of JUUL**, and to discuss technical aspects of vaping devices.



**Figure 2:**  
JUUL e-cigarette with a battery and flavoured pods



**JUUL launched in Germany** in 2018, complying with the European Union (EU) Tobacco Product Directive limiting the nicotine content to 20 mg/mL. While the United States (US) variants' nicotine levels were comparable to cigarettes, **no data exists for the European version**. Researchers anticipate lower nicotine delivery in the European version but speculate that vapour generation might be increased to offset the reduced nicotine content. A **new "Turbo" version** has been introduced in Germany, raising concerns over its heightened addictiveness.

#### METHODS

As part of the methodology, **benzoic acid and carbonyl compounds were quantified and the following assessed:**

Concentrations of nicotine, benzoic acid, propylene glycol and glycerol

Density and pH values of JUUL e-liquids

Several analytical assessments were conducted on the different flavoured JUUL pods, comparing initial and modified versions. **The nicotine content in the initial pods was lower than declared, which was also the case in the modified European pods.** Liquid composition, pH, and benzoic acid levels were consistent across flavours. The modified European version produced more total particulate matter (TPM), indicating increased vapour generation. The nicotine to benzoic acid ratio decreased in the modified version, suggesting higher benzoic acid application. Aldehyde formation patterns changed with pod design alteration, with increased acetone generation and decreased acetaldehyde and formaldehyde.

As shown in **Figure 3**, the American JUUL device emitted  $1.4 \pm 0.4$  mg of TPM per puff, showing comparable vapour generation to the initial European model, whereas **nicotine delivery in the American device was approximately three times higher** (approx.  $72 \pm 25$  µg per puff). The vapour generation of the modified European JUUL pods more than doubled compared to both the initial European pods and the US version, leading to a nicotine delivery similar to the high-nicotine US model.

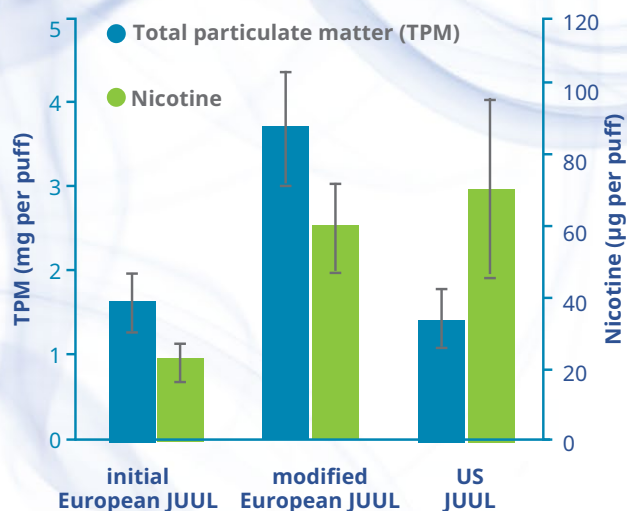
## RESULTS

This result has therefore confirmed that **technical adaptations can lead to enhanced nicotine delivery.** The increased vapourisation in the modified JUUL is attributed to a different wick material rather than higher power delivery, with an expansible wick material facilitating a faster and more stable resupply of unvapourised e-liquid to the coil. Although vapour generation by the modified JUUL is more stable, there are still significant **deviations in nicotine delivery consistency.** Despite containing the same volume of liquid, the modified version yields only half the number of puffs compared to the initial version, potentially impacting cost.

The other concern is that the modified JUUL version with increased nicotine delivery could lead to **higher addictiveness**, particularly among non-smokers who start vaping with such high nicotine levels per puff. Therefore **limiting nicotine delivery per puff might be a more effective regulation** than solely regulating the liquid nicotine content.

On the other hand, the **increased nicotine delivery could be advantageous for smokers** seeking harm reduction or cessation, as adequate nicotine delivery may help alleviate cravings and discourage dual use or a return to tobacco cigarettes. The **impact of high nicotine levels on complete cessation remains uncertain**, as eventually the use of e-cigarettes should also be discontinued.

The pod systems of an e-cigarette, typically use low electrical power and may offer advantages from a toxicological standpoint. This study showed that **levels of carbonyl compounds, in both the American and non-American JUUL devices, were comparable and lower than those found in tobacco cigarettes.** Furthermore, compared to other e-cigarettes, with higher power settings, the JUUL devices emitted comparatively lower levels of carbonyl compounds.



**Figure 3:**

Total particulate matter (TPM) in mg per puff and nicotine levels in µg per puff released during the first 160 puffs of 20 mg/mL initial European Rich Tobacco JUUL (20 pods), 18 mg/mL modified European Rich Tobacco JUUL (6 pods) and 58 mg/mL US-American Virginia Tobacco JUUL (5 pods).

## CONCLUSIONS

Therefore, **completely switching from tobacco cigarettes to e-cigarettes can reduce exposure to harmful tobacco cigarette toxins and potentially lower health risks for smokers.** However, non-smokers who initiate e-cigarettes may compromise their health and increase their risk of developing addiction. As such, **initiating e-cigarette consumption is strongly discouraged for non-smokers, regardless of age.**

**E-cigarettes and e-liquids are constantly evolving** products undergoing continuous development. This presents a **significant challenge for regulators and surveillance authorities**, who must not only keep pace with future product developments but also monitor existing products effectively.

## 4 Selected Harmful and Potentially Harmful Constituents Levels in Commercial e-Cigarettes

Maxim Belushkin, Donatien Tabin Djoko, Marco Esposito, Alexandra Korneliou, Cyril Jeannet, Massimo Lazzerini, and Guy Jaccard.

DOI: 10.1021/acs.chemrestox.9b00470 *Chem. Res. Toxicol.* 2020, 33, 657–668

### BACKGROUND



The article focuses on **analysing the levels of harmful and potentially harmful constituents (HPHCs) in commercial e-cigarettes**. E-cigarettes, also known as electronic cigarettes or vape pens, have gained popularity in recent years as an alternative to traditional combustible cigarettes. However, there is still ongoing debate about their safety and potential health risks.

### AIM



In this study, the researchers aimed to **evaluate the levels of 15 selected HPHCs** in e-cigarette aerosols for a comprehensive understanding of potential health risks associated with e-cigarette use.



A broad range of commercially available electronic cigarette (e-cigarette) systems were tested for levels of emissions of harmful and potentially harmful constituents (HPHC), with a particular focus on the carbonyls: acetaldehyde, acrolein, and formaldehyde.



**These HPHCs were chosen based on their known carcinogenic, respiratory, cardiovascular, and irritation effects.** The study included a total of 36 commercially available e-cigarette products, including disposable, cartridge-style, and tank-style e-cigarettes.

### METHODS

#### Commercial Devices and e-Liquid Samples:



**34 samples of commercial e-cigarette devices and 57 e-liquids were purchased in 2015, 2017, and 2018** at the point of sale or through Internet channels in U.K., Poland, France, South Africa, and Canada. Brands were selected to capture as much as possible the market diversity in terms of different manufacturers, device types (closed systems, such as disposable “cigalike” products or cartridge systems, and open systems with tanks and mods), and e-liquid designs.



The results of the study showed that the **levels of HPHCs in e-cigarette aerosols varied significantly between different products and brands**. Some products had higher levels of certain HPHCs, while others had lower levels. The study also found that **certain e-cigarette flavours and nicotine concentrations had an impact on the levels of HPHCs present in the aerosols**.



### RESULTS



Overall, the study concluded that **e-cigarettes do contain HPHCs**, albeit at lower levels compared to traditional cigarettes.



The results show that except for the levels of carbonyls, **all types of e-cigarettes performed in a similar manner, and emission levels for HPHCs were generally not quantifiable**.



However, the researchers emphasised the importance of **further research to fully understand the long-term health effects** of e-cigarette use, standardisation work on assessment of variable-voltage electronic cigarettes was emphasised.

### CONCLUSIONS

In conclusion, the article **highlights the need for continued monitoring and regulation of e-cigarettes** to ensure that consumers are aware of the potential risks associated with their use.

**Further research is necessary** to fully understand the **health implications** of e-cigarette use and to develop **evidence-based policies** to protect public health.

## 5 The Evolving E-cigarette: Comparative Chemical Analyses of E-cigarette Vapour and Cigarette Smoke

Anthony Cunningham, Kevin McAdam, Jesse Thissen and Helena Digard. *Front. Toxicol.* 2:586674. doi: 10.3389/ftox.2020.586674

### BACKGROUND



Electronic cigarettes (e-cigarettes) have gained popularity in recent years as a perceived safer alternative to traditional tobacco cigarettes. However, concerns have been raised regarding the potential health effects of e-cigarette vapour. This study aimed to compare the chemical compositions of e-cigarette vapour and cigarette smoke to provide insight into the potential risks associated with e-cigarette use.

### STUDY OBJECTIVES

The main objectives of the study were to conduct a **comparative analysis** of the **chemical constituents of e-cigarette vapour and cigarette smoke**, and to assess the potential health implications of e-cigarette use.

### METHODS



The researchers used a specialised analytical technique called gas chromatography-mass spectrometry (GC-MS) to analyse the chemical components of e-cigarette vapour and cigarette smoke. Samples were collected from both e-cigarettes and traditional cigarettes, and the results were compared to identify any differences in chemical composition.

#### Commercial Devices and e-Liquid Samples:

Cigarette smoke toxicants and e-cigarette emissions were measured by using Labstat standard methods, as described previously (Margham *et al.*, 2016). The 19 additional HPHCs proposed by the FDA were measured in e-cigarette aerosol using the following methods:

- Aromatic flavourants were determined in emissions from e-cigarettes by using Labstat method TMS-00175. In brief, e-cigarette aerosol was generated by an automated constant volume linear smoking machine.
- The sample was then analysed by gas chromatography-mass spectrometry (GC-MS).
- Propionic acid was determined in e-cigarette aerosol by using Labstat method TMS-00177.
- Acetic acid was determined in e-cigarette aerosol by using Labstat method TMS-00115A.

For all analyses, the researchers used 50 puffs of the ePen3 or ePen2 devices per collection. This was half the puff number used in previous studies (Margham *et al.*, 2016), as the ePen3 delivers approximately twice as much aerosol mass per puff. The researchers also conducted air/method blank determinations to identify any background contaminants or analytical artifacts.

### RESULTS



The study found that **e-cigarette vapour contained significantly lower levels of toxic chemicals compared to cigarette smoke**. Specifically, e-cigarette vapour had lower concentrations of harmful compounds such as nicotine, formaldehyde, and acetaldehyde.



Additionally, **e-cigarette vapour did not contain certain carcinogenic compounds found in cigarette smoke**, such as benzene and nitrosamines.

### CONCLUSIONS

The results of the study suggest that **e-cigarettes may pose fewer health risks** than traditional cigarettes due to their **lower levels of toxic chemicals**.

However, it is important to note that e-cigarettes **still contain some potentially harmful compounds**, and **further research is needed** to fully understand the long-term health effects of e-cigarette use.

Overall, this study provides valuable insights into the evolving nature of e-cigarettes and their potential impact on public health.



## 6 Electronic cigarettes for smoking cessation (Review)

Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Livingstone-Banks J, Morris T, Hartmann-Boyce J. *Cochrane Database of Systematic Reviews* 2024, Issue 1. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub8. doi: 10.3389/ftox.2020.586674

### BACKGROUND



**Electronic cigarettes (ECs)** have emerged as a potential smoking cessation aid. However, their **efficacy and safety compared to other cessation methods remain unclear**. People who smoke, healthcare providers and regulators want to know if ECs can help people quit smoking, and if they are safe to use for this purpose. This is a review update conducted as part of a living systematic review.

### STUDY AIM

To evaluate the effectiveness and safety of ECs in helping smokers achieve **long-term abstinence**, comparing them to non-nicotine ECs, other cessation treatments, and no treatment.

### METHODS



A systematic review was conducted, searching for randomised controlled trials (RCTs) that compared ECs to other interventions or control groups.

### STUDY OUTCOMES

#### PRIMARY OUTCOME

- Long-term smoking abstinence

#### SECONDARY OUTCOMES

- Safety, tolerability, and other relevant measures



### RESULTS

#### EFFECTIVENESS

- Nicotine ECs were more effective than nicotine replacement therapy (NRT) in helping smokers quit.
- Nicotine ECs were also more effective than non-nicotine ECs.
- Evidence for the effectiveness of nicotine ECs compared to usual care/no treatment was less certain due to study limitations.

#### SAFETY

- No significant differences in adverse events (AEs) were found between nicotine ECs and NRT or between nicotine and non-nicotine ECs.
- The overall incidence of serious adverse events (SAEs) was low across all study groups.

### CONCLUSIONS

**Nicotine ECs are more effective than NRT and non-nicotine ECs in helping smokers quit.**

While safety data is limited, no significant differences in AEs were found. More research is needed to assess the long-term safety and effectiveness of ECs and to identify optimal EC characteristics for smoking cessation.



## 7 Levels of Selected Carcinogens and Toxicants in Vapour from Electronic Cigarettes

Goniewicz Maciej Lukasz, PhD, Knysak Jakub, MPharm, Gawron Michal, MPharm, Kosmider Leon, MPharm, Sobczak Andrzej, PhD, Kurek Jolanta, MSc, Prokopowicz Adam, PhD, Jablonska-Czapla Magdalena, PhD, Rosik-Dulewska Czeslawa, PhD, Havel Christopher, Jacob Peyton III, PhD, and Benowitz Neal, MD. *Tob Control*. 2014 March ; 23(2): 133–139.  
doi:10.1136/tobaccocontrol-2012-050859.

### BACKGROUND



Electronic cigarettes (e-cigarettes) have gained popularity as alternatives to traditional cigarettes. While marketed as a safer option, the **exact composition and potential health risks of e-cigarette vapour remain unclear.**

### STUDY AIM

The study aimed to **analyse the levels of various potentially harmful compounds**, including carbonyls, volatile organic compounds (VOCs), nitrosamines, and heavy metals, in the vapour produced by different e-cigarette brands.

### METHODS



Researchers used a **modified smoking machine to generate vapour from 12 e-cigarette brands under controlled conditions.** A reference product, a medicinal nicotine inhaler, was also included for comparison. The vapour was collected and analysed using chromatographic and spectroscopic techniques to identify and quantify the target compounds.

### RESULTS



The vapour from e-cigarettes **contained some toxic compounds**, including formaldehyde, acetaldehyde, acrolein, nitrosamines, and trace amounts of metals.



**However**, the levels of these compounds were **9 to 450 times lower** than the levels found in cigarette smoke.



The **levels of some toxic compounds** in e-cigarette vapour were **comparable to the trace amounts** found in a **nicotine inhaler.**



### CONCLUSIONS

The findings suggest that **switching from traditional cigarettes to e-cigarettes could substantially reduce exposure to certain harmful compounds.** The study provides **evidence supporting the potential of e-cigarettes as a harm reduction strategy** for smokers unwilling to quit. However, **further research is needed to fully assess the long-term health implications** of e-cigarette use.

# 8 Chemical Composition and *in vitro* Toxicity Profile of a Pod-Based E-Cigarette Aerosol Compared to Cigarette Smoke

Kathryn Rudd, Matthew Stevenson, Roman Wiecek, Jutta Pani, Edgar Trelles-Sticken, Ole Dethloff, Lukasz Czekala, Liam Simms, Francesca Buchanan, Grant O'Connell, and Tanvir Walele. *APPLIED IN VITRO TOXICOLOGY* Volume 6, Number 1, 2020. DOI: 10.1089/aivt.2019.0015

## BACKGROUND



E-cigarette use has been rapidly increasing in recent years, with pod-based e-cigarettes being a popular choice among users. However, there is **limited research on the chemical composition and toxicity profile of aerosols produced by pod-based e-cigarettes** compared to traditional cigarette smoke.



Understanding the **potential health risks associated with pod-based e-cigarettes** is crucial for informing public health policies and promoting tobacco control efforts.

## STUDY OBJECTIVES

The study aimed to compare the chemical composition and *in vitro* toxicity profile of a pod-based e-cigarette aerosol to cigarette smoke.



Specifically, the researchers sought to assess differences in levels of harmful chemicals, such as nicotine and volatile organic compounds, as well as **evaluate the cytotoxicity and genotoxicity of the aerosols using *in vitro* cell-based assays.**

## METHODS



The study utilised a commercially available **pod-based e-cigarette device and a smoking machine to generate aerosols for analysis.** The researchers report comparative data for aerosol emissions and *in vitro* toxicity, using the neutral red uptake, the bacterial reverse mutation, and *in vitro* micronucleus assays, for a pod system e-cigarette compared with 3R4F reference cigarette smoke.



**Chemical analysis was performed to quantify levels of various constituents in the aerosols,** including nicotine, carbonyls, and volatile organic compounds. *In vitro* assays were conducted using human lung cells to assess the cytotoxic and genotoxic effects of the aerosols.

## RESULTS



The researchers found that the **pod-based e-cigarette aerosol contained lower levels of harmful chemicals,** such as nicotine and carbonyls, compared to cigarette smoke.



However, the **aerosol still exhibited cytotoxic effects on human lung cells,** with higher concentrations leading to increased cell death.



Additionally, the **aerosol induced genotoxic effects, as evidenced by DNA damage in the cells exposed to it.**



**E-cigarette aerosol was also found to be approximately 300-fold less cytotoxic** than cigarette smoke in the neutral red uptake assay.

## CONCLUSIONS

In conclusion, the study demonstrates clear differences of a tobacco cigarette versus a commercially available non-tobacco containing e-cigarette product in terms of emissions and *in vitro* toxicity profile.

**Pod-based e-cigarette aerosols may contain lower levels of some harmful chemicals** compared to cigarette smoke.

These findings highlight the importance of **further research on the health impacts of pod-based e-cigarettes** and the need for regulatory measures to protect public health.



# 9 Metal concentrations in electronic cigarette aerosol: effect of open-system and closed-system devices and power settings

Di Zhao, Ana Navas-Acien, Vesna Ilievski, Vesna Slavkovich, Pablo Olmedo, Bernat Adria-Mora, Arce Domingo-Relloso, Angela Aherrera, Norman J. Kleiman, Ana M. Rule, Markus Hilpert. *Environ Res.* 2019 July; 174: 125–134. doi:10.1016/j.envres.2019.04.003.

## BACKGROUND



Electronic cigarettes (e-cigarettes) have gained popularity as an alternative to traditional tobacco cigarettes. However, **concerns** have been raised about the **potential health risks** associated with the **inhalation of metal particles** present in **e-cigarette aerosol**.

## STUDY AIM

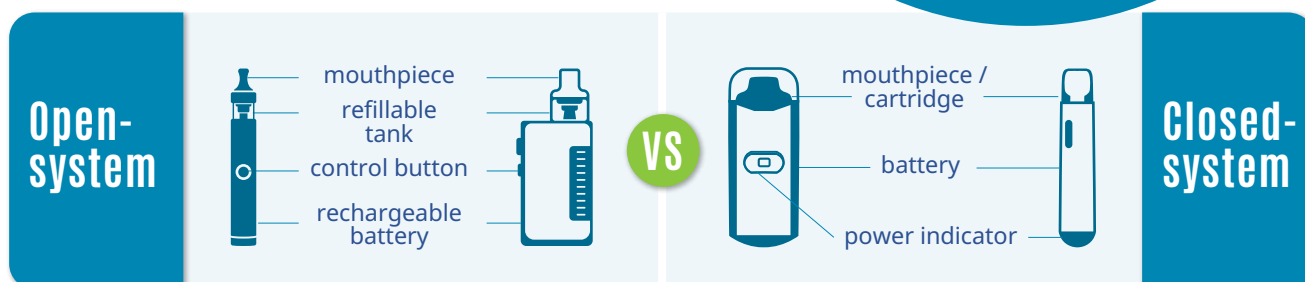


To quantify aerosol metal concentrations and to compare the effects of power setting and device type (open-system vs. closed-system) on metal release.



## STUDY OBJECTIVES

The study conducted by Zhao *et al.* aimed to **investigate the levels of metal concentrations in e-cigarette aerosols** produced by open-system and closed-system devices at different power settings. The study sought to **compare the metal content in aerosols** generated by different types of e-cigarettes and power settings, providing valuable insights into potential health risks associated with e-cigarette use.



**Figure 4. Comparison between open-system and closed-system device types**

Figure 4 illustrates the defining factors between an open-system versus a closed-system. An open system e-cigarette are the refillable tank and rechargeable battery. While closed-systems can be rechargeable, the defining factors are the pre-filled cartridges and disposable devices. *Adapted from: Mass General Research Institute*



## METHODS



The researchers used both open-system and closed-system e-cigarette devices to generate aerosols at various power settings. The aerosol samples were collected and analysed for metal concentrations using inductively coupled plasma-mass spectrometry.



Concentrations of 14 metals in e-cigarette aerosol collected via droplet deposition were measured using inductively coupled plasma mass spectroscopy. The levels of nine metals, including aluminium (Al), median arsenic (As), cadmium (Cd), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), nickel (Ni), and zinc (Zn), were measured in the aerosol samples.

## RESULTS



### The study found that metal concentrations varied among the different types of e-cigarette devices and power settings.

The levels of certain metals, such as nickel and chromium, were higher in aerosols produced by open-system devices compared to closed-system devices, except for aluminium (Al) and uranium (U).

|                                                                          | open-system                             |    | closed-system                           |
|--------------------------------------------------------------------------|-----------------------------------------|----|-----------------------------------------|
| For Cr, median (interquartile range) concentrations ( $\mu\text{g/kg}$ ) | 2.51 (1.55, 4.23) and 15.6 (7.88, 54.5) | vs | 0.39 (0.05, 0.72) and 0.41 (0.34, 0.57) |
| For Ni, concentrations ( $\mu\text{g/kg}$ )                              | 793 (508, 1169) and 2148 (851, 3397)    | vs | 1.32 (0.39, 3.35) and 11.9 (10.7, 22.7) |

#### For open-system device 1 (OD1),



median arsenic (As), chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), nickel (Ni), lead (Pb), antimony (Sb), tin (Sn), and zinc (Zn) concentrations increased 14, 54, 17, 30, 41, 96, 14, 81, 631, and 7-fold when the device power was increased from low (20 W) to intermediate (40 W) setting.

#### For open-system device 2 (OD2),



Cr and Mn concentrations increased significantly when device power was increased from low (40 W) to intermediate (120 W) setting, and then decreased significantly when power was further increased from intermediate (120 W) to high (200 W) setting.

**Additionally,** increasing the power setting of the e-cigarette devices also led to higher metal concentrations in the aerosols. Overall, the study identified differences in metal content between open-system and closed-system e-cigarettes, highlighting the influence of device type and power settings on metal exposure through e-cigarette aerosol.

Inhalation of 0% and 100% of samples from OD1, 7.4% and 88.9% from OD2 by typical e-cigarette users would exceed chronic minimum risk levels (MRL) of Mn and Ni, respectively. No MRL exceedance was predicted for the closed-system devices. A large fraction of users of OD1 (100%) and OD2 (77.8%) would be exposed to Ni levels higher than those from reference tobacco cigarette 3R4F.



## CONCLUSIONS

In conclusion, the study by Zhao *et al.* demonstrated that metal concentrations in e-cigarette aerosols are influenced by device type and power settings.

The findings suggest that open-system **e-cigarettes and higher power settings may result in increased metal exposure** during e-cigarette use.

These results have important **implications for public health**, emphasising the **need for further research and regulations** to minimise metal exposure and potential health risks associated with e-cigarette aerosols.



# 10 Tobacco smoking in Sub-Saharan Africa: A systematic review and meta-analysis

Belete H, et al. Tobacco smoking in Sub-Saharan Africa: A systematic review and meta-analysis. *Drug Alcohol Rev.* Feb 2025; 1-13.

In 2019, over 1.1 billion people smoked tobacco, causing around 8 million deaths and major health burdens, especially in low- and middle-income countries where over 80% of smokers live.



## AIM

To estimate smoking prevalence and frequency among both adolescents (10 – 17 years) and adults ( $\geq 18$  years) in SSA.

Global smoking rates have declined, but progress is slower in less developed regions, including Sub-Saharan Africa (SSA), where data is limited and likely underestimates actual prevalence.



Adolescent smoking remains concerning, with SSA showing a 23.5% lifetime prevalence in 2018 and no updated data to date. Male smoking rates are higher globally, with the gender gap especially wide in Asia and SSA.



The World Health Organization (WHO) aims to cut tobacco use by 30% by 2025, but projections suggest health and economic consequences will worsen, particularly in poorer regions.



SSA faces challenges in tobacco control due to political instability and limited resources, highlighting the urgent need for reliable data to guide effective policies.

## METHODS



**Databases** (PubMed, EMBASE, CINAHL, PsycINFO, African Journal Online, the Global Health Data Exchange and Google Scholar) were searched for peer-reviewed observational online studies (cohort and cross-sectional designs) published from January 2018 to 2023.



The prevalence of smoking (i.e., cigarette smoking, tobacco or nicotine use) was captured by:

- 'past 6-months'
- 'past 12 months' and
- 'lifetime use' (at any point in the participant's life)
- e-cigarette use was not included.



Daily smoking was defined as smoking at least once a day.



Weighted pooled prevalence was calculated using MetaXL, while meta-regression analysis was conducted with Stata version 17. For the estimation of pooled prevalence, the DerSimonian-Laird estimation method was used. The risk of bias tool was utilised to assess the quality of the studies.

## RESULTS

10 310 unique records were screened and 340 studies were included for full-text screening. A total of 195 studies were retained for the meta-analysis, which amounted to 1 304 723 participants.

## OVERALL SMOKING PREVALENCE

- Overall lifetime smoking prevalence in Sub-Saharan Africa (SSA) was 8.8% (CI 5.1%, 13.4%), with 10.8% (CI 4.0%, 19.9%), in the past year and 5.8% (CI 0.2%, 15.9%) in the past 6 months (Table 3).
- Among adolescents, lifetime smoking prevalence was 4.5% (CI 2.0%, 8.0%), with 4.1% (CI 0.0%, 13.4%) in the past year and 7.6% (CI 0.0%, 13.4%) in the past 6 months

— suggesting possible data inconsistencies.



**Table 3. Overall prevalence and gender differences in smoking by region in Sub-Saharan Africa.**

| Region                      | Overall prevalence |                     | Gender differences, male to female |                 |
|-----------------------------|--------------------|---------------------|------------------------------------|-----------------|
|                             | No. of studies     | Prevalence (95% CI) | No. of studies                     | RR (95% CI)     |
| <b>Lifetime prevalence</b>  | 143                | 8.8 (5.1, 13.4)     | 38                                 | 4.9 (3.8, 6.4)  |
| Southern SSA                | 26                 | 36.1 (21.2, 52.4)   | 9                                  | 3.3 (2.2, 4.9)  |
| Western SSA                 | 50                 | 5.2 (1.7, 10.2)     | 12                                 | 3.8 (2.2, 6.6)  |
| Eastern SSA                 | 64                 | 5.7 (3.0, 9.1)      | 16                                 | 6.5 (3.9, 10.8) |
| Central SSA                 | 2                  | 6.9 (4.5, 9.8)      | 1                                  | 7.0 (6.7, 7.3)  |
| <b>12 months prevalence</b> | 9                  | 10.8 (4.0, 19.9)    | —                                  | —               |
| Southern SSA                | 3                  | 16.9 (0.0, 71.1)    | —                                  | —               |
| Western SSA                 | 1                  | 11.1 (9.8, 12.5)    | —                                  | —               |
| Eastern SSA                 | 5                  | 8.2 (5.2, 11.8)     | 3                                  | 3.0 (1.6, 5.6)  |
| Central SSA                 | —                  | —                   | —                                  | —               |
| <b>6 months prevalence</b>  | 126                | 5.8 (0.2, 15.9)     | 48                                 | 4.0 (3.1, 5.2)  |
| Southern SSA                | 26                 | 20.2 (14.4, 26.6)   | 13                                 | 3.9 (2.7, 5.4)  |
| Western SSA                 | 56                 | 6.0 (4.1, 8.3)      | 21                                 | 4.5 (3.1, 6.8)  |
| Eastern SSA                 | 40                 | 8.1 (1.5, 18.5)     | 12                                 | 3.0 (1.9, 4.6)  |
| Central SSA                 | 1                  | 6.1 (5.3, 7.0)      | —                                  | —               |

Abbreviations: —, no data is available; CI, confidence interval; RR, relative risk; SSA, Sub-Saharan Africa.

- For adults, lifetime smoking prevalence was higher at 12.7% (CI 6.6%, 20.4%), with 12.1% (CI 2.6%, 26.2%) in the past year and 6.3% (CI 0.0%, 16.3%) in the past 6 months.

## PREVALENCE OF DAILY SMOKING

- Overall daily smoking prevalence was 3.5% (CI 0.0%, 9.5%) across all participants.
- Among adolescents, the daily smoking rate was 4.7% (CI 1.0%, 10.6%).
- For adults, daily smoking was more common at 8.2% (CI 4.9%, 13.8%).

## REGIONAL DIFFERENCES

| — in overall prevalence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | — among adolescents                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | — among adults                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li><b>Lifetime prevalence highest in:</b> <p>Southern SSA: 36.1%<br/>Central SSA: 6.9%<br/>Eastern SSA: 5.7%<br/>Western SSA: 5.2%</p> </li> <li><b>12-month prevalence:</b> <p>Southern SSA: 16.9%<br/>Western SSA: 11.1%<br/>Eastern SSA: 8.2%</p> </li> <li><b>6-month prevalence:</b> <p>Southern SSA: 20.2%<br/>Western SSA: 8.1%<br/>Central SSA: 6.1%<br/>Eastern SSA: 6.0%</p> </li> <li><b>By country:</b> <p><b>South Africa:</b><br/>Highest lifetime (37.0%) and 6-month (20.3%) prevalence.</p> <p><b>Namibia:</b><br/>Lifetime 28.9%, no 12-month data.</p> <p><b>Rwanda:</b><br/>Lifetime 19.8%, 6-month 8.6%.</p> </li> </ul> | <ul style="list-style-type: none"> <li> <p>Southern SSA: 19.8%<br/>Central SSA: 9.1%<br/>Eastern SSA: 4.6%<br/>Western SSA: 4.0%</p> </li> <li> <p>Western SSA: 11.1%<br/>Southern SSA: 3.0%</p> </li> <li> <p>Southern SSA: 22.9%<br/>Western SSA: 8.3%<br/>Eastern SSA: 4.7%</p> </li> <li> <p><b>Benin:</b><br/>Highest lifetime (43.5%), low 6-month (4.6%)</p> <p><b>South Africa:</b><br/>21.2% lifetime, 23.7% 6-month</p> <p><b>Botswana:</b><br/>18.2% lifetime, 13.0% 12-month</p> <p><b>Nigeria:</b><br/>Highest daily smoking (4.9%) among adolescents</p> </li> </ul> | <ul style="list-style-type: none"> <li> <p>Southern SSA: 37.1%<br/>Central SSA: 7.0%<br/>Eastern SSA: 6.3%<br/>Western SSA: 6.1%</p> </li> <li> <p>Southern SSA: 59.2%<br/>Eastern SSA: 8.2%</p> </li> <li> <p>Southern SSA: 19.5%<br/>Western SSA: 8.8%<br/>Eastern SSA: 7.2%<br/>Central SSA: 6.1%</p> </li> <li> <p><b>South Africa:</b><br/>59.2% (12-month), 19.6% (6-month)</p> <p><b>Namibia:</b><br/>28.9% (lifetime), no recent data</p> <p><b>Gambia:</b><br/>27.9% (lifetime), no recent data</p> <p><b>Burkina Faso:</b><br/>19.4% (lifetime), 10.7% (6-month)</p> <p><b>Rwanda:</b><br/>19.8% (lifetime), 8.0% (12-month)</p> <p><b>Congo:</b><br/>7.0% (lifetime), no 12- or 6-month data</p> </li> </ul> |



## DAILY SMOKING HIGHEST IN:



South Africa  
**24.5%**



Ghana  
**18.8%**



Seychelles  
**14.8%**



Kenya  
**11.8%**



## DISCUSSION

### SMOKING IN ADULTS

- **Adult lifetime smoking prevalence in SSA** was comparable to the United States (US) (19%).
- **Annual adult smoking prevalence in SSA** (12.7%) was higher than in Latin America/Caribbean (7.6%) and SSA's earlier estimates (2.9%).
- The **past 6-month smoking prevalence** in SSA adults is lower (6.3%) than the 15.5% in the US and may be due to differences in the population and data collection period.
- **Daily smoking** among adults in SSA (3.3%) is lower than Economic Co-operation and Development member countries (OECD) countries (16.5%), likely due to weaker health data systems and underreporting.



### SMOKING IN ADOLESCENTS

- **Adolescent lifetime smoking** (4.5%) is lower than prior SSA estimates (23.5%) and global youth figures (12.7%).
- **Annual adolescent smoking** (4.1%) is also lower than global youth figures (12.7%) and earlier SSA reports (5.8%).
- The **past 6-month smoking prevalence** (7.6%) was also lower than low- and middle income countries (14%) and Global School-based Student Health Survey (GSHS) 2013–2022 in Africa (10.1%).
- **Daily smoking** among adolescents (4.7%) is higher than in many low- and middle-income countries (1.2%) and the US in 2016–2019 (1.3–1.9%).
- **Differences in definitions and data collection periods** may explain discrepancies.



### GENDER AND SMOKING

- **Males consistently show higher smoking rates** than females, especially among adults (RR = 8.2 for daily smoking).
- The RR of smoking is also higher in males than females in low-income countries and more notably in SSA countries due to cultural and societal norms
- **Gender gap** in smoking is smaller in adolescents, possibly due to higher rates among younger females.
- Highlights the need for gender-sensitive tobacco control strategies.

## STUDY LIMITATIONS

- **Uneven distribution of studies** across SSA countries.
- **Potential publication bias** i.e. studies with favourable results are more likely to be published.
- **Inconsistencies in age classifications** between adults and adolescents.
- Cultural, language, economic and health system differences limit generalisability.
- **E-cigarette use was not assessed**, leaving a gap in understanding emerging trends.
- **Irregularities in data** (i.e., lower lifetime vs 12 month smoking) suggest inconsistent data monitoring.



These results underscore the **growing rates of tobacco use** in SSA, reinforcing the idea that high smoking prevalence is **increasingly concentrated in low-income regions like SSA**



Without collective action, smoking rates in SSA could rise, triggering serious health and economic issues.



The smoking epidemic is shifting toward low-income countries.



Without urgent policy action, SSA risks falling short of the WHO's 2025 goal to cut tobacco use by 30%.



Weak smoking policies in Africa demand urgent regulation of tobacco marketing banned in higher-income countries for decades.



South Africa's Parliament is reviewing the Tobacco Control Bill.

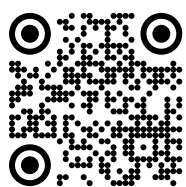
## CONCLUSIONS



Smoking is prevalent in SSA, with a notably high 12 month smoking rate among adults at 12.7%. Despite this, comprehensive national data on smoking prevalence and frequency remain scarce across many SSA countries. To bridge this gap, it is essential for nations in the region to strengthen their tobacco monitoring systems and adopt innovative strategies for smoking prevention and trend surveillance. Equally important is the consistent enforcement of international tobacco control measures to effectively reduce smoking rates.

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# ADVOCACY IN ACTION

