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Emissions from electronic cigarettes: Assessing vapers' intake of toxic compounds, secondhand exposures and the associated health impacts

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Abstract

E-cigarettes likely represent a lower risk to health than traditional combustion cigarettes, but they are not innocuous. Recently-reported emission rates of potentially harmful compounds were used to assess intake and predict health impacts for vapers and bystanders exposed passively. Vapers' toxicant intake was calculated for scenarios in which different e-liquids were used with various vaporizers, battery power settings and vaping regimes. For a high rate of 250 puff day^{-1} using a typical vaping regime and popular tank devices with battery voltages from 3.8 to 4.8 V, users were predicted to inhale formaldehyde (up to 49 mg day^{-1}), acrolein (up to 10 mg day^{-1}) and diacetyl (up to 0.5 mg day^{-1}), at levels that exceeded US occupational limits. Formaldehyde intake from 100 daily puffs was higher than the amount inhaled by a smoker consuming 10 conventional cigarettes per day. Secondhand exposures were predicted for two typical indoor scenarios: a home and a bar. Contributions from vaping to air pollutant concentrations in the home did not exceed the California OEHHA 8-h reference exposure levels (RELs), except when a high emitting device was used at 4.8 V. In that extreme scenario, the contributions from vaping amounted to as much as 12 µg m^{-3} formaldehyde and 2.6 µg m^{-3} acrolein. Pollutant concentrations in bars were modeled using indoor volumes, air exchange rates and the number of hourly users reported in the literature for US bars in which smoking was allowed. Predicted contributions to indoor air levels were higher than those in the residential scenario. Formaldehyde (on average 135 µg m^{-3}) and acrolein (28 µg m^{-3}) exceeded the acute 1-h exposure REL for the highest emitting vaporizer/voltage combination. Predictions for these compounds also exceeded the 8-h REL in several bars when less intense vaping conditions were considered. Benzene concentrations in a few bars approached the 8-h REL, and diacetyl levels were close to the lower limit for occupational exposures. The integrated health damage from passive vaping was derived by computing disability-adjusted life years (DALYs) lost due to exposure to secondhand vapor. Acrolein was the dominant contributor to the aggregate harm. DALYs for the various device/voltage combinations were lower than –or comparable with– those estimated for exposures to secondhand and thirdhand tobacco smoke.

Introduction

Electronic cigarettes produce an aerosol –often referred to as "vapor"– that is primarily inhaled by the user, but the vapor can also be partially released by exhalation and/or leaked from the mouth into the environment, raising concerns about secondhand exposures. Use of e-cigarettes is increasing rapidly in the US and many other countries, particularly among young consumers, as vaping technology and practices continue to evolve.[1] In May 2016 the US Federal Drug Administration (FDA) finalized a ruling that authorized regulation of their manufacture, import, packaging, labeling, advertising, promotion, sales and distribution.[2] Before this development, e-cigarettes had not been subject to the same restrictions as conventional tobacco products. While e-cigarettes are likely to be less harmful than conventional tobacco products, misleading marketing often portrays these products as generating non-toxic emissions that can safely be used indoors.[3, 4] The FDA ruling indicates that limiting exposures to secondhand e-cig vapor must be considered, and more research on this topic is needed. At least six states in the USA currently ban the use of e-cigarettes in public spaces to ensure 100% smoke free environments, and a large number of municipalities, universities and private companies have adopted similar measures.[5] The objective of this study is to address the critical need for exposure assessments and prediction of the health effects associated with inhalation of mainstream and secondhand vapor, e.g. by establishing valid quantitative comparisons with harm caused by conventional cigarettes and other known exposures to toxicants.

In a recently-published study, we quantified emissions from three e-liquids used in two different e-cigarettes operated over a range of voltages from 3.3 V to 4.8 V under conditions that reproduced a typical vaping regime.[6] Emission factors for nine toxicants were determined for initial and steady-state puffing regimes. Toxicants present in the vapor included formaldehyde, acetaldehyde, acrolein, diacetyl, acetol, glycidol, nicotine, nicotyrine and benzene. In the current study these emission factors are the inputs to calculations that predict users' intakes of toxicants in mainstream vapor, and non-users' exposures to secondhand vapor. The fractions of these toxicants retained by users were derived from published results for electronic and conventional cigarettes, and incorporated into the calculation that generated the inhaled doses and the contributions of vaping to indoor pollutant concentrations. Secondhand exposures were derived for two scenarios corresponding to a typical home and bars that allowed vaping, an occupational setting commonly found in the hospitality industry. By quantifying these exposures, the resulting potential harm to passive vapers could be predicted using disability-adjusted life years (DALYs). This metric enables direct comparison of the impacts of particular e-cigarettes with those associated with second- and thirdhand tobacco exposures. DALYs are hereby proposed as a tool to predict the magnitude of the harm caused by e-cigarette vapor in indoor environments.

Materials and Methods

Users' retention of e-cigarette emissions

The extent to which inhaled individual vapor constituents are retained in the mouth cavity and upper respiratory tract was predicted from literature data for conventional and electronic cigarettes as described below, assuming that the relevant physical, chemical and biological processes are comparable for vaping and smoking. As the device is removed from the mouth at the end of a puff, part of the undiluted vapor is pulled out, together with an additional amount that can be voluntarily or involuntarily discharged prior to inhalation, becoming a source of indoor air pollutants. In addition, exhaled breath contains toxicants that have not been fully absorbed during puffing and also contribute to increasing indoor pollutant concentrations. Hence, two quantities are used to establish the extent of retention by the vaper: the fraction of vapor spilled from the mouth prior to inhalation, defined as mouth spill (*MS*), and the compound-specific respiratory retention (R_R) during an inhalation/exhalation cycle. The retention factor for each compound (R) is thus computed as:

$$R = (1 - MS) \times R_R \quad (1)$$

Two different clinical studies described by St Charles et al [7] showed significant agreement in the quantitative evaluation of *MS* for conventional cigarettes. In order to account for the amount of spilled smoke, the daily nicotine dose for each subject was compared with a nicotine mass equivalent determined from urinary cotinine and other five urinary metabolites in both studies. The results showed a broad normal distribution centered around *MS* = 30%. For our assessment we adopted the range 20% < *MS* < 40%, which captures roughly the two central quartiles. It should be noted that puff duration and other topography parameters are different for conventional and electronic cigarettes[8], and for that reason using *MS* derived from tobacco cigarettes may be a source of bias.

Compound-specific R_R values have been determined for only a few compounds [9-12], among which formaldehyde, acetaldehyde, acrolein and nicotine are relevant to this study and reported in Table S1 (Supporting Information). Values for the other compounds considered here were predicted using a correlation between R_R and the vapor pressure proposed by St Charles et al [7], and are also listed in Table S1. Due to the high volatility of these toxicants, predicted R_R values are in the range 93-99%, consistent with almost quantitative absorption into the respiratory tract. For that reason, *MS* is the dominant contributor to concentrations of e-cigarette toxicants in indoor air.

Modeling intake of mainstream vapor

We estimated the user's daily intake *I* as a function of vaping topology, device characteristics and user retention, as follows:

$$I_{i,j,k,l,m} = [(P_i^{initial} \cdot E_{i,j,k,l}^{initial} + P_i^{st-state} \cdot E_{i,j,k,l}^{st-state}) R_{l,m}] N \qquad (2)$$

Subscripts *i* refers to the applied voltage, *j* to the device considered, *k* to the e-liquid used, *l* to the compound being considered, and *m* to the user. *P* is the number of puffs for a single puffing session, *E* is the mass emitted per puff, *R* is the retention factor and *N* is the number of puffing sessions in a day. Vapers' intake was estimated for a worst-case scenario of 250 puffs per day, near the maximum daily number of puffs reported by a large number of vapers (n = 812).[13] A key observation in our previous study was that emission rates were not constant during a puffing session. Emission rates increased during the initial 5-15 puffs (depending on the device/voltage combination), reaching a steady state for subsequent puffs after that point. For that reason, we investigated three different vaping regimes:

a) **Frequent short sessions** corresponding to 25 daily sessions of 10 puffs each. The emission rates for this computation were only those that corresponded to the initial conditions, since steady-state was never reached;
b) **Intermediate "typical" conditions**, with 10 daily sessions of 25 puffs each, combining initial and steady-state emission rates in roughly equal amounts, and
c) **Infrequent long sessions**, with only 5 daily sessions of 50 puffs each, in which steady-state emission rates predominate.

This matrix of puffing regimes allowed for a sensitivity analysis of our model, because vapers' behavior is one of the variables with most influence on the levels of exposure.

The two vaporizers considered were the same used in our previous study: an eGO CE 4 single-coil vaporizer ("EGO") and a dual-coil device, the Kangertech Aerotank^{TM} Mini ("AERO"). Similarly, the three e-liquids were those used previously in our group: Apollo Classic Tobacco ("CT"), Drip Mojito Mix ("MOJ") and Drip Bubblicious ("BUB").

Modeling intakes of secondhand vapor

Two indoor environments were considered, in which non-users could be exposed to e-cigarette vapor: 1) a residential setting where a non-user lives with a user, and 2) a bar that allows vaping indoors. The per-puff mass emission rates in exhaled vapor, *EXH*, were defined as the non-retained fraction of the e-cigarette emissions for initial and steady-state regimes, as follows:

$$EXH^{initial}_{i,j,k,l,m} = E^{initial}_{i,j,k,l} \cdot (1 - R_{l,m}) \tag{3}$$

$$EXH^{st-state}_{i,j,k,l,m} = E^{st-state}_{i,j,k,l} \cdot (1 - R_{l,m}) \tag{4}$$

These emission rates were used as inputs to calculate indoor air pollutant concentrations using home and bar scenarios as described in the Supporting Information.

Health impact assessment

The integrated chronic harm caused by inhalation of secondhand vapor constituents was predicted for the residential and occupational scenarios by calculating the corresponding DALYs lost due to resulting illness, disability and premature death. DALYs are a measure of the overall disease burden and incorporate both disease likelihood and severity.[14, 15] This metric, used by the World Health Organization, makes it possible to aggregate mortality and morbidity into a parameter that can be used to compare across different health outcomes, chemical exposures and affected populations. DALYs have recently been incorporated into health impact assessments of exposures to indoor pollutants, including thirdhand smoke gases and particles.[16,17] This approach estimates, on a compound-by-compound and device-by-device basis, the population-averaged health damage per year of exposure.[16] In this study, DALYs were computed from exposure estimates and toxicology-derived damage factors (*δDALYs/δintake*) for VOCs as developed by Huijbregts et al.[18] Using these values, the DALYs lost for one person breathing chemical *l,* for one year, based on exposure were calculated with equation 5:

$$\Delta DALY_l = \Delta C \cdot B \cdot \left(\frac{\partial DALY_{cancer}}{\partial intake_l} + \frac{\partial DALY_{non-cancer}}{\partial intake_l} \right) \tag{5}$$

where ΔC is the difference in exposure concentration for the non-user compared to levels predicted in the absence of vaping, and B is the breathing volume. The average breathing volume used for adults over 16 years old was 15 m^3 day^{-1}, or 5475 m^3 $year^{-1}$, assuming that the damage-intake relationship is linear in the range of interest.[16] We did not use this approach for primary users inhaling mainstream vapor because exposures are high and likely to be outside of the linear range.

Damage factors were available for five of the toxicants considered in this study: formaldehyde, acetaldehyde, benzene, acrolein and glycidol. A Monte-Carlo simulator (100,000 repetitions) was used to develop a distribution of aggregate health damage for chronic intake of each toxicant in the home and bar scenarios. Both exposures had similar toxicant profiles. Aggregate harm was compared across scenarios using the same stochastically selected damage profiles for each toxicant.

Results and discussion

Impact on the user (vaper)

Predicted toxicant intake. Figure 1 illustrates the effects of key parameters on the vapers' toxicant intake, as predicted by Equation 2. These parameters include the choice of vaporizer, operation voltage and vaping regime, thus accounting for the key drivers of the impacts on users' intake. Uncertainty in the determination of the retention factor led to additional variability, described with error bars in Figure 1. The effect of uncertainty in the retention factor is further illustrated for one set of conditions in Figure S1 (Supporting Information). The variability associated with switching from one e-liquid to another is presented in Figure S2 (Supporting Information).

The AERO device operated at lower temperatures than the EGO vaporizer at the same voltage.[6] As a consequence, using the EGO device led to higher toxicant intakes than those predicted for the AERO device when both were run at 3.8 V. By increasing the voltage of the EGO device from 3.8 V to 4.8 V, the intake of formaldehyde, acetaldehyde and acrolein grew by an order of magnitude. These volatile aldehydes are highly irritating to eyes and the respiratory system. Formaldehyde and acetaldehyde are also possible carcinogens (WHO/IARC Group 2B; US EPA Group B2). These compounds were produced in larger amounts when the combinations of device and voltages led to higher vapor temperatures.[6] Such increases were not observed for compounds such as nicotine and nicotryine, which are not pyrolysis byproducts. Diacetyl is often considered to be a flavoring, but it was not present in the formulation of the e-liquids. Its emission rates in the vapor increased by changing from AERO to EGO, and from 3.8V to 4.8V. This similarity to volatile aldehydes suggests that diacetyl is formed as a decomposition byproduct. Benzene has recently been reported as being formed as decomposition byproduct as well.[19]

For formaldehyde, acrolein and diacetyl, the daily doses predicted for a relatively high usage rate of 250 puffs day^{-1} were comparable to or exceeded those derived from occupational health guidelines. The maximum limit recommended by the National Institute for Occupational Exposure and Health (NIOSH) for an 8- or 10-h time-weighted average exposure and/or a ceiling is 20 µg m^{-3} for formaldehyde and 250 µg m^{-3} for acrolein.[20] For diacetyl, NIOSH recommended a level of 5 ppb (1.4 µg m^{-3}) for up to 8-h daily exposures in a 40-h workweek.[21] Assuming a constant breathing rate of 15 m^3 day^{-1},[22] the amounts inhaled during an 8-h work day at the NIOSH-determined limits are estimated as 0.1 mg formaldehyde, 1.3 mg acrolein and 7 µg diacetyl. These values are either comparable to or lower than daily intake rates from vaping. For formaldehyde and diacetyl, the predicted daily intakes from e-cigarettes were higher than NIOSH guidelines by more than an order of magnitude under all vaping regimes, for both devices and both voltage settings. This suggests that NIOSH limits could be exceeded even with a lower, more typical vaping rate (e.g., 100 puff day^{-1}). Predicted acrolein intake was comparable to or higher than NIOSH guidelines only for the more extreme vaping conditions (i.e., using the EGO device at 4.8 V under the typical or intense vaping regimes).

Different vaping regimes had major effects on the predicted toxicant intakes. A sensitivity analysis for each toxicant is presented in Table S2 (Supporting Information). Average increases in the intake rates were between 11 and 63% when switching from the less intense to the intermediate "typical" regime. Switching from the intermediate to the more intense vaping regime showed average changes in intake rates between 8 and 30 %.

Comparing aldehyde intake from electronic and conventional cigarettes. E-cigarette vapor contains fewer compounds than tobacco smoke, and many of the known carcinogens in cigarette smoke are absent from the vapor. However, relatively high levels of volatile aldehydes are found in e-cigarette vapor. A comparison of aldehyde intake by smokers and vapers was carried out to quantify the relative exposures. We assumed a moderate vaping scenario of 100 puffs per day following the previously described three vaping regimes. Intake from smoking was estimated for an average of 10 cigarettes per day using emission rates reported in the literature (Table S3, Supporting Information). Mainstream emission rates for conventional cigarettes were obtained following the ISO, CORESTA and Health Canada Intense methods. [23-25] The reported range of emission rates reflects differences in yields obtained for each method and the variability observed among commercial and reference cigarettes. Daily intakes presented in Figure 2 were calculated as the product of the retention factors (Table S1) and emission rates for each compound present in e-cigarette vapor or in mainstream cigarette smoke, respectively. We assumed that the retention factors are the same for vaping and smoking. It should be noted that smokers are exposed not only to mainstream smoke during active puffing, but they also inhale undiluted sidestream smoke in close proximity to the smoldering tip of the cigarette, an additional source of exposure not included in this analysis. Results from Figure 2 indicate that formaldehyde intakes for all e-cigarettes, voltages and vaping regimes were higher than for mainstream tobacco smoke. The intake of acrolein and acetaldehyde using the EGO device were comparable to combustion cigarettes for most conditions. Intake of diacetyl from e-cigarettes was below values predicted for smoking in all cases. In summary, the overall intake of volatile aldehydes from e-cigarettes was comparable to that from conventional cigarettes.

Biomarkers of human exposure are available for acrolein and benzene, but not for formaldehyde or acetaldehyde. Three studies tracking biomarkers of acrolein found that exposure was much lower for e-cigarette users than for smokers, and generally similar to that of non-smokers. [26-28] Our predictions for the more frequent, shorter vaping sessions are consistent with those findings. However, similar levels of acrolein exposure in smokers and e-cigarette users were predicted with less frequent, longer puffing sessions. The discrepancies between biomarker studies and our model simulations for more extreme vaping regimes are likely due to differences in the devices and vaping regimes used in each case.

Impacts on non-users

Figure 3 shows the incremental concentrations (ΔC) of indoor air pollutants attributed to e-cigarette's exhaled mainstream vapor. Conditions reported correspond to typical puffing sessions of 25 puffs each. Results for more moderate –frequent short sessions– and extreme vaping conditions –infrequent long sessions– are presented in Figure S3 and S4 (Supporting Information), respectively. Increases in indoor air concentrations were evaluated for the AERO vaporizer operating at 3.8 V, and for the EGO vaporizer operating at both 3.8 and 4.8 V. In all cases, the e-liquid considered was CT. Values plotted in Figures 3, S3 and S4 correspond to average determinations, and the error bars illustrate the range of values considered.

Residential exposures. Figure 3(A) presents results corresponding to a scenario in which both the vaper and the non-vaper stay at home most of the time, a worst-case setting for residential exposures. Household pollutant levels were impacted by toxicants exhaled by the user, and the magnitude of those changes strongly depended on the emission rates for each device/voltage combination, the vaping topography and the retention factors for each compound. The error bars reflect the variability of retention factors considered in this study. In most cases, higher contributions to indoor concentrations were predicted for the EGO vs. the AERO vaporizer.

Similarly, higher levels were predicted for the higher power setting of 4.8 V, compared to 3.8 V. In most cases, toxicant concentrations did not exceeded the health-based 8-h reference exposure levels (RELs) established by the California Office of Environmental Health Hazard Assessment (OEHHA). Only the EGO device at the highest voltage produced increments in formaldehyde concentration that exceeded the 8-h REL (9 μg m^{-3}) and acrolein levels that were comparable to the 1-h REL (2.5 μg m^{-3}). The 40-h workweek occupational exposure limits for diacetyl (1.4 μg/m^3) was not exceeded under any operation conditions. Acetaldehyde and benzene concentrations were far below the corresponding 8-h REL in all cases (300 μg m^{-3} and 27 μg m^{-3}, respectively).

Results presented in Figure S3 (Supporting Information) provide the corresponding sensitivity analysis. When a vaping regime with lower emissions was used (frequent short sessions), all ΔC values were below the 8-h RELs. However, when a more intense puffing regime was considered, the EGO vaporizer at 4.8 V led to predicted contributions to indoor levels that exceeded the 1-h REL for acrolein, and the 8-h REL for formaldehyde, but remained below the 8-h RELs for acetaldehyde and benzene and the occupational exposure levels for diacetyl. These results suggest that residential indoor air quality can be impacted by a single vaper, although under most conditions and exposure scenarios the contribution of vaping to indoor pollutant levels is expected to be minor.

Exposures in a vaping bar. Figure 3(B) shows the predicted increases in indoor concentrations in a bar that allows vaping. Three parameters were used to characterize each bar: the physical dimensions of the indoor space (350 – 2500 m^3), the air exchange rate (0.6 – 6.5 h^{-1}) and the average number of vaping patrons (3.3 – 13 vapers per hour). These parameters were adapted from those determined by Waring and Siegel for 17 different smoking bars in Austin TX (Table S4, Supporting Information).[29] Values reported in Figure 3(B) represent the average for all bars, and the error bars the variability due to the diversity of building characteristics and vaping prevalence. The indoor air concentration of toxicants varied by up to a factor of 7.6 due to changes in these parameters. Overall, increments in pollutant concentrations predicted in bars were higher than those predicted in the home, and concentrations changes for the EGO device were in general higher than for the AERO vaporizer. The difference observed between the two voltage settings in the EGO device was partially offset by a combination of building characteristics (e.g., low ventilation rates, reduced space volume) or by the presence of a larger number of vapers. Changes in formaldehyde, acetaldehyde and acrolein concentrations in bars could span up to two orders of magnitude. For vaping conditions corresponding to the EGO vaporizer at the higher setting of 4.8 V, formaldehyde levels exceeded the OEHHA REL for 1-h exposure (55 μg m^{-3}) in several bars and the 8-h REL (9 μg m^{-3}) in all cases. Acrolein concentrations exceeded the acute exposure REL (2.5 μg m^{-3}) in all bars. For both compounds, the milder vaping condition (e.g., EGO device at 3.8 V) also exceeded the 8-h exposure RELs in several bars. In addition, results for the EGO vaporizer at the higher setting showed some bars approaching the 8-h REL for benzene (27 μg m^{-3}) and the 40-h workweek occupational exposure limit for diacetyl (1.4 μg/m^3).

Results shown in Figure S4 (Supporting Information) indicate that for some bars, when a less intense vaping regime with lower emissions was used, all tested conditions exceeded the formaldehyde 8-h REL. In some bars the more intense vaping regime (EGO at 4.8 V) caused the 1-h REL to be surpassed. The same extreme regime also exceeded the acrolein 8-h REL in most cases. When a more intense puffing regime was modeled, results resembled those presented in Figure 3(B): formaldehyde and acrolein exceeded the 8-h REL for at least some bars, considering all three vaping regimes, and exceeded the 1-h REL for the more intense regime. The latter setting led also to high diacetyl and benzene concentrations that approached reference limits. These results indicate that indoor air quality can be affected in bars where vaping is allowed, leading to potentially significant occupational exposures for bar personnel, in addition to affecting non-vaping patrons.

Integrated health damage

The predicted health damage associated with lifetime exposures was computed assuming average intakes for the home and bar scenarios. The results are consistent with the typical large uncertainties in modeling population-based health impacts of specific compounds, spanning several orders of magnitude. Toxicant-specific contributions to DALYs are shown in Figure 4(A) for the residential scenario in which a non-vaper is exposed to secondhand vapor from an EGO vaporizer operating the device at 3.8 V, following a typical vaping regime of 10 vaping sessions of 25 puffs each. Acrolein was the dominant contributor to the aggregate harm (75%), with formaldehyde contributing 21% and much smaller contributions from other compounds (glycidol, acetaldehyde and benzene). This is consistent with the fact that acrolein levels were close to or exceeded the 1-h OEHHA REL and formaldehyde levels exceeded the 8-h REL.

In Figure 4(B) results are shown for the aggregate damage integrating all toxicants for residential and bar exposures, taking account of the three device/voltage combinations analyzed in this study. The figure presents DALYs for these six modeled scenarios alongside previous results for combined second- and thirdhand tobacco smoke (SHS/THS) in the same residential scenario used in this study.[17] We compared the impacts of VOCs found in e-cigarette vapor with those of the VOC fraction of SHS/THS, as well as with the full impact of SHS/THS (VOCs + $PM_{2.5}$). Overall, vaping scenarios led to DALYs that were lower than those calculated for the VOC fraction of SHS/THS. When $PM_{2.5}$ from conventional cigarettes was included in the analysis, the impact associated with SHS/THS was even higher, and the gap with e-cigarettes larger. $PM_{2.5}$ was the largest contribution to aggregate heath damage for SHS/THS using concentration-response functions derived from outdoor air particles.[30] Aerosols emitted by e-cigarettes are predominantly composed of liquid droplets that evaporate fairly quickly and may contribute differently to long-term $PM_{2.5}$ exposures. Most of the compounds described in this study are initially associated with aerosol particles.[31] There is recent evidence of metal nanoparticles present in e-cigarette vapor at high concentrations, but the chemical nature and toxicity of these nanoparticles are unknown. [32]

In Figures S5 and S6 (Supporting Information) we present the same analysis carried out when emission rates are calculated using frequent short vaping sessions and infrequent long vaping sessions, respectively. Results presented in Figure S5 show DALYs that were between one and two orders of magnitude lower than those calculated for the VOC fraction of SHS/THS due to the lower emission rates achieved with that vaping topography. By contrast, Figure S6 shows predicted DALYs for the home and bar scenarios that, when vaping was carried out with the EGO device at 4.8 V, were comparable to those estimated for the VOCs present in SHS/THS. This result is consistent with vaping scenarios showing high acrolein concentrations at similar orders of magnitude as the SHS/THS VOCs results, since acrolein was the main contributor to DALYs for both exposures. In all cases, our analysis suggests that long-term exposure to e-cigarette vapor would cause a lower impact on non-users' health than exposure to SHS/THS.

These predictions could be considered to be preliminary evaluations for a subset of the compounds detected in the vapor, based on the partial information that is currently available. DALYs were calculated with the incomplete information available from epidemiological and/or toxicological data. Damage factors could not be developed for diacetyl, acetol, nicotine and nicotyrine, and the contribution of particles was not considered. Similarly, regulatory limits and/or guidance to estimate safe exposure levels for acetol, nicotine and nicotyrine were not available in the literature. Despite these limitations, this methodology can serve as a tool to predict the magnitude of the harm caused by e-cigarette vapor in indoor environments.

Implications

This study predicted that mainstream emissions contained significantly different levels of harmful chemicals depending on the choice of atomizer, the voltage used and vaping patterns.

These factors were most directly correlated to changes in intake doses and secondhand exposure levels. Switching the e-liquid did not have a major effect on emissions. Regulating e-liquid formulation may help reduce exposures to toxic compounds used as flavorings (e.g., cinamaldehyde, 2-methoxycinnamaldehyde)[33], but the main toxic burden of e-cigarettes is likely associated with thermal decomposition byproducts of the main constituents (propylene glycol and glycerin). Some of the same byproducts also originate in decomposition of flavorings.[34] Those compounds are generally in low concentration or absent in e-liquid formulations, and our study shows that the amounts produced can vary by up to two orders of magnitude. For that reason, controlling exposure to volatile aldehydes and other toxicants formed during vaporization is challenging.

A limited number of vaporizers and e-liquids were investigated, although all of them were popular in California at the time of the study (2015). We have also made assumptions about puffing regimes throughout the day that may differ from the way many vapers behave. While our predictions are not indicative of toxicant exposures for all vapers, the methodological approach for estimating exposures could be adapted for testing any particular device and e-liquid, different puffing behavior and patterns. The methods presented here could be useful for regulatory purposes, to assess potential harms caused by electronic nicotine delivery systems.

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Supporting Information

A description of model use to predict exposures to secondhand vapor; calculation of retention factors; the effect of retention factors and different e-liquids on intake; a sensitivity analysis considering three vaping regimes; estimation of daily intake of aldehydes from conventional cigarettes; change in indoor VOC concentrations and the associated DALYs for different vaping regimes.

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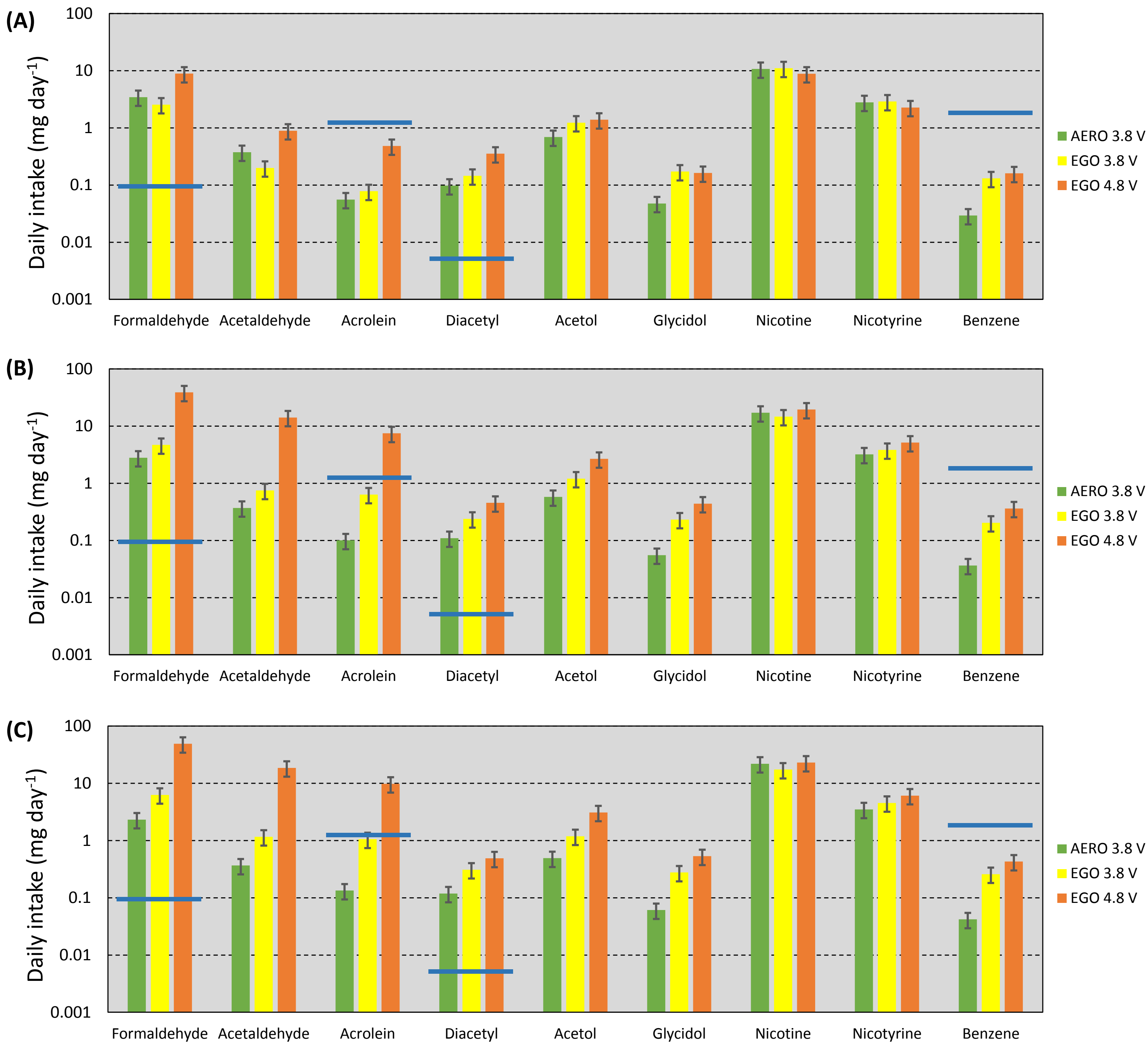

Figure 1. *Impact of the choice of vaporizer and voltage used to consume the CT e-liquid on the mass intake predicted for a high-usage rate of 250 puffs per day, distributed in (A) 25 sessions of 10 puffs each; (B) 10 sessions of 25 puffs each, and (C) 5 sessions of 50 puffs each. The blue lines correspond to daily doses derived from occupational health guidelines.*

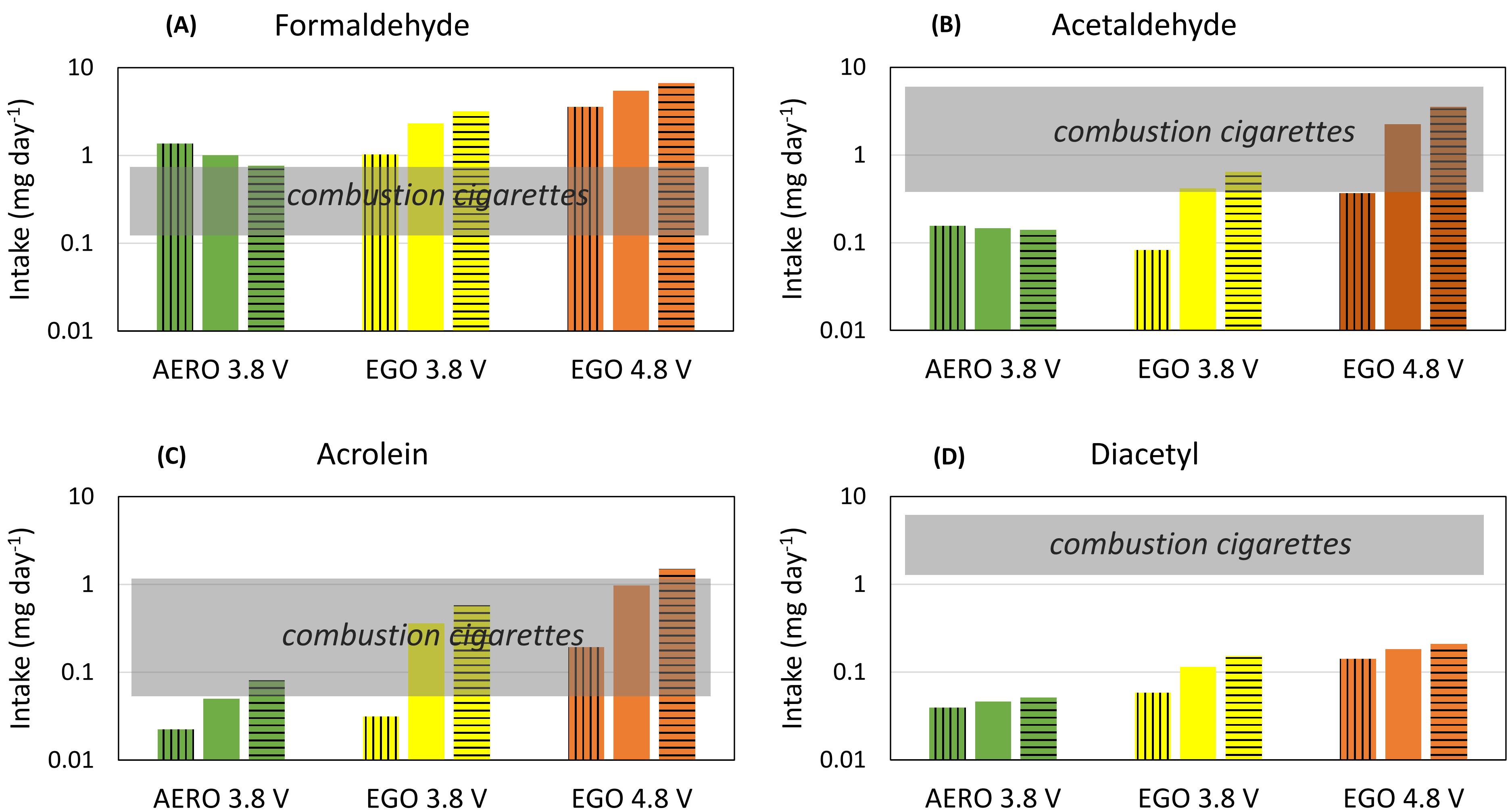

Figure 2. *Comparative estimates of vapers' and smokers' daily intake of (A) formaldehyde, (B) acetaldehyde, (C) acrolein and (D) diacetyl. Calculations were based on a moderate usage rate of 100 e-cigarette puffs per day vs. 10 combustion cigarettes smoked per day. Vaping regimes included short and frequent sessions (10 sessions of 10 puff each, vertical stripes), intermediate conditions (4 sessions of 25 puffs each, no stripes) and long, infrequent sessions (2 sessions of 50 puffs each, horizontal stripes).*

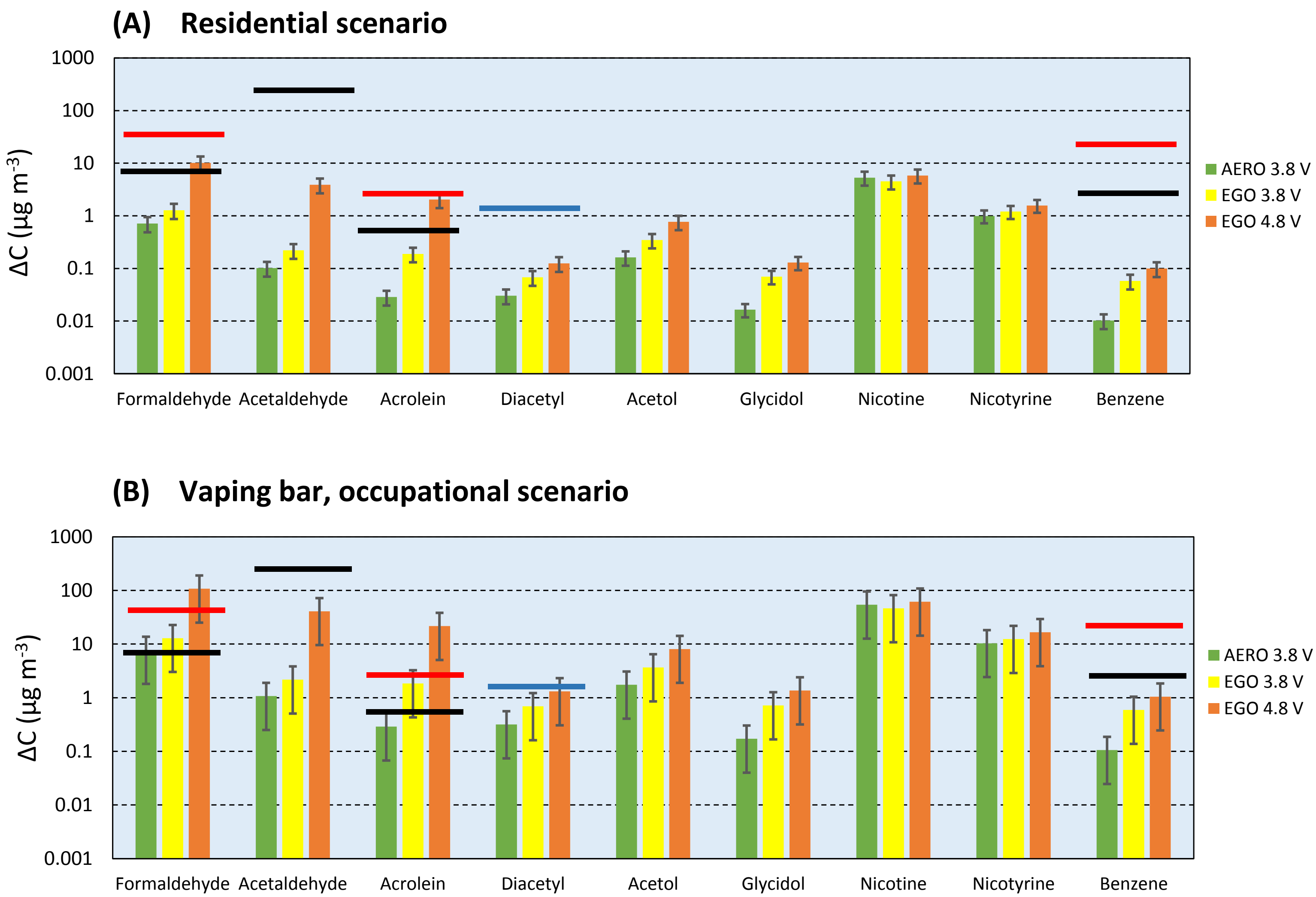

***Figure 3**. Change in average indoor air VOC concentrations for (A) a residential scenario in which the vaper stays at home most of the time, corresponding to an elevated usage rate of 250 puffs per day, and (B) a bar that allows vaping. Three different device/voltage combinations using the CT e-liquid were used to determine emission rates for typical puffing sessions of 25 puffs each. Black and red lines represent California OEHHA Reference Exposure Levels for 8-h and 1-h exposures, respectively, for formaldehyde, acetaldehyde, acrolein and benzene. The blue line represents the NIOSH recommended 40-h workweek exposure limit for diacetyl.*

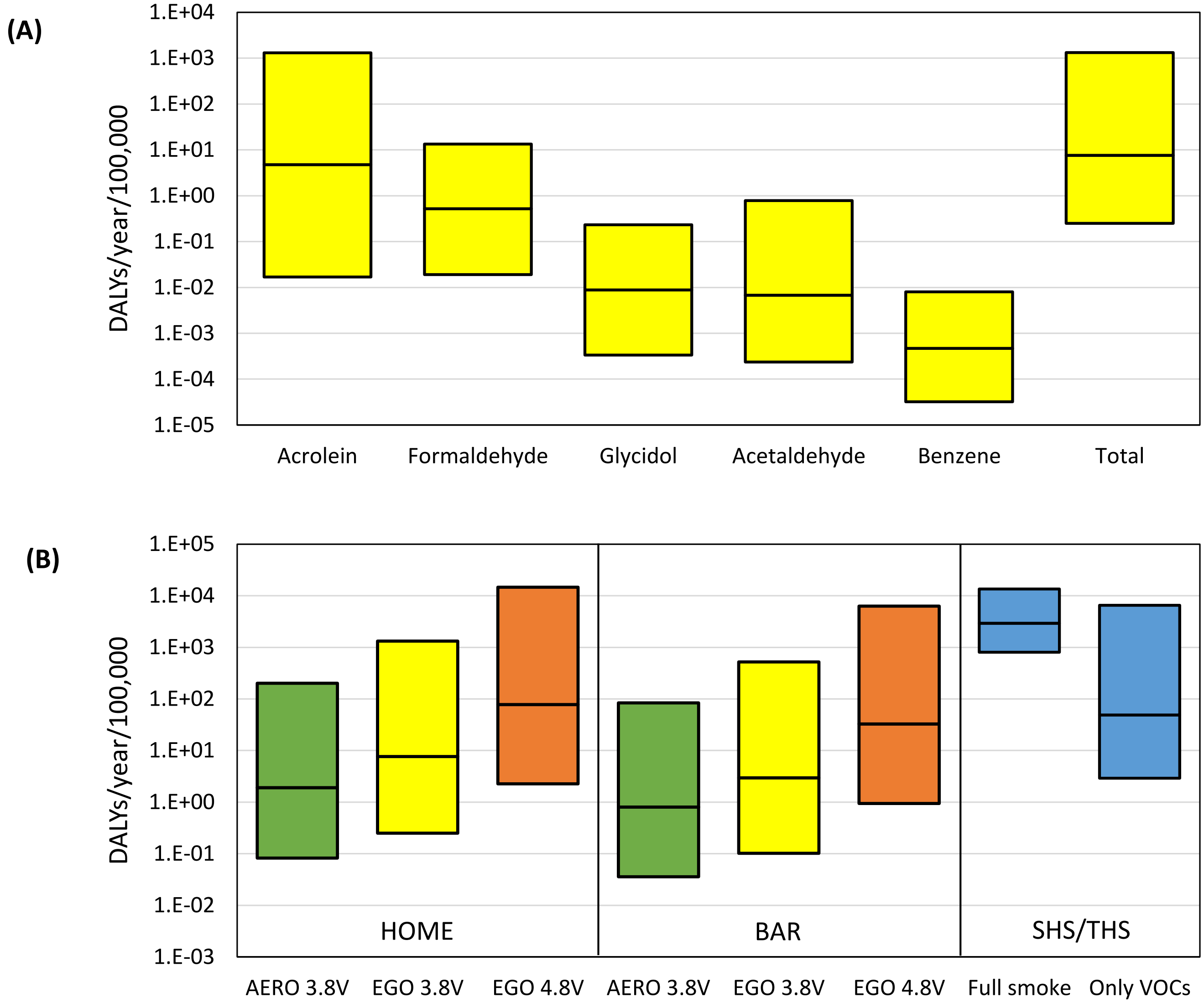

Figure 4: *Estimated DALYs for selected modeled scenarios. The boxes show the median and 95th percentile range of predicted health damage. (A) toxicant-specific impact estimated for the residential scenario in which the vaper consumes CT e-liquid using the EGO device at 3.8 V; (B) aggregated damage for six scenarios of home and bar exposures using three device/voltage combinations. In all cases, emission rates correspond to typical vaping sessions of 25 puffs each. The figure includes the estimated damage due to second- and thirdhand smoke (SHS/THS) from combustion cigarettes as calculated in our previous study.* [11] *The DALYs are presented for full smoke and for the VOCs alone (excluding $PM_{2.5}$).*