

Commentary

Exposure to Benzene, Toluene, and Xylenes from Electronic Cigarette Use Compared to Working Environment Permissible Exposure Limits: A Risk Assessment Analysis of a Recent Publication

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A recent study tested 20 electronic cigarette (e-cigarette) samples and reported that e-cigarette use was associated with far higher exposure to benzene, toluene, and total xylenes compared to Permissible Exposure Limits (PELs) for working environments. However, we noticed several errors in that study, such as incorrect conversions of measuring units from ppm to $\mu\text{g}/\text{L}$ and, more importantly, an irrelevant comparison between environmental levels in 1 L of air (corresponding to 2 breaths) and levels in 1 L of aerosolized e-cigarette liquid (corresponding to 200–250 days of consumption). In this study, we performed a risk assessment analysis using total daily exposure limits. PELs were used to estimate total exposure considering an 8-hour work shift with an inhalation rate of $0.027\text{m}^3/\text{min}$ for moderate activity. Conversions from ppm to $\mu\text{g}/\text{L}$ were made using an appropriate formula considering the molecular weight. Levels of emissions per L of aerosolized liquid were used to estimate daily exposure from e-cigarette use considering a 5 mL consumption based on surveys. The ratio of working exposure to e-cigarette use exposure was calculated. For benzene, daily exposure from e-cigarette use was 865 to 15,990-fold lower compared to the working PEL, with the average exposure from all samples being 3,115-fold lower. For toluene, daily exposure from e-cigarette use was 748 to 844,866-fold lower compared to the working PEL, with the average exposure from all samples being 3,841-fold lower. For xylenes, daily exposure from e-cigarette use was 6811 to 1,411,167-fold lower compared to the working PELs, with the average exposure from all samples being 70,451-fold lower. In conclusion, benzene, toluene, and xylenes exposure from e-cigarette use is orders of magnitude lower compared to working in an environment that is considered safe according to air quality guidelines.

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Introduction

E-cigarettes (ECs) have become popular substitute products for conventional cigarettes given the broad scientific consensus on the significant reduction of users' exposure to toxic compounds with respect to tobacco smoke^[1]. Nevertheless, toxic byproducts are produced in the heating process during aerosol formation, so it is important to assess their safety profile by comparing the concentrations and inhaled doses of these byproducts with appropriate toxicological standards, either those used in medication^[2] or occupational safety exposure limits, such as the Threshold Limit Values (TLVs), Permissible Exposure Limit (PEL), and Short Term Exposure Limit (STEL) of the Occupational Safety and Health Administration (OSHA) of the USA.^[3] Evidently, this assessment requires an adequate chemical analysis of the emissions and the correct evaluation of exposures.

A recently published article^[4] conducted a chemical analysis of e-liquids and aerosols from a sample of 20 illegal disposable vaping devices collected in Mexico City. The authors only quantified (in both e-liquids and aerosols) a group of aromatic hydrocarbons:

benzene, toluene, and the xylene isomers (known as BTX), compounds that are generally not expected to occur in EC emissions in meaningful levels. They reported the measured BTX concentrations for the 20 devices in Table S1 of their Supporting Information file, arguing that in most samples they exceed tobacco smoke levels and the PELs and STELs as defined by the California Division of Occupational Safety and Health (Cal/OSHA)^[5]. However, we have noticed several errors in their methodology, calculations, and comparisons, making the results and conclusions unreliable.

Cal/OSHA provides a comprehensive list of concentrations in ppm units (and many in mg/m³ too) for assorted compounds as PELs, defined by the “TWA” (time-weighted average concentration) for up to an 8-hour workday during a 40-hour workweek, and as STEL, a 15-minute TWA exposure that should not be exceeded at any time during a workday. The normal respiratory rate of adults in resting conditions is 12 breaths/min, meaning that the average adult human takes more than 5760 breaths during an 8-hour working shift (since we cannot assume resting conditions during working hours). Thus, threshold concentrations set by PELs involve exposure for every single one of thousands of breaths during a working shift. In contrast, EC use is intermittent in nature, with users taking approximately 200 puffs per day^[6], with over 300 daily puffs when users compensate for lower nicotine concentrations^[7]. Thus, concentrations in environmental air, resulting in continuous exposure with every single breath for 8 hours (in the case of PELs), and concentrations in EC aerosol, resulting in intermittent exposure for a number of breaths orders of magnitude lower than the number taken during a working shift, would not be comparable.

However, the authors did not even compare concentration values in air vs. EC aerosol. Instead, they compared threshold concentrations from PELs with the total amount of BTX emitted from 1 L of EC liquid when aerosolized. Specifically, they measured aerosol BTX levels by generating two puffs only, a puffing procedure that prevents statistically reliable outcomes and grossly deviates from recommended experimental standards^[8], and they mentioned: “*The quantitative analysis of aerosols for BTX was conducted, with concentrations reported in ng/2 vapes. For comparison purposes, these values were converted to µg/L, considering the number of puffs and the volume declared for each device*”. Thus, the reported µg/L values for EC emissions were not concentrations per L of inhaled air but the total amount of BTX emitted from using 1 L of EC liquid. The latter represents approximately 200 days of average EC use, since surveys have shown a daily consumption of 3–5 mL of liquid for vapers^{[9][10][11]}. At the same time, the PELs expressed in µg/L would in fact represent exposure from 2 breaths in resting conditions (since the average human tidal volume is 0.5 L per breath). Thus, the authors literally compared 200 days of vaping with just 2 breaths in a working environment. Furthermore, their method introduces another uncontrolled factor since their calculations were based on declarations by the manufacturers on puff number and volume of each device, which were assumed to be accurate. Instead, they should have measured the amount of liquid aerosolized when taking the two puffs and then making the calculations for larger amounts (e.g., per Kg or even per L by assuming a liquid specific weight of 1).

Another substantial error by Svarch-Pérez et al. was that they converted ppm values of PELs and STELs to µg/L by multiplying them by 1000. This is an elementary error since values in ppm in ambient air are converted to weight per volume of air volume after considering the molecular weight of each compound, using a specific formula (see methods section)^[12]. Thus, all values in µg/L for PELs and STELs mentioned by Svarch-Pérez et al. were wrong, making all comparisons invalid.

In this study, we attempted to make more reliable comparisons between occupational setting safety limits and EC exposure by examining total exposure of BTX during an 8-hour working shift using PELs and calculating daily exposure from EC use based on the measurements reported by Svarch-Pérez et al. for all devices. This is a methodology that more reliably addresses the discrepancy between continuous exposure with every single breath for PELs during a working shift and intermittent exposure for a few hundred breaths per day for EC use and has been used previously in a risk assessment analysis of metal exposure from ECs^[13].

Additionally, we correctly converted the ppm values of STELs to $\mu\text{g/L}$ using either the respective values reported in Cal/OSHA (for toluene and xylenes) or the appropriate formula (for benzene).

Methods

Aerosol BTX concentration

For this analysis, we used the aerosol results reported for each sample tested by Svarch-Pérez et al.^[4] from Supplementary Table 1 of their manuscript. We focused on the aerosol results only, since e-cigarette use involves aerosol inhalation instead of liquid use. The results were reported in μg of BTX per Liter of liquid, after measuring BTX levels in 2 puffs. The authors assumed that the manufacturers' reported total liquid volume in their device and total number of usable puffs of their devices were accurate. Thus, they made the calculations based on that information, using the following formula:

$$\text{BTX concentration } (\mu\text{g/L}) = [\text{BTX}_{2p} \times (\text{N}_{pd}/2)] \times (1000/V_d) \quad (1)$$

where BTX_{2p} : BTX amount measured in 2 puffs; N_{pd} : number of usable puffs reported in the device; V_d : liquid volume reported in the device.

We find this inaccurate because it assumes that manufacturer labelling values are accurate. The authors could have easily measured the weight of liquid consumption for the two puffs used to make the analysis (by precision weighing the device before and after each puff) and then made the conversions to $\mu\text{g/kg}$, although using two puffs would still be inadequate to adjust for emissions interpuff variability. Since no data was provided in the manuscript in order to make calculations more reliable, we proceeded with the analysis based on the results reported by Svarch-Pérez et al.^[4].

PELs

For PELs, we used the threshold values provided by Cal/OSHA. However, as mentioned above, we noticed that the authors incorrectly calculated the $\mu\text{g/L}$ of PELs by multiplying the ppm values reported in CAL/OSHA by 1000. Furthermore, units of g/L were mentioned in some tables while the text referred to all of them as $\mu\text{g/L}$, with the latter being the correct units. To correctly convert ppm to $\mu\text{g/L}$, we used the following formula^[12]:

$$\mu\text{g/L} = (\text{ppm} \times \text{molecular weight})/24.45 \quad (2)$$

(based on 25 °C and 1 bar atmospheric pressure)

In fact, the CAL/OSHA table^[5] reports values in both ppm and mg/m^3 for toluene (10 ppm, 37 mg/m^3) and xylenes (100 ppm, 435 mg/m^3). For benzene, we used the formula (molecular weight: 78.11) to calculate that the 1 ppm PEL equates to 3.19 mg/m^3 . The same values are applicable when expressed in units of $\mu\text{g/L}$ instead of mg/m^3 , so throughout the results and table, we use $\mu\text{g/L}$ as did Svarch-Pérez et al.^[4].

Comparison between e-cigarette exposure and PELs

As mentioned above, Svarch-Pérez et al.^[4] compared the PELs, which represent amounts per volume of breathing air in an occupational setting, with the exposure from using 1 L of e-cigarette liquid. In reality, and based on an average daily consumption of 3-5 mL of liquid for vapers, the authors attempted to compare the exposure concentration (not even the total amount of exposure) from breathing ambient air in 8 hours with the total amount of exposure from using ECs for 200-250 days. In this study, we performed a more appropriate comparison by calculating daily exposure based on PELs (for 8 hours of exposure in a working environment) and daily exposure from EC use.

For this comparison, we assumed a 5 mL per day average liquid consumption for vaping. Therefore, the formula for calculating total daily exposure from e-cigarette use was:

$$\text{Exposure } (\mu\text{g}/\text{d}) = \text{reported levels } (\mu\text{g}/\text{L})/200 \quad (3)$$

For PELs, we used the EPA assessment of an inhalation rate of $0.027\text{m}^3/\text{min}$ for moderate activity, resulting in $12.96\text{m}^3/8$ hours ($12,960$ L/8 hours) that corresponds to a working shift^[14]. Therefore, using the correct thresholds in $\mu\text{g}/\text{L}$ mentioned above, we calculated the total amount of exposure from an 8-hour shift using the formula:

$$\text{Exposure } (\mu\text{g}/8\text{h}) = \text{PEL } (\mu\text{g}/\text{L}) \times 12,960(\text{L}^3) \times 1000 \quad (4)$$

Finally, we calculated the ratio between the 8-hour total exposure based on the PELs threshold and the total daily exposure from vaping 5 mL per day.

	Benzene (PEL: 1 ppm = 3.19 µg/L)				Toluene (PEL: 10ppm = 37.68 µg/L)				Xylenes (PEL: 100 ppm = 435 µg/L)			
	Aerosol reported (µg/L)	Aerosol (µg/d) ¹	PEL exposure (µg/8h) ²	Ratio PEL/Aerosol	Aerosol reported (µg/L)	Aerosol (µg/d) ¹	PEL exposure (µg/8h) ²	Ratio PEL/Aerosol	Aerosol reported (µg/L)	Aerosol (µg/d) ¹	PEL exposure (µg/8h) ²	Ratio PEL/Aerosol
1	1462.6	7.31	41342.4	5653	33270.3	166.35	488332.8	2936	3735.3	18.68	5637600.0	301855
2	577.7	2.89		14313	1010.4	5.05		96661	52484.4	262.42		21483
3	7797.4	38.99		1060	8119.8	40.60		12028	3183.1	15.92		354221
4	1256.8	6.28		6579	22264.9	111.32		4387	1952.7	9.76		577416
5	577.2	2.89		14325	3532.2	17.66		27650	3399.2	17.00		331702
6	1225.1	6.13		6749	4501.4	22.51		21697	1163.9	5.82		968743
7	2158.6	10.79		3830	4234.9	21.17		23062	165555.8	827.78		6811
8	1326.6	6.63		6233	130618.7	653.09		748	16827.4	84.14		67005
9	2104.3	10.52		3929	6598.9	32.99		14800	4015.2	20.08		280813
10	517.1	2.59		15990	15652.1	78.26		6240	10171.9	50.86		110847
11	1168.4	5.84		7077	19334	96.67		5052	6574.2	32.87		171507
12	6227.4	31.14		1328	9166.4	45.83		10655	2891.8	14.46		389902
13	1508.6	7.54		5481	115.6	0.58		844866	799.0	4.00		1411164
14	2169.6	10.85		3811	619.9	3.10		157552	1526.2	7.63		738776
15	9562.2	47.81		865	39176.6	195.88		2493	18365.5	91.83		61393
16	1755.1	8.78		4711	39924.4	199.62		2446	1045.8	5.23		1078141
17	ND	ND		-	1007.4	5.04		96949	1767.3	8.84		637990
18	1733.1	8.67		4771	102795.4	513.98		950	11831.4	59.16		95299
19	1242.5	6.21		6655	2005.1	10.03		48709	1319.9	6.60		854247
20	3023.9	15.12		2734	64564.6	322.82		1513	11477.9	57.39		98234
Average	2494.4	12.47		3315	25425.65	127.1283		3841	16004.4	80.02		70451

Table 1. Levels of BTX reported by Svarch-Pérez et al.^[4], their corresponding daily exposure from vaping 5 mL of EC per day and the daily exposure in a working environment with BTX at PEL levels.

¹ For daily consumption of 5 mL EC liquid.

² Based on an inhalation volume of 12.96 m³ (12,960 L) in 8 hours in a working environment.

ND: not detected.

Results

Results for the 20 devices tested by Svarch-Pérez et al. are shown in Table 1. For benzene, the average daily exposure from EC use ranged from 2.89 to 47.81 μg , while benzene was not detected (ND) in one sample. The PEL for benzene (3.19 $\mu\text{g}/\text{L}$) corresponds to an 8-hour working exposure of 41,342.4 μg . Therefore, EC use would expose users to 865 to 15,990-fold lower levels of benzene compared to working for 8 hours in an environment with benzene levels at the PEL, a more than 3 to 4 orders of magnitude difference. The average levels of benzene for the 19 samples reported by Svarch-Pérez et al. would result in a daily exposure of 12.47 μg from EC use, which is 3,115-fold lower than daily exposure in a working environment with the PEL for benzene.

For toluene, the average daily exposure from EC use ranged from 0.58 to 653.09 μg . The PEL for toluene (37.68 $\mu\text{g}/\text{L}$) corresponds to an 8-hour working exposure of 488,332.8 μg . Therefore, EC use would expose users to 748 to 844,866-fold lower levels of toluene compared to working for 8 hours in an environment with toluene levels at the PEL, a more than 3 to 5 orders of magnitude difference. The average levels of toluene for the 20 samples reported by Svarch-Pérez et al. would result in a daily exposure of 127.13 μg from EC use, which is 3,841-fold lower than daily exposure in a working environment with the PEL for toluene.

For xylenes, the average daily exposure from EC use ranged from 4.00 to 827.78 $\mu\text{g}/\text{d}$. The PEL for xylenes (435 $\mu\text{g}/\text{L}$) corresponds to an 8-hour working exposure of 5,637,600 μg . Therefore, EC use would expose users to 6811 to 1,411,167-fold lower levels of xylenes compared to working for 8 hours in an environment with xylenes levels at the PEL, a more than 3 to 6 orders of magnitude difference. The average levels of xylenes for the 20 samples reported by Svarch-Pérez et al. would result in a daily exposure of 80.02 μg from EC use, which is 70,451-fold lower than daily exposure in a working environment with the PEL for xylenes.

Discussion

On the grounds of their chemical analysis of e-liquids and aerosols in a sample of 20 disposable vaping devices collected in Mexico, Svarch-Pérez et al.^[4] conclude that, in most devices, BTX concentrations surpassed the PELs and STELs listed for these compounds by Cal/OSHA^[5]. They also claim that these concentrations also surpassed BTX levels in tobacco smoke. However, as we have shown in this analysis, the authors' conclusions are invalid, as they were derived from the various methodological flaws we described. The main findings of our study show orders of magnitude lower exposure from EC use compared to working in an occupational setting with PELs for BTX.

The main and most serious problem in the study by Svarch-Pérez et al. is the liquid volume they used to define their reported concentrations in their Table S1. Comparisons with Cal/OSHA standards require concentrations in air volumes, which result in exposure through breathing. Taking a puff from an EC leads to a mixture of environmental air with aerosol from the device being inhaled by the user. Had the authors wanted to compare concentrations that would result in exposure through breathing, they should have compared PELs in the occupational setting with the concentration of BTX in an EC puff. The latter could be calculated by measuring the amount of BTX emissions in a single puff and assuming that this would be dissolved in 0.5 L air volume, since this is the average tidal volume. Instead, the authors compared PELs (in $\mu\text{g}/\text{L}$, with 1 L air volume corresponding to 2 breaths) with the amount of BTX in 1 L of aerosolized e-liquid, corresponding to 200-250 days of EC consumption.

To illustrate the huge discrepancy between their analysis and a comparison of breathing concentrations, we make such a calculation using the results from the sample device marked with the number 8 in their figure 1, a Fly EVO disposable device available in the Mexican market, which produced the highest reported total xylenes concentration of 166,555 $\mu\text{g}/\text{L}$. That device is labelled as containing 16 mL of liquid and delivering 8000 puffs. Using formula (1) from the Methods Section, we calculated that each puff would contain 0.667 μg of total xylenes, resulting in an inhaled concentration of 1.33 $\mu\text{g}/\text{L}$ considering a tidal volume of 0.5L. This is 327-fold lower than the PEL for total xylenes and more than 5 orders of magnitude lower than the concentration Svarch-Pérez et al.

reported in their study^[4] (which of course referred to 1 L of aerosolized EC liquid). The same error appears in all their calculations and comparisons, making their conclusions obsolete.

Still, while a methodology of comparing air concentrations would appear reasonable, it does not address the problem that toxicological comparisons should also be linked to exposure times. While Cal/OSHA respiratory occupational standards are defined for continuous inhalation (with every single breath) during a work shift of 8 hours, EC use involves intermittent inhalation only, when users are taking a puff. The normal resting respiratory rate of adults is 12 breaths/min, meaning that the average person would take at least 5760 breaths in an 8-hour working shift, even if we assume resting conditions while working. In contrast, vapers take approximately 200–300 puffs per day. Thus, we compared total daily exposure levels, considering the 8-hour exposure to PELs and the average daily EC use consumption, with the latter being spread throughout the waking hours and not involving continuous exposure. Such a method has been used previously in publications to address the discrepancy between intermittent exposure from vaping and continuous exposure in a working environment^{[13][15]}.

Another problem in the study by Svarch-Pérez et al. was that their calculations using the labelled puff number in the devices are extremely unreliable since the number of puffs that can be delivered depends on users' habits that exhibit enormous interindividual variation. It would have been preferable to weigh the devices before and after taking puffs for analysis, and thus measure emissions per weight of liquid aerosolized based on true measurements rather than manufacturers' labelling specifications. Still, it would be inappropriate to compare emissions per Kg of aerosolized liquid, which corresponds to a consumption for 200–250 days, with an amount per L of environmental air, which corresponds to 2 breaths.

BTX compounds are mostly, but not exclusively, combustion-related and, thus, are not expected to be detected at significant levels in EC aerosols that are generated at temperatures below 300 °C, which do not involve combustion. Using e-liquids prepared by intentionally adding these (and other) compounds, Wagner et al.^[16] showed that BTX transfer efficiently to the aerosols but are unstable when injected in the e-liquid, with full evaporation happening in 90 hours. These results suggest that reported detection of trace amounts of BTX in e-liquids and aerosols likely originates from contamination from background air, analytical equipment, or laboratory reagents. Therefore, it is important to exclude the possibility that these compounds were also present in blank samples. Similar findings were reported by Margham et al.^[17]. Pankow et al.^[18] targeted and quantified benzene in aerosols generated by prefilled pod systems which contained nicotine salt prepared with benzoic acid as well as by two other unspecified tank devices. They also used e-liquids spiked with benzoic acid and benzaldehyde. Benzene was not detected in the prefilled pod system and appeared in minuscule concentrations, below 1.9 µg/m³, in the two tank devices puffed in their normal operational power. Benzene concentrations only reached higher levels when puffing the devices with excessive power (up to 25 W) under overheating conditions. With heavily spiked e-liquids, concentrations reached up to 5000 µg/m³, which (even under such abnormal conditions) were way below the benzene concentration of 200,000 µg/m³ in tobacco smoke. In general, detection of BTX compounds in e-liquids and vaping aerosols is very infrequent. LeBouf et al.^[19] examined aerosols from 146 commercial e-liquids, detecting benzene in 5 samples (maximal concentration 1.6 ppm), m, p-xylene in 5 samples (maximal concentration 0.18 ppm), o-xylene in 4 samples (maximal concentration 0.14 ppm) and toluene in 4 samples (maximal concentration 0.38 ppm). Goniewicz et al.^[20] found toluene and m, p-xylene in 10 of 12 samples of aerosols from devices in Poland, but the concentrations were comparable to those of the blank samples. Harrison and Myers^[21] detected benzene and toluene without quantifying them, but both were also detected in blank samples. Czoli et al.^[22] detected without quantifying benzene in one sample out of 166 commercial e-liquids.

The study by Svarch-Pérez et al. also has problems in the testing methodology. As mentioned before, generating aerosols with only two puffs leads to unreliable results and deviates from testing standards^[8]. The authors' analytic method (thermal desorption^[23]) has been used to analyze gaseous, liquid, and solid samples, but might not be appropriate to analyze vaping aerosols. Svarch-Perez

et al. puffed the devices at 0.25 L/min, the maximum airflow possible for the vacuum pump SKC 224-PCXR8, an airflow rate unrepresentative of user inhalation and far below the recommended standards of 1 L/min. The authors mention briefly testing blank samples, but the outcomes of these tests are not disclosed, and no further information is supplied. Also, there is no information on how the devices were obtained, handled, stored, and transported. This, together with the lack of disclosure of blank samples, are serious flaws when analyzing illicit devices that could have been contaminated or mishandled.

In conclusion, we identified serious methodological and interpretational problems in the study by Svarch-Pérez et al. measuring BTX emissions in ECs. This risk assessment analysis, based on total daily exposure to BTX, identified that ECs expose users, on average, to approximately 3000 to 70,000-fold lower BTX levels compared to exposure during an 8-hour work shift in an environment containing BTX at PELs based on Cal/OSHA. The difference is so enormous that even extreme consumption of ECs is associated with far lower exposure to BTX compared to working in an environment that is considered safe according to air quality guidelines. The study by Svarch-Pérez et al. contains so many errors, including errors in converting between different units (ppm to µg/L), that editors should consider the possibility of retraction.

Statements and Declarations

Author Contributions

"Conceptualization, FK and RAS.; Methodology, FK and RAS.; Formal Analysis, KF and RAS.; Investigation, KF and RAS.; Writing – Original Draft Preparation, KF and RAS.; Writing – Review & Editing, KF and RAS.

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Conflicts of interest

The authors declare no conflict of interest.

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