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1 Q&A Dialogue

Q

Alex

Roberto, there is a lot of concern that vape aerosols contain toxic substances, especially metals and other harmful chemicals. What does the evidence actually show?

Roberto

It is true that e-cigarette aerosols can contain toxic compounds.

However, when devices are used as they were designed, these substances usually appear only as **very small trace amounts**. Users can actually sense when a device is working properly - if the aerosol tastes normal and feels comfortable, the device is operating as intended and toxicity remains minimal.

A

On this issue of toxic compounds in e-cigarette aerosols, I recommend you to look at my Substack entries (especially posts 5 and 6):

robertosussman.substack.com/publish/posts/published

SCAN
THE QR TO
READ THE
SUBSTACK



with
Dr. Roberto Sussman
& **Dr. Alex Wodak**

Q

Alex

So the harm reduction claim for vaping compared with smoking is evidence-based?

Roberto

Yes. The reduction in harm when switching from cigarettes to vaping is not just an opinion.

A

It is supported by empirical evidence based on the properties of the emissions. Cigarette smoke contains far higher levels of harmful compounds. Some studies report high toxicity in vape aerosols, but these are often conducted under **abnormal laboratory conditions** that real users would never tolerate.

Q

Alex

You mentioned metals in vape aerosols. This is often used as an argument against e-cigarettes. What is the reality?

Roberto

Metals such as nickel, lead, cadmium, and copper have been detected in e-liquids and aerosols, but detection alone does not mean there is a health risk.

A

Similar trace metals are found in **many everyday exposures**, including food, medicines, and even the air we breathe. What matters is the **dose**, not simply whether a substance can be detected.

Q

Alex

So are the metal levels in vaping significant?

Roberto

Under normal vaping conditions, the concentrations are extremely low, often at nanogram levels.

A

In addition, metals appear mainly as metal oxides, not pure elements. Studies reporting high metal levels typically used **overheated devices in laboratory experiments**, producing aerosols with a burnt taste that real users would find unpleasant and avoid. In the end authors report high metallic content assuming this is "normal" use. Unfortunately, the media takes care to spread these results and panic and disinformation spreads.



Alex

Does the same issue apply to other chemicals like aldehydes?



Roberto

Yes. Organic by-products such as aldehydes and other carbonyl compounds can form when e-liquids are heated.

Under normal conditions they appear only in **very small concentrations**, often close to the detection limit of instruments. High levels usually occur when devices are **overheated in laboratory tests**, again producing aerosols that people would not actually inhale.



Alex

Have you studied this issue extensively?

the research



Roberto

Yes. Together with colleagues Sébastien Soulet and Federica Sipala, I have co-authored several open-access reviews examining emissions from e-cigarettes and heated tobacco products.

SCAN THE QRs TO READ THE OPEN-ACCESS REVIEWS



Critical Review of the Recent Literature on Organic Byproducts in E-Cigarette Aerosol Emissions
doi.org/10.3390/toxics10120714



A Critical Review of Recent Literature on Metal Contents in E-Cigarette Aerosol
doi.org/10.3390/toxics10090510



Analytical methods and experimental quality in studies targeting carbonyls in electronic cigarette aerosols
doi.org/10.3389/fchem.2024.1433626



Aerosol Emissions from Heated Tobacco Products: A Review Focusing on Carbonyls, Analytical Methods, and Experimental Quality
doi.org/10.3390/toxics11120947



Critical Appraisal of Exposure Studies of E-Cigarette Aerosol Generated by High-Powered Devices
doi.org/10.2478/cttr-2025-0019

These papers analyse metals, carbonyls, and experimental methods used in laboratory studies, and they highlight how unrealistic testing conditions can lead to misleading conclusions.



Alex

And why is this important for public health discussions?



Roberto

Because some laboratory studies with unrealistic conditions are widely circulated and can create unnecessary alarm.

To understand the real risks, it is essential to evaluate whether studies use **realistic puffing conditions, proper analytical methods, and transparent experimental procedures**. Only then can we accurately assess the emissions and the potential benefits of tobacco harm reduction.

Dr. Alex Wodak

Member of the Order of Australia (AM)

Doctor Alex Wodak AM, a retired physician, was the Foundation Director of the Alcohol and Drug Service at St Vincent's Hospital in Sydney, Australia (1982-2012). He was very involved in harm reduction efforts to control HIV among and from people who inject drugs initially in Australia but subsequently in many Low- and Middle-Income Countries. He was the Foundation President of the International Harm Reduction Association (1996-2004). Dr Wodak is the Tobacco Harm Reduction Adviser to the Harm Reduction Australia Board. He has never received funds from the tobacco or vaping industries.

Dr. Roberto Sussman

Associate Professor, National University of Mexico (UNAM)

Doctor Roberto Sussman is an Associate Professor and senior researcher at the Institute of Nuclear Sciences at the National Autonomous University of Mexico (UNAM). He is a prominent advocate for tobacco harm reduction, specifically focusing on the legalisation and regulation of non-combustible nicotine products (e-cigarettes and heated tobacco products) in Mexico.

2 Critical Review of the Recent Literature on Organic Byproducts in E-Cigarette Aerosol Emission

Soulet S, Sussman RA. Critical Review of the Recent Literature on Organic Byproducts in E-Cigarette Aerosol Emissions. *Toxics*.2022;10:714.

Aim

To critically assess current laboratory testing of electronic cigarette (EC) emissions

by analysing experimental methodologies, with a particular focus on the detection of organic byproducts (aldehydes, carbon monoxide, and free radicals), while also examining the physical principles underlying optimal EC operation, defining conditions representative of typical vaping habits, and providing a comprehensive evaluation of the existing literature. [E1-2,p2,p42,E3,p11]

Methods

38 A total of 38 articles

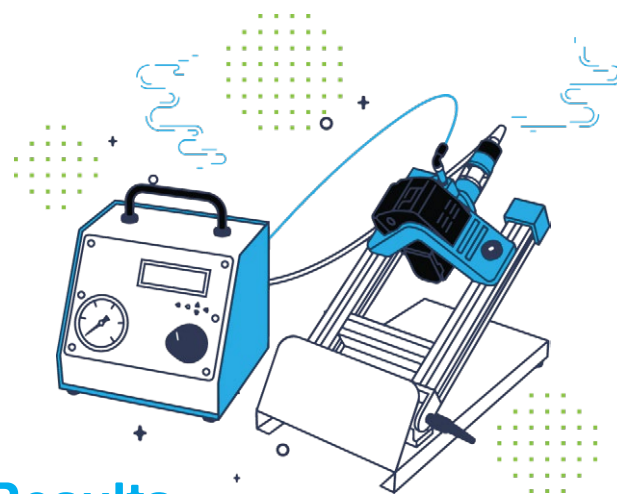
- published after January 2018
- including 2 previous review articles

36 A total of 36 studies

- 22 studies on **carbonyls and byproducts**
- 3 on **carbon monoxide (CO)**
- 4 on **reactive oxygen species (ROS)**
- 5 on **byproduct formation**
- 2 comparing **carbonyls with nicotine**

Reviewed with the following criteria: [E1,p2,E3,p11]

- ✓ **Experimental consistency** [E4,p11]
Alignment of experimental conditions (puffing parameters, devices, analytical methods) with realistic user behaviour.
- ✓ **Reproducibility of experiments** [E4,p11]
Studies must provide sufficient detail for replication, including device specifications, coil information, e-liquid composition, and vaping regime (puff duration, airflow, frequency, number of puffs).
- ✓ **Toxicological confidence** [E4,p11]
Clear reporting of results to enable accurate estimation of daily exposure and comparison with established toxicological limits. Reliability depends on consistency and reproducibility; otherwise, risk assessments may be inaccurate or not generalisable.
- ✓ **Old and/or used devices** [E4,p11]
Studies must report device condition, storage, and justification for use, as ageing may affect performance and emissions.



Results

Among 35 studies quantifying organic byproducts, **the most common issue was testing sub-ohm devices with a CORESTA or CORESTA-like protocol.**

Of these, 10 studies used excessively high power, likely causing overheating and producing results irrelevant to typical users, while 8 used power near recommended levels, with limited relevance to a small minority. [E5,p36]

35

studies



12

unreliable

12

restricted reliability

11

reliable

Toxicological confidence grading indicated 12 studies as unreliable, 12 as of very restricted reliability, and 11 as reliable, closely linked to these testing issues.

Overall, **this highlights frequent inappropriate testing of sub-ohm devices,** likely leading to overestimation of health risks and emphasising the need to improve laboratory standards. [E6,p36-37]

Table 1. Studies on carbonyls 2018–2022. [E7,p37]

	Experimental Consistency		Reproducibility			
First Author	Vaping Regime	Power Range	Emissions Generation	Trapping & Analysis	Toxicological Confidence	Comments
CARBONYLS						
2018						
Vreeke	+/-	+/-	✓	✓	●	1
Korzun	✓		✓	✓	●	1
El Hellani	+/-	✓	✓	✓	●	1 3 3
2019						
Beauval	+/-	+/-	✓	✓	●	2
Ooi	x	x	?	?	●	1 3 3 3 3
Balushkin	+/-	+/-	✓	✓	●	2 10
Reilly	✓	✓	✓	✓	●	-
2020						
Son	✓	+/-	✓	✓	●	3
Talih	x	+/-	✓	✓	●	1 3
Zelinkova	x	✓	✓		●	2
Uchiyama	x	x	✓	x	●	1 3 3
Cunningham	✓	✓	✓	✓	●	-
Noël	x	x	?	✓	●	1 3 3
Mallock	✓	✓	✓	✓	●	-
2021						
Chen	✓	✓	✓	✓	●	-
Crosswhite	✓	✓	✓	✓	●	-
Li	+/-	✓	✓	✓	●	2 3 4
Yan	x	x	✓	✓	●	1 3 4
Tehrani	x	x	✓	✓	●	1 3 3 3 3
Cancelada	+/-	+/-	✓	✓	●	2 3
2022						
Xu	✓	✓	✓	✓	●	-
Visser	✓	✓	✓	✓	●	-

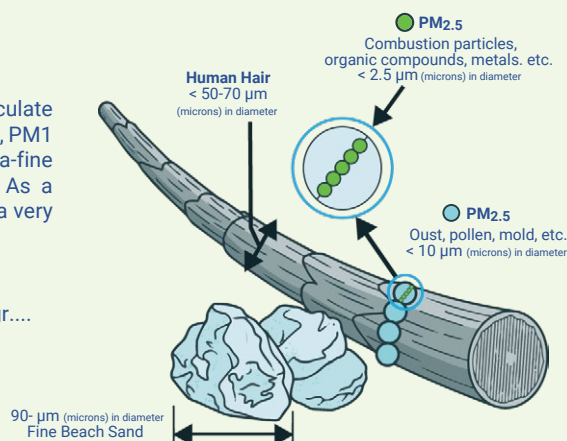
Table 2. Studies on CO, ROS, degradation pathways and nicotine vs. carbonyls. [E8,p38]

	Experimental Consistency		Reproducibility		Toxicological Confidence	Comments
First Author	Vaping Regime	Power Range	Emissions Generation	Trapping & Analysis		
CO						
Casebolt	x	x	+/-	✓	●	1 3
ElHellani	x	x	+1	✓	●	1 3 4
Son	+/-	✓	✓	✓	●	2 3
ROS						
Bitzer(a)	x	+/-	✓	✓	●	2 3
Bitzer(b)	x	x	✓	✓	●	2 3
Son	✓	+/-	✓	✓	●	3 4
Haddad	x	x	+/-	✓	●	1 3 3
Degradation reactions & carbonyl formation						
Jensen	✓	✓	✓	✓	●	9
Wang	N/A	+/-	+/-	✓	●	3
Li	✓	✓	✓	✓	●	3 9
Melvin	✓	✓	+/-	✓	●	3 9 10
Jaegers	N/A	N/A	✓	✓	N/A	-
Nicotine compensation vs. carbonyls						
Dawkins	✓	✓	✓	✓	●	-
Kosmider	✓	✓	✓	✓	●	-

Key: Experimental Consistency: ✓: Fully Consistent; +/-: Restricted Consistency; x: Completely Inconsistent; ?: Missing Information | **Toxicological Confidence:** ●: Fully Reliable; ●: Restricted Reliability; ●: Completely Unreliable; ●: Missing Information | **Comments:** 1: Sub-ohm device with CORESTA high powers; 2: Sub-ohm device with CORESTA recommended powers; 3: Other forms of inconsistent protocol; 4: Incorrect computation of exposure; 5: Outliers not properly identified; 6: Devices not fully identified; 7: Testing power not identified; 8: Too frequent puffs; 9: Too long puffs; 10: Used old devices [E9,p38]

Very small "particles" deposit deeply in the lungs. Sizes of particulate matter "PM" (particles in aerosols) are classified as PM₁₀, PM_{2.5}, PM₁ (all particulates below 10, 2.5 and 1 micrometers), while "ultra-fine particles" (UFPs) are much smaller (below 0.3 micrometers). As a reference, human hair thickness is between 50-70 micrometers, a very large molecule is 0.001 micrometers.

Figure 1. Comparison of diameters between a hair, a sand gr....



Discussion

Testing Sub-Ohm Devices with Insufficient Airflow [E11,p38-39]



CORESTA protocols, designed for low-powered, MTL devices, are unsuitable for sub-ohm devices used for DTL vaping.



Half (18 of the 35 studies) of the reviewed studies tested sub-ohm devices with CORESTA-like parameters, often at excessive power, causing overheating and unrealistic results.



Only a small minority (~5% of vapers) use sub-ohm devices in MTL style, making most results irrelevant for the majority.



Sub-ohm devices are typically used by experienced ex-smokers; most vapers use low-powered devices or disposables.

Arbitrarily Fixing Power, Temperature and Puff Duration [E12,p39-40]



Some studies fixed combinations of puffing parameters (power, temperature, airflow, puff volume), which do not reflect realistic sub-ohm use.



Fixed parameters neglect the dynamic interaction between airflow, puff volume, power, and temperature needed for proper aerosol formation.



Lack of experimental validation for device-reported temperatures makes these approaches artificial and disconnected from user experience.

Conclusions

Most studies failed to meet minimal consistency criteria, particularly in testing high-powered sub-ohm devices with CORESTA or CORESTA-like protocols.

Physical Limitations on Chemical Processes [E13,p40-41]



Laboratory control of temperature does not replicate the dynamic, open-system environment of vaping devices.



Assumptions that higher power linearly increases vaporisation and chemical degradation are conceptually flawed.



Experiments using closed systems, ovens, or reactors exaggerate byproduct formation and are not representative of real device operation.



Realistic vaping involves specific power ranges and open-system thermodynamics; extrapolations from inappropriate lab conditions lead to overestimation of risks.

Assessment of Risk Communication [E14-15,p41-42]

Laboratory testing of EC emissions aims to provide objective guidance on health risks from HPHCs. Many studies report potential hazards and recommend regulatory restrictions, but most fail to meet basic consistency criteria, limiting the reliability of their risk assessments.

A major issue is testing sub-ohm devices with CORESTA-like protocols. Risk assessments from low-powered pods and disposables are generally inapplicable to the majority of users.

Additional flaws include miscalculated exposures, reliance on outlier data, insufficient methodological details, excessive puffing frequencies, and testing of old devices without reporting storage. The most reported HPHCs are aldehydes (formaldehyde, acetaldehyde, acrolein) and free radicals, which are negligible in low-powered devices tested under consistent protocols.

Involving vapers in testing procedures could improve the objectivity of risk assessments, though this has rarely been implemented.



Many studies used excessive power or unrealistic puffing parameters, producing overheating and “dry puff” conditions, making risk assessments largely irrelevant for the majority of vapers. Other common issues include insufficient reporting of device and experimental details, miscalculated exposures, reliance on outliers, testing of old devices, and excessive puff frequencies. Despite residual health risks from harmful and potentially harmful constituents, well-designed, self-consistent studies confirm that vaping is substantially safer than smoking. [E16,p42-43]

The review emphasises the urgent need to update laboratory standards, incorporate realistic usage and end-user input, and develop databases of optimal regimes, longitudinal cohort studies of puffing behaviour, inbuilt device safety features, and guidelines for maintenance and storage of devices. Laboratory testing remains essential for health risk estimation, quality control, product comparison, and technological development, but only when aligned with realistic usage and physical constraints of efficient aerosol generation. [E17,p44]

3 A Critical Review of Recent Literature on Metal Contents in E-Cigarette Aerosol

Soulet S, Sussman RA. Critical Review of Recent Literature on Metal Contents in E-Cigarette Aerosol. *Toxics*. 2022;10:510.

Aim

To critically evaluate 12 laboratory studies (post-2017) on metal element content in electronic cigarette (EC) aerosols, with a focus on assessing the compatibility of puffing protocols with realistic usage patterns and the implications for risk evaluation through comparison with toxicological reference standards. [D1,p1-2,D2,p30]

Definitions and Methods

Realistic Usage Conditions and Toxicological Markers

1 Vaping Styles [D3,p3-4]

- Two main vaping styles exist: Mouth-to-Lung (MTL) and Direct-to-Lung (DTL).
- MTL is the most common, especially among beginners and former smokers, and mimics cigarette smoking with lower airflow and smaller puff volumes.
- DTL is used by more experienced users and involves deeper inhalation, larger puff volumes, higher airflow, and longer puff duration, resulting in greater aerosol intake.
- DTL requires higher-powered devices and differs significantly from smoking behaviour.
- Current standard puffing protocols (CORESTA) are unsuitable for DTL devices, and no standardised testing method exists for this style.

2 Puffing Habits of Vapers in Natural Settings [D4,p4-5]

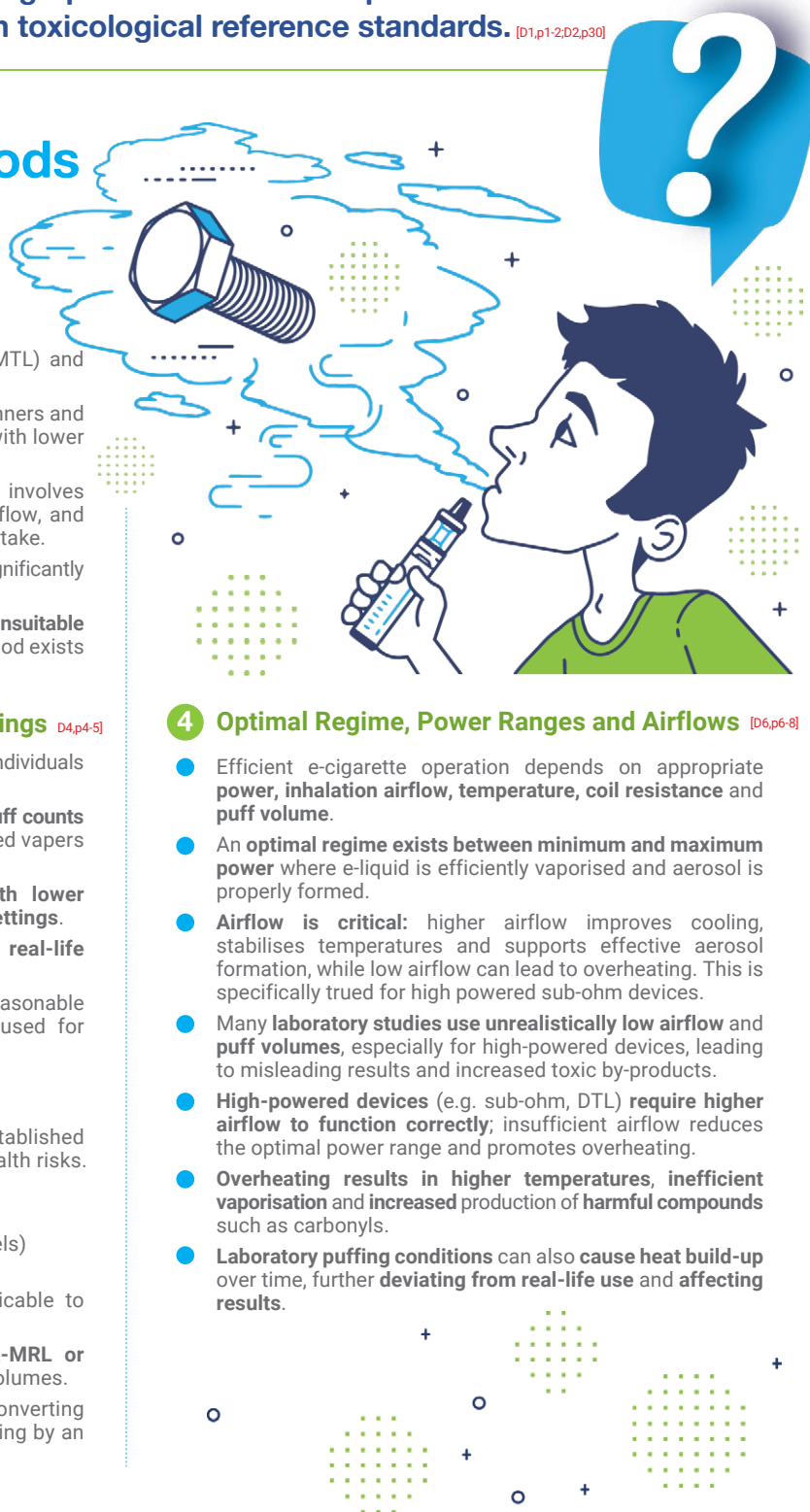
- Real-life vaping behaviour varies widely between individuals and over time.
- Earlier studies on older devices show lower daily puff counts (156–225), while newer devices used by experienced vapers show higher counts (around 272–338).
- Puff numbers and duration can increase with lower nicotine concentrations and adjustable device settings.
- Intervals between puffs are generally longer in real-life settings than in laboratory conditions.
- An average of 250 puffs per day is considered a reasonable estimate for typical vaping behaviour and is used for exposure calculations.

3 Toxicological References [D5-6,p5]

- Laboratory results are compared against established toxicological benchmarks to assess potential health risks.
- Three main references are used:
 - PDE-ICH (pharmaceutical inhalation limits)
 - ATSDR-MRL (safe environmental exposure levels)
 - NIOSH REL/PEL (workplace exposure limits).
- PDE-ICH is prioritised as it is strict and applicable to general population inhalation exposure.
- When PDE-ICH values are unavailable, ATSDR-MRL or NIOSH limits are used with adjusted inhalation volumes.
- Daily exposure to metals is estimated by converting laboratory results to per-puff values and multiplying by an average of 250 puffs per day.

4 Optimal Regime, Power Ranges and Airflows [D6,p6-8]

- Efficient e-cigarette operation depends on appropriate power, inhalation airflow, temperature, coil resistance and puff volume.
- An optimal regime exists between minimum and maximum power where e-liquid is efficiently vaporised and aerosol is properly formed.
- Airflow is critical: higher airflow improves cooling, stabilises temperatures and supports effective aerosol formation, while low airflow can lead to overheating. This is specifically true for high powered sub-ohm devices.
- Many laboratory studies use unrealistically low airflow and puff volumes, especially for high-powered devices, leading to misleading results and increased toxic by-products.
- High-powered devices (e.g. sub-ohm, DTL) require higher airflow to function correctly; insufficient airflow reduces the optimal power range and promotes overheating.
- Overheating results in higher temperatures, inefficient vaporisation and increased production of harmful compounds such as carbonyls.
- Laboratory puffing conditions can also cause heat build-up over time, further deviating from real-life use and affecting results.



Findings [D7,p8-9]

Table 3. Laboratory studies on metal content in aerosol emissions published post 2017.

Study	Device and Properties	Puffing Parameters	Analytic Technique
Grey <i>et al.</i> , 2020	Juul myblu Vuse Alto	3 s, 30 s, 55 mL, 16.67 mL/s 50 puffs	ICP-MS
Halstead <i>et al.</i> , 2019	Juul Blu Vuse Obsolete disposables	3 s, 30 s, 55 mL, 16.67 mL/s 75 puffs	ICP-MS
SECOND GENERATION			
Beauval <i>et al.</i> , 2017	Lounge	3 s, 30 s, 55 mL, 16.67 mL/s 96 puffs	Various techniques
Palazzolo <i>et al.</i> , 2017	eGO	5 s, 10 s, 6.67 mL/s 45 puffs	Scanned microscopy
Williams <i>et al.</i> , 2019	EgoC Twist Protank EgoX Twist Nautilus iTaste MVP Kanger	4.3 s, 60 s, 17-81 mL, 4-19 mL/s 60 puffs: continuous & 10 min clusters	ICP-OES ICP-OES ICP-OES
THIRD GENERATION TANK MODELS			
Zhao <i>et al.</i> , 2019 & 2022	Smok, 6-220 W, 0.6 Ω Istick, 0-85 W, 0.2 Ω	4 s, 26 s, 66 mL, 16.67 mL/s 15-120 puffs 15-120 puffs	ICP-MS
Kapiamba <i>et al.</i> , 2022	Voofoo, 5-60 W Unspecified resistance	2 s, 60 s, 35 mL, 16.67 mL/s 30 puffs	ICP-MS
Liu <i>et al.</i> , 2020	Unspecified 3rd Generation Tank Model	4 s, 30 s, 66 mL, 16.67 mL/s Unspecified puff number	ICP-MS Arsenic Species
Williams <i>et al.</i> , 2019	Smok Alien, sub-ohm iPV6X, Tsunami 2.4 RDA + Nemesis Clone RDA	4.3 s, 60 s, 30.1 mL, 7 mL/s 60 puffs	ICP-OES
Olmedo <i>et al.</i> , 2018	56 assorted tank devices	4 s, 30 s, 66 mL, 16.67 mL/s 30-50 puffs	ICP-MS
Halstead <i>et al.</i> , 2019	Joyetech eGO 2016 Model	3 s, 30 s, 55 mL, 16.67 mL/s 50 puffs	ICP-MS
Kim <i>et al.</i> , 2018	Aspire Cleito, 0.2 Ω Kanthal coil, cotton wick	4 s, 18 s, 50 mL, ~20 mL/s 150 puffs	GC-MS
PODS			
Kapiamba <i>et al.</i> , 2022	Vapor4Life Juul	2 s, 60 s, 35 mL, 16.67 mL/s 30 puffs	ICP-MS
		2 s, 60 s, 35 mL, 16.67 mL/s 30 puffs	ICP-MS
Chen <i>et al.</i> , 2021	Juul (not intense) Juul (intense)	4 s, 30 s, 55/70 mL, 16.67 mL/s 3 blocks of 100 puffs	ICP-MS
		6, 30 s, 110 mL, not specified 3 blocks of 100 puffs	ICP-MS
Zhao <i>et al.</i> , 2019 & 2022	myblu Juul	4 s, 11 s, 66 mL, 16.67 mL/s 50-100 puffs	ICP-MS
		4 s, 11 s, 66 mL, 16.67 mL/s 290-330 puffs	ICP-MS

Abbreviation: ICP-MS - Inductively Coupled Plasma Mass Spectroscopy

Discussion

1 High Powered Sub-Ohm Devices [D8,p24]

- All studies **testing** high powered sub-ohm devices (mostly used and recommended for DTL vaping) did so **by means of CORESTA or CORESTA-like puffing protocols** that are **appropriate** for low powered devices used for MTL vaping, **but not for DTL vaping** that requires much larger airflows and puff volume
- Most findings showed metal **exposure below toxicological limits**.
- Three studies reported **high metal levels**, likely due to **unrealistic overheating** conditions.
- Overall, testing conditions **do not reflect real-world use**, limiting relevance.

2 Pod Devices [D9,p24-25]

- Three out of five studies found negligible **metal levels below safety thresholds**.
- One study reported **unusually high metals** (copper, nickel, lead) in a specific cartridge, **likely due to defects** (e.g. corrosion or leaching).

3 Testing Old Devices: Corrosion [D10,p25]

- **Several studies tested aged devices** acquired years before testing
- No studies reported **storage conditions**.
- **Older devices** showed **higher metal levels** due to corrosion and leaching.
- **Corrosion** is more likely in closed systems **with long storage times**.
- Such conditions are **not representative of typical user behaviour** (most users consume within a few days of purchase).

4 Comparison with Toxicological References [D11,p25-26]

- Some studies **overestimated exposure** due to incorrect assumptions (e.g. puff volume vs tidal volume, continuous exposure).
- Vaping **exposure is intermittent** and much **shorter than assumed** in comparisons.
- **Proper calculations show** most metal exposures fall **below occupational safety limits**.
- Comparing concentrations **without accounting for exposure time can be misleading**; dose-based comparisons are more appropriate.

5 Information Vacuum [D12,p27]

- Many studies **lack key details** on devices, puffing protocols, and results.
- **Missing data** (e.g. coil resistance, device specifications) limits interpretation.
- Some studies **grouped incompatible data**, reducing reliability.
- **Poor reporting** hinders reproducibility and evaluation.



6 Aerosol Collection [D13,p27]

- Ceramic containers and glass and quartz fiber filters, vary widely and may introduce **contamination**.
- Leaching from certain materials (e.g. tubing, filters) can **overestimate metal levels**.
- Only two studies **adequately addressed contamination risks**.
- **Improved, standardised methods** are **needed** for accuracy.

7 Metal Biomarkers [D14,p28]

- Three studies showed **no significant difference in metal levels between vapers and non-users** when metal biomarkers were measured on body fluids of human vapers as opposed to machines.
- Suggests limited concern for **metal exposure** under normal acute vaping conditions.
- **Biomarkers** provide **more realistic evidence** than laboratory aerosol studies.

8 Comparison with Tobacco Smoke [D15,p28]

- **Several studies tested aged devices** acquired years before testing
- No studies reported **storage conditions**.
- **Older devices** showed **higher metal levels** due to corrosion and leaching.
- **Corrosion** is more likely in closed systems **with long storage times**.
- Such conditions are **not representative of typical user behaviour** (most users consume within a few days of purchase).

8 Comparison with Toxicological References [D11,p25-26]

- **Comparisons of metals** are common but **must be interpreted carefully**.
- **Metal profiles differ** between vaping aerosol and tobacco smoke.
- **Some metals are higher in EC aerosol** (nickel and zinc), **others are higher in tobacco smoke** (cadmium/mercury).
- **Direct comparisons may be misleading** due to different sources and compositions.

Assessment of the Risk Communication

[D16,p28-29]



Most of the reviewed metal studies reported alarmingly high health risks from metals in e-cigarette emissions, often leading to calls for stricter regulation, despite most findings being below toxicological limits and affected by significant methodological flaws.



Risk communication is therefore questioned, as it frequently relies on unrealistic laboratory conditions that do not reflect real-world vaping, leading to exaggerated conclusions.



Comparisons with tobacco smoke are often misleading, as metals play only a minor role in cigarette toxicity and are present merely as trace byproducts in e-cigarette aerosols.



The studies compared measured metal levels from 12 experiments with strict safety limits (PDE-ICH and MRL-ATSDR) for 14 metals.



Cases where exposure exceeded these limits were found to have major flaws, such as unrealistic testing conditions, lack of proper sample details, or other methodological issues.



When devices were tested under normal or reasonable conditions, metal exposure remained below these safety thresholds.



While strict toxicological benchmarks are useful, occupational exposure limits may also be appropriate given that vaping is a voluntary activity for adult smokers.



Overall, current risk communication tends to be overly precautionary and fails to account for the fundamental differences between vaping and smoking, indicating the need for more proportionate and evidence-based evaluation.

Conclusions

The review highlights that accurate assessment of metal exposure from e-cigarettes depends on using laboratory methods that are consistent with real-life device operation, including appropriate puffing protocols, device characteristics, and avoidance of overheating.

The authors argue that many existing studies rely on CORESTA-type protocols, which are unsuitable for high-powered sub-ohm devices, leading to artificially elevated metal levels—particularly for nickel, lead, copper, and manganese—sometimes exceeding strict toxicological thresholds.

In contrast, when low-powered devices are tested under appropriate conditions, metal emissions are consistently well below safety limits, and high readings in such devices are generally linked to flawed methodologies.

The review stresses that while laboratory testing is useful for comparison and quality control, it does not replicate actual user behaviour, and results obtained under unrealistic conditions have limited relevance for health risk assessment.

A major issue identified is the lack of essential methodological detail in many studies, such as device specifications and operating parameters, which undermines transparency and reproducibility. The authors recommend incorporating user experience, manufacturer guidelines, and real-world usage data into experimental design to ensure more realistic and meaningful results.

There is a clear need to update current testing standards, which were developed for older devices and do not reflect the diversity of modern products. Improved standards should align with real-world usage, include appropriate puffing regimes, and consider user sensory feedback, benefiting regulators, researchers, and consumers alike.

The review also identifies emerging disposable pod devices as an important area for future research, particularly regarding their metal emissions.

Further work is needed to replicate prior studies under realistic conditions and to expand research into other harmful emissions, with the overall aim of improving testing practices and enabling more accurate public health evaluations of vaping products.



4 Analytical methods and experimental quality in studies targeting carbonyls in electronic cigarette aerosols

Sussman RA, Sipala FM, Ronsisvalle S, Soulet S. Analytical methods and experimental quality in studies targeting carbonyls in Electronic Cigarette aerosols. *Front Chem.* 2024;12:1433626.

Conventional tobacco cigarette smoking causes millions of deaths each year, leading to efforts to reduce harm through **alternatives** such as **processed oral smokeless tobacco** and **Electronic Nicotine Delivery Systems (ENDS)** i.e. **Electronic Cigarettes (ECs)** and **heated tobacco products (HTPs)**, both delivering nicotine through an aerosol generated electronically without combustion. [C1,p1;C2-C3,p2]



However, e-cigarette aerosols can still contain **carbonyl compounds** (such as **formaldehyde**, **acetaldehyde** and **acrolein**), which may form when e-liquid ingredients are heated. [C1,p1;C2-C3,p2]



To evaluate potential **health risks** of these compounds for users, researchers measure **harmful and potentially harmful compounds (HPHCs)** in e-cigarette aerosols using **laboratory tests** where machines simulate puffing. Although these **standardised tests do not perfectly reflect real use**, they provide a **basic estimate of possible risks**. [C1,p1;C2-C3,p2]



ECs vary widely in devices, **coils**, **e-liquids**, **nicotine levels**, and **flavours**, study results also vary. Therefore, it is important to assess whether studies meet **key quality standards**. These include providing enough detail for results to be reproduced, using **puffing conditions similar to real device use**, applying **appropriate analytical methods**, and including **blank samples** to check for contamination. Meeting these criteria helps ensure the results are **reliable**. [C4,p2]

Aim

To provide a **comprehensive review of emission studies conducted on ECs**, with a particular focus on the **assessment of the analytical methods employed in measuring carbonyls**. [C5,p3]



Method

PubMed database searched for studies on **carbonyl compounds** in aerosols from cigarettes, ECs, and heated tobacco products. [C8,p4;C9,p3]



Four criteria were **evaluated** for experimental quality:

- 01 Reproducibility
- 02 Adequacy of puffing regime
- 03 Analytical methods (used to measure carbonyls in aerosols)
- 04 The usage of blank samples. [C6,p12]

14

Fourteen studies, published after 2018*, that met the criteria were **reviewed**.

*Studies published ≤2018 excluded as evaluated devices now obsolete

Results

Table 4. Evaluation of the revised studies in terms of fulfilment of the four conditions of experimental quality. [C10,p6]

First author	Provided sufficient information to reproduce results?	Adequate Puffing regime	Adequate Analytical methods	Blanks	Score and Comments
Conklin <i>et al.</i>	✓	✓	✓	✗	● 3.0 Reliable
El Mubarak <i>et al.</i>	✓	✓	✓	✓	● 4.0 Reliable
Lee <i>et al.</i>	Computerise system. Ω NOT disclosed.	?	✓	✗	● 1.5 Unreliable
Stephens <i>et al.</i>	Ω NOT disclosed.	✓	✓	✗	● 2.5 Partially reliable
Gillman <i>et al.</i>	✓	✓	✓	✗	● 3.0 Reliable
Nicol <i>et al.</i>	✓	✓	✓	✓	● 4.0 Reliable
Talih <i>et al.</i>	✓	Unrealistic puffing regime	✓	✗	● 2.5 Partially reliable
Rajapaksha <i>et al.</i>	(1/2) Some results not quantifiable	✓	✓	✗	● 2.5 Partially reliable
Son <i>et al.</i>	(1/2) Ω of sub-ohm coil not disclosed	(1/2)	✓	✓	● 2.0 Partially reliable
El-Hellani <i>et al.</i>	"do-it-yourself" e-liquids, W not disclosed	Unrealistic puffing regime	✓	✗	● 1 Unreliable
Lalonde <i>et al.</i>	✓	✓	✓	✗	● 3.0 Reliable
McGuigan <i>et al.</i>	Devices not disclosed	?	✓	✓	● 2.0 Partially reliable
Pinto <i>et al.</i>	✓	✓	✓	✓	● 3.0 Reliable
Talih <i>et al.</i>	✓	✓	✓	✗	● 3.0 Reliable

Key: ✓: one point; ✗: zero points; 1/2: half a point when a condition was partially fulfilled | **Reliability:** ● Green: ≥3.0 points (reliable); ● Orange: 2.0 - 3.0 (partially reliable); ● Red: < 2.0 (unreliable)

1 Analytical method [C11,p10;C12,p11]

- Most studies measuring carbonyls in e-cigarette aerosols used the High-Performance Liquid Chromatography Ultraviolet (HPLC-UV) method, recommended by Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA), though not always following the standard protocols.
- While effective for formaldehyde and acetaldehyde, this method can be affected by e-liquid flavours and is less suitable for higher-molecular-weight carbonyls. More sensitive techniques, like liquid chromatography (LC-MS), provide better quantification of low-concentration carbonyls.
- Accurate analysis also depends on fully characterising e-liquids, as their composition, including the Propylene Glycol/Vegetable Glycerin or Glycerol (PG/VG) ratio and flavourings, affects carbonyl formation.

2 Blank analysis [C13,p11]

- Only 5 of the 14 studies used blank samples.
- Blank analysis plays a key role in quantitative investigation because it excludes contamination from the results of the analysis. Among the studies reviewed, only 6 performed or presented a blank analysis of the air.

3 Storage [C14,p11]

- Most of the reviewed studies did not report how devices, e-liquids, or samples were stored before analysis, which makes it difficult to reproduce their results. Proper storage conditions—such as appropriate temperature, light exposure, and sealed containers—are important to prevent chemical changes that could affect measurements. Guidelines recommend storing devices and aerosols at room temperature for short periods, or at -10 °C if stored longer.
- Storage conditions can also influence metal concentrations in e-liquids and may affect comparisons with conventional cigarette emissions, highlighting the need for clear reporting of storage and environmental conditions during analysis.

4 Puffing Regime [C15,p11-p12]

- Laboratory puffing regimes strongly affect the amount of carbonyls produced in e-cigarette emissions. These regimes are defined by parameters such as puff duration, puff volume, time between puffs, and airflow rate, and changes in any of these can alter emission levels. Most studies use the ISO 20768:2018 CORESTA standard (3 s puff, 30 s inter-puff, 55 mL puff volume, airflow 1.1 L/min), which provides a consistent testing method and approximates typical use of low-powered, mouth-to-lung devices. While such protocols cannot fully replicate real user behaviour, they offer a practical way to compare devices and estimate potential exposure.

5 Evaluation [C16,p12]

- 7 studies were reliable
- 5 studies were partially reliable
- 2 studies were unreliable
- 1 out of the 7 reliable studies used blank samples (only three studies used blank samples).
- 6 studies failed the reproducibility criterion
- Most studies used reasonable values of puff duration (around 3s) and inter-puff intervals (30s and 60s).

Conclusion

Accurate evaluation
of EC risk depends on
high-quality emission studies.

Our review of 14 recent studies shows that, while most report negligible carbonyl levels compared with cigarette smoke, serious methodological flaws, such as incomplete reporting, lack of blanks, and limited reproducibility persist. Updating laboratory testing standards to ensure rigorous, reproducible methods that reflect real consumer use is essential to provide reliable information for all stakeholders. [C17,p13]

5 Aerosol Emissions from Heated Tobacco Products: A Review Focusing on Carbonyls, Analytical Methods, and Experimental Quality

Sussman RA, et al. Aerosol Emissions from Heated Tobacco Products: A Review Focusing on Carbonyls, Analytical Methods, and Experimental Quality. *Toxics*. 2023;11:947.

Aim

To describe the analytical methods used to characterise Heated Tobacco Product (HTPs) emissions, focusing on studies that analysed carbonyl compounds. [A1,p1,p19]

Background

Cigarette smoking is a major preventable cause of death worldwide, responsible for over 7 million deaths each year. [A2,p1]

Tobacco Harm Reduction (THR) aims to reduce this harm by replacing traditional cigarettes with alternative nicotine delivery systems that avoid combustion, thereby lowering exposure to harmful and potentially harmful compounds (HPHCs). [A2,p1]



Electronic Nicotine Delivery Systems (ENDS), such as e-cigarettes (ECs) and HTPs, produce nicotine-containing aerosols without burning tobacco. [A2,p2]



Unlike conventional cigarettes, which burn at very high temperatures (800-950°C), and generate thousands of harmful chemicals, ENDS operate at lower temperatures (<400°C). [A2,p2]



This fundamental difference results in markedly reduced chemical complexity and substantially lower concentrations of toxicants in emitted aerosols. [A2,p2]

Mechanistic Overview



HTPs operate below combustion temperatures, preventing oxidative reactions responsible for toxic smoke formation. Instead, aerosol formation occurs via evaporation and low-temperature pyrolysis, yielding fewer and less complex toxicants. [A3,p6-7]

Method

A PRISMA-based literature review was conducted using PubMed. [A4,p3]



Studies were selected based on standardised puffing protocols, proper analytical methods, reproducibility, and sample handling. A total of 17 studies were included. [A5,p4]



Results

HTPs show consistent reductions (80–95%) in major carbonyl compounds including formaldehyde, acetaldehyde, and acrolein **compared to conventional cigarettes**. Despite variability in methods, most studies show consistent reductions in toxic compounds. However, these toxicants remain present and biologically relevant . [A5,p4]

Table 5. Carbonyl Reduction Comparison. [A7,p11;A8,p12]

Compound	HTP Level (approx.)	Reduction vs Cigarettes
Formaldehyde	5–6 µg/stick	80–95% lower
Acetaldehyde	144–176 µg/stick	Significantly lower
Acrolein	10–11 µg/stick	Major reduction

Discussion and Clinical Interpretation



There is broad agreement that **HTPs reduce exposure to harmful compounds compared to cigarettes**. However, reduced toxicant exposure does not equate to safety and long-term clinical outcomes remain uncertain and require longitudinal data. Furthermore, **methodological inconsistencies** and the **presence of residual toxicants remain concerns**. [A9,p3]



This review **critically assessed the analytical approaches used to quantify carbonyl compounds in HTP emissions**, highlighting that **reliability of reported findings is strongly dependent on methodological rigour**. [A13,p19]



Most studies employed 2,4 Dinitrophenylhydrazine (DNPH) derivatisation to measure carbonyls; however, **incomplete reporting** of key parameters such as pH control, reaction time, and quenching procedures **limits reproducibility and may affect accuracy**. [A13,p19]



Alternative methods, including o-(2,3,4,5,6-Pentafluorobenzyl) hydroxylamine (PFBHA) derivatisation with Gas Chromatography–Mass Spectrometry (GC-MSHPLC), **offer improved sensitivity** but were **less frequently used**, while studies lacking derivatisation risk underestimating reactive compounds such as formaldehyde. [A14,p20]



High-performance liquid chromatography with UV detection (HPLC-UV) was the **most applied analytical technique**, though it was **originally developed for cigarette smoke** and may not be fully optimised for ENDS aerosols. More advanced methods such as **liquid chromatography with mass spectrometry (LC-MS)** provide **greater sensitivity** and may be **more appropriate** for trace-level detection. [A15,p20-21]



The review also identified important **gaps in quality control**, with few studies reporting blank analyses to account for contamination and limited detail provided on sample storage conditions, both of which are critical for ensuring data validity. [A16,p21]



In addition, **puffing regimes** (e.g., International Organization for Standardization (ISO) vs Health Canada Intense) **significantly influence measured emissions**, with more intensive regimes producing higher toxicant yields and highlighting the difficulty of replicating real-world use. [A17,p22]



Overall, **most studies were considered broadly reliable** despite minor methodological limitations; only one study was identified as unreliable due to unclear or inconsistent analytical methods, and three studies were deemed only partially reliable because of incomplete reporting (e.g., missing units or insufficient validation). [A18,p28]

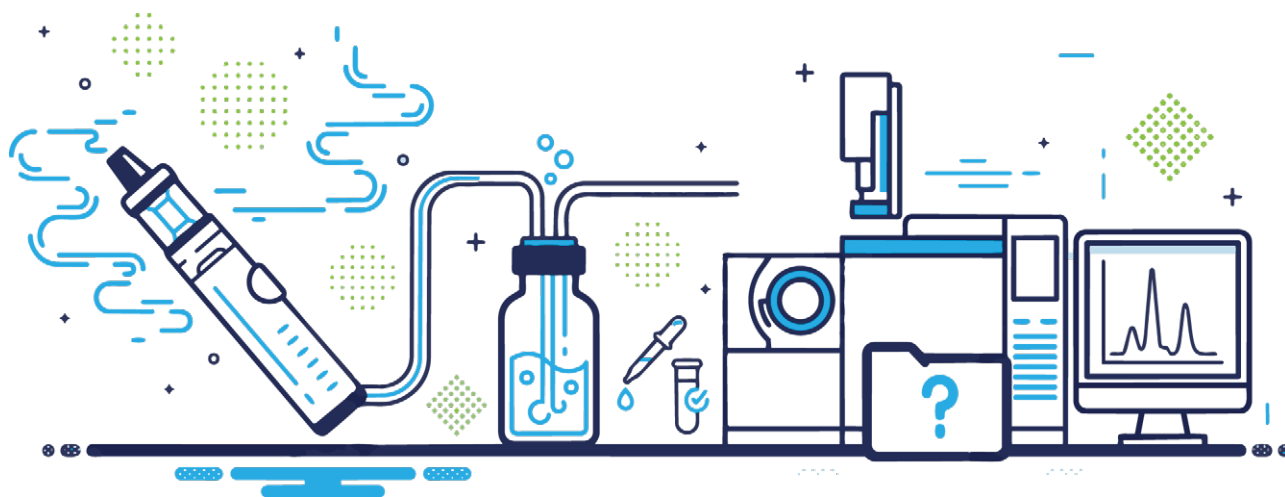


These findings underscore that, although the **overall evidence base is consistent**, interpretation of HTP emission data must account for variability in study quality, and highlights the **need for standardised, rigorously applied analytical protocols**. [A18,p28]

Table 6. Assessment of the reliability of the revised studies [A19,p28-29]

Authors	Puffing Conditions	Analytical Methods	Derivatisation Methods	Other Information	Score and Comments
Auer <i>et al.</i>	✓	✗	✗	✗ Several flaws	1.0 ●
Farsalinos <i>et al.</i>	✓	✓	✓	✓	4.0 ●
Mallock <i>et al.</i>	✓	✓	✓	✓	4.0 ●
Uchiyama <i>et al.</i>	✓	✓	½	✓	3.5 ●
Salman <i>et al.</i>	½	✓	✓	✗ Flawed conclusions on IQOS pollution	2.5 ●
Heide <i>et al.</i>	✓	✓	½ No derivatisation	✗ Poor Validation	2.5 ●
Wang <i>et al.</i>	✓	✓	✓	✗ Number of puffs per cigarette not specified	3.0 ●
Dusautoir <i>et al.</i>	½	✓	✓	✗ HCI regime for sub-ohm devices	2.5 ●
Schaller <i>et al.</i>	✓	✓	✓	✓	4.0 ●
Schaller <i>et al.</i>	✓	✓	✓	✓	4.0 ●
Jaccard <i>et al.</i>	✓	✓	✓	✗ No description of conventional cigarettes analysed	3.0 ●
Poynton <i>et al.</i>	✓	✓	✓	✓	4.0 ●
Buratto <i>et al.</i>	✓	✓	✓	Number of puffs per cigarette not specified	3.0 ●
Crooks <i>et al.</i>	✓	✓	✓	½ Internal methods not available	3.5 ●
Eaton <i>et al.</i>	✓	✓	✓	½ Internal methods not available	3.5 ●
Forster <i>et al.</i>	✓	✓	✓	½ Internal methods not available	3.5 ●
Bentley <i>et al.</i>	✓	✓	½ No derivatisation	✓	3.5 ●

Key: ✓: one point; ✗: zero points; ½: half a point when a condition was partially fulfilled | Reliability: ● Green: ≥3.0 points (reliable); ● Orange: 2.0 - 3.0 (partially reliable); ● Red: < 2.0 (unreliable)



Limitations

Findings are influenced by device variability, puffing regimes, and methodological inconsistencies. Some compounds not routinely monitored may also contribute to risk. [A10,p11]

Conclusion

Almost all studies support that HTP emissions represent significant **reduced-exposure** alternative to tobacco smoke. [A11,p29] However, this does not suggest a risk-free alternative. Interpretation should remain cautious, particularly in clinical and public health contexts. [A12,p29-30]

6 Critical Appraisal of Exposure Studies of E-Cigarette Aerosol Generated by High-Powered Devices

Soulet S, Sussmann RA. Critical Appraisal of Exposure Studies of E-Cigarette Aerosol Generated by High-Powered Devices. *CTNR*.2025;34:(5).

Aim

This review critically evaluates the aerosol generation procedures in 41 experimental studies assessing toxicant emission exposure from high-powered (sub-ohm) e-cigarette (EC) devices to examine the effects in biological systems (cell lines and rodents).

[B6, p215]

Background

Current patterns of EC use increasingly include low-powered and disposable pod-based devices; however, a substantial proportion of experimental studies continue to assess aerosol toxicity using third-generation high-powered, low-resistance (sub-ohm) devices. [B1,p202]



In many cases, these devices are operated under conditions that do not reflect typical user behaviour, including excessive power settings and inappropriate puffing regimes. Such conditions can lead to overheating and “dry puff” phenomena, resulting in artificially elevated production of toxic compounds. [B1,p202]



Consequently, these methodological limitations may generate exposure data that are not representative of real-world use and may lead to misinterpretation of the risk profile of vaping products by medical practitioners, policymakers, and consumers. [B1,p202]



Image source: freepik.com

Literature Search Methodology



The literature search was conducted using Google Scholar due to its ability to identify keywords within full-text articles. A structured query targeting e-cigarette terminology and Scientific Respiratory Equipment Inc. (SCIREQ) yielded 263 references after duplicate removal.



A multi-stage manual screening process was applied to exclude irrelevant material and identify studies using appropriate aerosol generation systems. Following detailed assessment, 41 studies met inclusion criteria. [B2,p207]

Table 7. Classification of Studies [B3, p209]

Category	Number of Studies	Description
Certain / Almost Certain / Suspicious	14	Sufficient detail to assess aerosol generation
Uncertain	16	Incomplete reporting; inference required
Unknown	10	Insufficient detail; non-reproducible

Key results

A **key finding** of the review is that **methodological quality is the primary determinant of reported toxicant levels**. [B3,p209; B5, p212]



Only a **minority** of studies assessed devices under realistic conditions, while the **majority** employed flawed experimental designs. [B3,p209; B5, p212]



These flaws include inappropriate power-coil combinations, unrealistic puffing regimes, and failure to identify or exclude dry puff conditions. [B3,p209; B5, p212]



As a result, **many studies report artificially elevated toxicant levels that are not representative of actual user exposure**. [B3,p209; B5, p212]

Discussion

The review emphasises the lack of standardised testing protocols for high-powered devices. While frameworks such as Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) Method 81 exist, they are **not fully suitable for sub-ohm systems**. [B1,p202]

The authors **highlight** the InExpose protocol (SCIREQ aerosol exposure system) as a **more appropriate approach**, as it incorporates realistic puffing parameters and minimises overheating artifacts. [B9,p215]

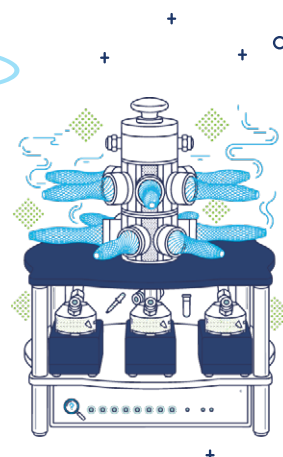


Table 8. Study-by-Study Appraisal [B4, p209-211]

Study	Focus	Issue	Mechanism	Interpretation
Noël et al. 2018	Carbonyl emissions	High power use	Overheating	Non-representative results
Jensen et al. 2015	Formaldehyde	High voltage	Dry puff	Overestimated toxicity
Talih et al. 2016	Power variation	Mismatch	Thermal instability	Variable results
Sleiman et al. 2016	Puffing regime	Unrealistic	Thermal stress	Overestimated emissions
Ogunwale et al. 2017	Toxicant profile	Incomplete data	Unknown conditions	Non-reproducible

Coil Resistance and Power Settings



Methodological flaws were frequently associated with inappropriate combinations of coil resistance and applied power. [B8,p203-204]



Sub-ohm coils (typically 0.15–0.5 ohms) were often tested at **excessively high-power levels**, leading to overheating and dry puff conditions. [B8,p203-204]



In contrast, studies operating within manufacturer-recommended ranges demonstrated **stable aerosol generation** and substantially lower toxicant levels. [B8,p203-204]

Conclusion

The appraisal demonstrates that **methodological inconsistencies** — particularly **unrealistic power settings, inadequate reporting, and failure to detect dry puff conditions** — are key drivers of variability in reported toxicant emissions.

Accurate interpretation of e-cigarette exposure data requires careful consideration of experimental design and adherence to validated testing protocols. [B7, p218]

7

Multiple Choice Questions for CPD points

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Questions 1 to 4 based on: Critical Review of the Recent Literature on Organic Byproducts in E-Cigarette Aerosol Emissions

1. What was the main aim of the review by Soulet S and Sussman RA?

- a) ☐ To compare vaping devices with traditional cigarettes in clinical trials
- b) ☒ To assess laboratory testing methods and detection of organic byproducts in e-cigarette emissions
- c) ☐ To determine the effectiveness of vaping for smoking cessation
- d) ☐ To evaluate nicotine addiction in e-cigarette users

2. Which of the following was one of the key criteria used to evaluate the studies?

- a) ☐ Cost of vaping devices
- b) ☐ Marketing strategies of manufacturers
- c) ☒ Experimental consistency with realistic user behaviour
- d) ☐ Popularity of device brands

3. What was the most common issue identified among the reviewed studies?

- a) ☐ Lack of nicotine measurements
- b) ☒ Testing sub-ohm devices using CORESTA or CORESTA-like protocols
- c) ☐ Using too many participants
- d) ☐ Failure to measure carbon monoxide

4. According to the review, unrealistic laboratory testing conditions may lead to:

- a) ☐ Underestimation of vaping risks
- b) ☐ Accurate simulation of real vaping conditions
- c) ☒ Overestimation of health risks from e-cigarettes
- d) ☐ Elimination of harmful byproducts

Questions 5 to 8 based on: A Critical Review of Recent Literature on Metal Contents in E-Cigarette Aerosol

5. Which of the following is considered a typical estimate of daily vaping behaviour used for exposure calculations in the review?

- a) ☐ 50 puffs per day
- b) ☐ 100 puffs per day
- c) ☒ 250 puffs per day
- d) ☐ 500 puffs per day

6. Which of the following best describes Direct-to-Lung (DTL) vaping?

- a) ☐ Low airflow, short puffs, and low-powered devices
- b) ☐ Similar to cigarette smoking behaviour
- c) ☒ Larger puff volumes, higher airflow, and higher-powered devices
- d) ☐ Only used with disposable e-cigarettes

7. According to the review, why did some studies report high metal levels in e-cigarette aerosols?

- a) ☐ High nicotine concentrations
- b) ☐ Use of flavoured e-liquids
- c) ☒ Unrealistic testing conditions causing overheating
- d) ☐ Increased puff intervals

8. What did studies measuring metal biomarkers in human vapers generally find?

- a) ☐ Extremely high metal exposure compared to smokers
- b) ☒ No significant difference between vapers and non-users
- c) ☐ Higher exposure than occupational safety limits
- d) ☐ Increased heavy metal accumulation over time

Questions 9 to 12 based on: Analytical methods and experimental quality in studies targeting carbonyls in electronic cigarette aerosols

9. Which analytical method was most commonly used to measure carbonyls in e-cigarette aerosols?

- a) ☐ Gas chromatography–mass spectrometry (gc-ms)
- b) ☒ High-performance liquid chromatography ultraviolet (hplc-uv)
- c) ☐ Infrared spectroscopy
- d) ☐ Atomic absorption spectroscopy

10. Why are blank samples important in carbonyl emission studies?

- a) ☐ To increase aerosol production
- b) ☐ To measure nicotine levels
- c) ☒ To detect and exclude contamination
- d) ☐ To standardise puff duration

11. Which of the following puffing conditions is commonly used in the ISO 20768:2018 CORESTA protocol?

- a) ☐ 1 second puff duration and 10 second interval
- b) ☒ 3 second puff duration and 30 second interval
- c) ☐ 5 second puff duration and 5 second interval
- d) ☐ 10 second puff duration and 60 second interval

12. What was a common limitation identified in many reviewed studies?

- a) ☐ Excessive participant recruitment
- b) ☐ Lack of nicotine measurement
- c) ☒ Insufficient reporting of storage conditions
- d) ☐ Use of clinical trials instead of laboratory testing

Questions 13 to 16 based on: Aerosol Emissions from Heated Tobacco Products: A Review Focusing on Carbonyls, Analytical Methods, and Experimental Quality

13. Which carbonyl compound showed a major reduction in heated tobacco products compared with conventional cigarettes?

- a) ☐ Benzene
- b) ☒ Acrolein
- c) ☐ Carbon monoxide
- d) ☐ Ammonia

14. Which analytical technique was most commonly used to measure carbonyl compounds in heated tobacco product emissions?

- a) ☐ Liquid chromatography–mass spectrometry (lc-ms)
- b) ☐ Gas chromatography only
- c) ☒ High-performance liquid chromatography with uv detection (hplc-uv)
- d) ☐ Infrared spectroscopy

15. What factor was identified as influencing measured toxicant levels in heated tobacco product emissions?

- a) ☐ Packaging material
- b) ☒ Puffing regimes such as ISO or Health Canada Intense
- c) ☐ Nicotine warning labels
- d) ☐ Device colour

16. Which derivatisation method was most frequently used to quantify carbonyls in htp studies?

- a) ☐ o-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine (pfbha)
- b) ☒ 2,4 dinitrophenylhydrazine (dnph)
- c) ☐ Ninhydrin
- d) ☐ Dansyl chloride

Questions 17 to 20 based on: Critical Appraisal of Exposure Studies of E-Cigarette Aerosol Generated by High-Powered Devices

17. What is a major source of variability in reported toxicant levels from high-powered e-cigarette studies?

- a) ☐ User age and sex
- b) ☒ Methodological inconsistencies such as unrealistic power and puffing regimes
- c) ☐ Battery brand only
- d) ☐ Flavour of e-liquid

18. Why are many toxicant measurements from sub-ohm device studies not representative of real-world vaping?

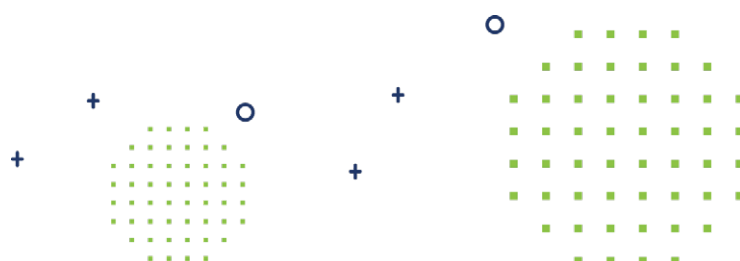
- a) ☐ The devices do not produce aerosol in lab conditions
- b) ☒ Studies often use excessive power and inappropriate puffing, causing overheating and dry puffs
- c) ☐ Nicotine levels are too low to detect
- d) ☐ Aerosol is filtered before measurement

19. Which protocol was highlighted as more appropriate for testing high-powered sub-ohm devices?

- a) ☐ ISO 20768
- b) ☐ CORESTA Method 81
- c) ☒ InExpose (SCIREQ aerosol exposure system)
- d) ☐ Health Canada Intense

20. What combination is frequently associated with overheating and dry puff conditions in high-powered e-cigarette studies?

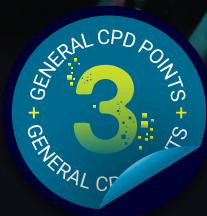
- a) ☐ High coil resistance with low power
- b) ☒ Sub-ohm coil resistance (0.15–0.5 ohms) with excessive applied power
- c) ☐ Low nicotine e-liquid with short puff duration
- d) ☐ Disposable pod devices with standard puffing





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