Electronic cigarettes and indoor air quality: a review of studies using human volunteers

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Abstract

Objective: This paper is primarily aimed to review articles on electronic cigarettes (e-cigarettes) focusing on indoor air quality (IAQ) assessment that were conducted using human volunteers under natural settings that mimic actual vaping scenarios. Such studies may give a better representation of the actual potential exposure towards e-cigarettes emissions in indoor settings.

Methods: A systematic literature search was conducted using PubMed search engine database. Search terms such as “electronic cigarette”, “e-cigarette”, “electronic nicotine delivery system”, and “indoor air quality” were used to identify the relevant articles to be included in this review. Articles that involved human volunteers who were asked to vape in natural settings or settings that mimic the actual vaping scenario were chosen to be reviewed. The search yielded a total of 15 published articles. Eleven articles were excluded due to 1) unavailability of its full-text (n = 1), 2) did not involve human volunteers (n = 5) and 3) did not involve an IAQ study (n = 5). Four articles were critically reviewed in this paper.

Results: From the four selected articles, two of the papers focused on the determination of nicotine level released by e-cigarettes whereas the other two covered IAQ parameters namely; particulate matters (PM), propylene glycols, formaldehyde, metals and polycyclic aromatic hydrocarbons (PAHs). Only two of the studies involved determination of biomarkers of exposure. The level of chemical contents released varied between studies. The differences in the brands of e-cigarette used, number of vapers recruited and the sensitivity of the methodologies employed in these studies may be the possible causes for such differences. However, studies using human volunteers conducted in a natural setting are more relevant to portray the actual exposure to vapors among e-cigarettes users and non-users compared to studies using a smoking machine/an exposure chamber. This is because such studies take into account the behavior of consumers and individual retention of nicotine. Such method will therefore avoid the possibility of overestimation in terms of exposures toward e-cigarettes users and non-users.

Conclusion: There are limited e-cigarette studies on the impact of IAQ performed using human volunteers in natural settings. The available studies however, provided inconsistent scientific evidence on the actual exposure towards the vapor contents as unstandardized methodology were used in conducting such research. Therefore, there is a need to conduct IAQ studies in natural settings by using a standardized protocol in terms of the number of vapers recruited, the size of the indoor settings, the methods used in detecting and quantifying the contents and levels of emissions and the sensitivity of the equipment used in analyzing the contents. This will help in better utilization of the findings from such studies for the use of risk assessment of the exposures towards e-cigarette emissions. There is also a need to emphasize that it is the onus of the manufacturers in providing and proving scientifically sound safety claims for their products prior to commercializing it in the market.

Keywords: e-cigarettes; exhaled aerosol; indoor air quality; nicotine; vaping.

Introduction

Electronic cigarettes (e-cigarettes) are battery-powered nicotine delivery systems which deliver nicotine-containing aerosols or vapors to its users by heating a...
solution commonly known as e-liquid or e-juice. E-liquids are commonly packaged and sold in a fancy and exclusive looking 30 mL dropper bottle. The e-liquids are typically made of propylene glycol or glycerol (glycerine), nicotine and assorted flavoring agents (1, 2). When users draw air on the mouthpiece of the e-cigarettes or manually switch on the fire button of the device, a sensor detects the draw and activates the heater to vaporize the e-liquid, producing a saturated vapor at a temperature greater than 350°C (3, 4). Upon leaving the heating element, the vaporized e-liquid immediately condensed to form aerosol of sub-micron liquid droplets that appears to be as clouds of smoke or fog. This mimics the experience of smoking conventional cigarettes.

E-cigarettes are marketed with the claims that it is a healthier, cleaner and cheaper smoking alternative compared to conventional cigarettes (5–9). Several studies have shown e-cigarette assists in smoking cessation or promotes reduction in the use of conventional cigarettes on a daily basis (5, 10, 11). These claims led to a sharp increment of e-cigarettes users’ population every year (12). In the United States of America (USA), the percentage of users was reported to increase from 0.6% in 2009 to 8.5% in 2013 (13, 14). From 2011 to 2014, the population of ever-user among adults increased from 6% in 2011 to 8% 2014 (15–18). However, there is no definite conclusion as several population-based studies have shown the highest rate of e-cigarette users were among those who were current smokers and former smokers (11, 15, 16). There are also those who interchangeably use e-cigarette and conventional cigarettes; commonly known as ‘dual-users’ (19, 20).

Concerns arise due to reports that e-cigarettes are being used to circumvent smoke-free policies especially in public places where smoking restriction are in place (2, 5, 7, 21). This is often because “vaping” or e-cigarettes are not included in the legislative definition of tobacco products, thus any smoking-restriction law does not apply to e-cigarettes usage. In countries where e-cigarettes are not currently regulated, vaping activities are common in smoking prohibited places (22–25). A few countries have already developed regulatory guidelines for e-cigarettes such as Canada, Brazil, Uruguay and Singapore (26). On 20th May 2016, a revised European Union’s Tobacco Product Directive (TPD) came into force in which it sets out new regulations covering e-cigarettes (27). The regulations cover the aspects of safety, packaging, labeling, sale and promotions of e-cigarette products. For instance, packaging size for refill containers will be limited up to 10 mL whereas for disposable e-cigarettes, cartridges and tanks, the allowable limit is set at 2 mL. The packaging must be child and tamper proof and the concentration of nicotine must not exceed 20 mg/mL. However, the TPD does not include any ban on vaping in public.

Beliefs regarding e-cigarettes only emitting harmless water vapor led to the unrestricted usage of this device in public places (28–30). This erroneous belief may be due to the fact that e-cigarettes have been marketed with the emphasis that they do not release harmful smoke like conventional cigarettes do (2, 31, 32). However, studies done so far have showed that the use of e-cigarettes exposes the users and non-users to nicotine, glycols, carbonyls, formaldehyde, nitrosamines, heavy metals and flavorings from the aerosols produced by the e-cigarettes (33–38). Although the level of exposures of some of these elements were reported to be much lower than conventional cigarette smoke, studies have also indicated the presence of new toxic components or chemicals which are produced from the heating process and the flavorings of the e-liquids (39–41). Among the toxic chemicals is the formation of formaldehyde and acetaldehyde in e-cigarette vapors. These chemical substances are not initially present in e-liquid but its formation in vapor is due to the (oxy) dehydration of glycerol which is one of the main ingredients of e-liquids. Formaldehyde is categorized as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), while acetaldehyde is listed in Group 2B which are possibly carcinogenic to human (42). In addition, recent studies revealed that higher power output used to operate e-cigarettes has resulted in higher concentration of these two chemicals (43–45).

Several studies have shown compelling evidence on the harmful health effects arising from the chemicals in e-liquids and vapors. Schober et al. (24) found increased levels of exhaled nitric oxide among volunteers who use nicotine-containing e-cigarettes. The study attributed the increased nitric oxide levels as an indication of pulmonary inflammation (24). Another study showed that an acute ad lib puffing of e-cigarette by healthy smokers after 4 h of abstinence from conventional cigarettes showed no effect on the spirometry test but a significant increase in dynamic airway resistance of 18% (46). This study suggested that the use of e-cigarettes constricts peripheral airways due to the irritant effects of propylene glycol. In terms of reducing the intake of nicotine between the use of conventional and e-cigarettes, a study has shown that passive smoking of e-cigarette vapors among non-smokers causes the elevation of serum cotinine concentration on a level which is similar to non-smokers who were exposed to passive smoking from conventional cigarette smoke (47).

In order to determine and quantify the exposure of e-cigarette vapors, studies have so far been conducted by using two different approaches. E-cigarette vapors were either produced by a smoking machine and were
collected to be analyzed or human volunteers were asked to vape for a length of a determined session while the exhaled vapors were analyzed. The latter approach allows researchers to detect any potential toxic substances that may be produced due to reactions between the chemicals released such as the formation of tobacco-specific nitrosamines (TSNA) (48). Furthermore, the latest generation of e-cigarette devices allows users to use different settings of voltages according to their preferences and higher voltages may affect the levels of chemical contents released with the vapors. Thus this approach provides a better picture of the real extent of exposure to the chemicals released by the e-cigarettes towards the users and non-users and avoid any overestimation of exposure.

In this paper, we examined available studies focusing on indoor air quality (IAQ) due to the use of e-cigarettes that were carried out using human volunteers that were asked to vape in natural settings (vapers used their e-cigarettes in their home) or mimics the actual vaping scenario (vapers were asked to vape in a specified room). The differences and similarities between these studies in terms of the method used and the outcomes of each study were discussed. The strengths and limitations of such studies were also reviewed. It is expected that this review will provide a concise conclusion on the effect of e-cigarettes released on the indoor air quality focusing on studies involving human volunteers.

Methods

Systematic literature searches were conducted to identify published scientific studies related to e-cigarettes and indoor air quality. A set of relevant search terms were used separately or in combination in PubMed, EBSCO, Science Direct and Google Scholar search engines using the search terms included the following: ('electronic nicotine devices' OR 'electronic nicotine delivery system' OR 'electronic cigarettes' OR 'e-cigs') AND ('indoor air' OR 'indoor air quality'). The search date was set between 2000 to June 2016. The inclusion criteria of the articles selected are 1) written in English, 2) publicly available, 3) dealt mainly or partly with e-cigarette and/or indoor air and 4) experiments or indoor air measurements were done in natural settings/mimicking the real-scenario of vaping. The search yielded a total of 15 articles that met the inclusion criteria. Article titles, keywords and abstracts were then screened for relevance, which left a total of four studies suitable for full-text review. The exclusion of the 11 other articles from this review was summarized as in Figure 1.

Results and discussion

We found four relevant studies that were conducted to determine and quantify indoor air pollutants arising from e-cigarette emissions (24, 49–51). These four studies were conducted using human volunteers in which they were asked to vape according to their preferences within a specified period of time upon which the levels of selected indoor air quality parameters were measured. Some of these studies measured only one specific indoor air parameter while others covered a wider range of e-cigarette emissions. The studies are as summarized in Table 1.

The study by Schober et al. (24) showed that vapors released from e-cigarette contains substantial amounts of 1,2-propanediol, glycerine and nicotine. This study compared the levels of a wide range of indoor air parameters in a room prior to the vaping activities and after 2 h of vaping activities. The level of possible carcinogenic content of polycyclic aromatic hydrocarbons (PAHs) in indoor air showed an increment of 20% to a total of 147 ng/m³ compared to the measurement prior to vaping. High concentrations of particulate matters (PM) were also measured but the chemical composition and size distribution of these particles differs from those produced by the combustion of conventional cigarettes (24). The PM from e-cigarette vapors are micro-droplets of 1,2-propanediol and glycerine. In terms of heavy metals, the concentration of aluminum in the room increased twofold from 203.0 ng/m³ to 482.5 ng/m³ before and after the vaping sessions. Thus, this study concluded that e-cigarettes are not emission-free as claimed by the manufacturers.

Ballbè et al. (50) reported an observational study comparing the exposure to airborne nicotine of non-smokers living at homes either with conventional cigarettes smokers or e-cigarettes users. The results were further compared with exposures of non-smokers living in...
Table 1: Summaries of articles regarding indoor air quality related to e-cigarette.

<table>
<thead>
<tr>
<th>No</th>
<th>Author, year (country)</th>
<th>Title</th>
<th>N (number of human samples)</th>
<th>Area and conditions of experiment room</th>
<th>IAQ parameters measured</th>
<th>Physiological/biomarkers measured</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Schober et al. (24) (Munich, Germany)</td>
<td>Use of electronic cigarettes (e-cigarettes) impairs indoor air quality and increases FeNO levels of e-cigarette consumers</td>
<td>9</td>
<td>Room size: 18 m² Air exchange rate: 0.56 h⁻¹ Volume: 45 m³ Equipped with three chairs, table and wardrobe (café-like settings)</td>
<td>PM, PNC, VOCs, PAHs, carbonyls, metals</td>
<td>eCO, FeNO, urinary nicotine and mercapturic acids</td>
<td>PM: (mean: 197 μg/m³, highest: 514 μg/m³) PNC: 48,620–88,386 particles/cm³ (peak at diameter 24–36 nm) Distinct increase of 1,2-propanediol (mean ± SD, 199.2 ± 93.2 μg/m³), glycerine (72.7 ± 6.9 μg/m³) and nicotine (2.2 ± 1.7 μg/m³) PAHs: 7 probable carcinogens (conc. increase by 20% during vaping)</td>
</tr>
<tr>
<td>2</td>
<td>O’Connell et al. (49) (United Kingdom)</td>
<td>An assessment of indoor air quality before, during and after unrestricted use of e-cigarettes in a small room</td>
<td>5 (3 vapers and 2 non-vapers)</td>
<td>Room size: 12.8 m² Naturally ventilated Volume: 38.5 m³</td>
<td>VOCs, nicotine, Low molecular weight carbonyls, PAHs, TSNAs, Metals</td>
<td>None</td>
<td>Total VOC: 379.8 μg/m³ CO₂: (mean: 5813 mg/m³, highest: 6800 mg/m³) Nicotine: &lt; 7.0 μg/m³ PG: highest 203.6 μg/m³ Formaldehyde: 37.6 μg/m³</td>
</tr>
<tr>
<td>3</td>
<td>Ballbè et al. (50) (Barcelona, Spain)</td>
<td>Cigarettes vs. e-cigarettes: Passive exposure at home measured by means of airborne marker and biomarkers</td>
<td>54 non-smokers (25 living with smokers, 5 living with nicotine-vapers, 24 control homes)</td>
<td>Non-smokers houses</td>
<td>Airborne nicotine</td>
<td>Salivary cotinine</td>
<td>Urinary cotinine</td>
</tr>
<tr>
<td>4</td>
<td>Bush and Goniewicz et al. (51) (New York, USA)</td>
<td>A pilot study on nicotine residues in houses of electronic cigarette users, tobacco smokers, and non-users of nicotine-containing products</td>
<td>22 (eight non-smoking households, six cigarette smoking households, and eight e-cigarettes user households)</td>
<td>Varied from 16–70 m² (room size where the samples were taken in homes) Nicotine deposited on 10 cm x 10 cm surfaces (window, wall and floor)</td>
<td>None</td>
<td>None</td>
<td>– E-cigarettes users: 7.7 ± 17.2 μg/m³ – Cigarette smokers: 1303 ± 2676 μg/m³</td>
</tr>
</tbody>
</table>
non-smoking homes. The average airborne nicotine exposure among non-smokers who lived with conventional cigarette smokers was 0.74 μg/m³ while for those who lived with e-cigarette smokers, the nicotine level was lower (0.13 μg/m³). The airborne nicotine level in homes without smokers was 0.02 μg/m³ (50). This study also compared the levels of salivary and urinary cotinine of the non-smokers. Cotinine is the predominant metabolite of nicotine which is the substance that causes addiction and it is widely used as the biomarker for exposure to tobacco smoke as it has a longer half-life compared to nicotine (20 h vs. 1–2 h) (52). For the three groups of non-smokers, the geometric mean (GM) for salivary cotinine level were 0.38 ng/mL, 0.19 ng/mL and 0.07 ng/mL among those living with conventional cigarette smokers, e-cigarette smokers and those living in non-smoking homes, respectively. The concentration of urinary cotinine among those living with conventional cigarettes smokers, e-cigarettes users and control homes were 2.46 ng/mL, 1.75 ng/mL and 0.70 ng/mL, respectively. Although conventional cigarettes produce more airborne nicotine levels and result in higher nicotine exposures compared to e-cigarettes, the results showed that non-smokers who lived with e-cigarettes users were also passively exposed to nicotine. However, due to the small number of volunteers exposed to e-cigarettes at home (n = 5), the results of this study needs to be interpreted with care. Furthermore, the study did not take into account other potential sources of nicotine exposure such as those occurring in public places and vehicles, thus assuming the exposure to be only limited from the smokers and e-cigarettes users themselves. There was also potential for recall-bias among the volunteers in terms of their exposure during 1 week of the study.

The experimental study by O’Connell et al. (49) compared several parameters of the IAQ before, during and after unrestricted use of e-cigarettes in a meeting room with a size of 12.8 m². This was done to create or mimic a natural environment of indoor vaping which occurs outside the framework of the experiment. In contrast to the studies by Schober et al. (24) and Ballbè et al. (50), this study showed no measurable increase in airborne nicotine concentration before, during or after vaping sessions. All measurements of airborne nicotine were below 70 μg/m³. However, the level of propylene glycol in air increased from less than 0.5 μg/m³ before the vaping session to an average concentration of 203.6 μg/m³ for the total of 3 h of vaping. There was a slight change in formaldehyde levels from 32.0 μg/m³ to 37.6 μg/m³. Compared to existing indoor air guidelines established by the World Health Organization (WHO), the formaldehyde level was below the threshold limit of 100 μg/m³ or an equivalent of 0.1 ppm (53). Although there was only a slight change in concentration of formaldehyde, the fact that it is listed as a Group 1 human carcinogen by IARC is a concern. In normal conditions where sources of formaldehyde exist, the range of levels were from 0.03 ppm to 0.09 ppm (54, 55). However, indoor concentrations of formaldehyde can vary according to; 1) the age of the building, 2) the temperature and relative humidity indoor, 3) the air exchange rate and 4) the weather season (55, 56). When compared to other regulatory standards, the concentrations of volatile organic compounds (VOCs) including nicotine and low molecular weight carbonyls, PAHs, TSNAs and trace metals which are present in indoor air due to the use of e-cigarettes did not exceed the limits permitted and did not pose an air quality issue to non-users.

The levels of nicotine on surfaces in the homes of eight e-cigarettes users, six conventional smokers, and eight non-users of any nicotine-containing products were measured and compared by Bush and Goniewicz (51). Nicotine was found to be significantly lower in half of the homes of e-cigarettes users compared to the homes of conventional smokers. The average (standard deviation) concentration of nicotine in the homes of e-cigarette users was 200-fold lower [77 (17.2) μg/m³] compared to the homes of conventional smokers [1303 (2676) μg/m³]. There was no significant difference in the amount of nicotine in the homes of e-cigarette users compared to the homes with non-users. This study suggested that the exposure to nicotine from e-cigarettes is low; however, prolonged exposures may be of a serious health concern especially to vulnerable populations such as asthma patients, children and pregnant women. Although this study involved a very small number of volunteers; the results provided evidence that the emission of e-cigarettes does not only contain water vapors as many have claimed as prolonged exposures may still have the potential to be a health hazard to the users.

Studies by Ballbè et al. (50) and Bush and Goniewicz (51) focused on determining the concentration of nicotine released by e-cigarettes whereas the other two studies covered several IAQ parameters namely; PM, propylene glycols, formaldehyde, metals and PAHs (24, 49). Overall, the concentrations of nicotine measured in these four studies were between the range of 2.2 mg/m³ to 7.7 mg/m³. The variety of concentrations measured in these studies may be due to several factors. The different brands of e-cigarettes used in which in the study by O’Connell, a 16 mg/mg disposable original flavored Puritane™ EC (Fontem Ventures by Imperial Tobacco, UK) was used; whereas other brands of e-cigarettes namely Totally wicked® (Blackburn, UK), Puff® (USA) and Free Life® (USA) were used in the study by Ballbè. The study by Schober...
et al. (24) did not state the brand of the e-cigarettes used but mentioned that their study used rechargeable e-cigarettes with refillable tanks. These brands were among the commonly used e-cigarettes at the location of these studies and were available during the study period. The engineering differences between the e-cigarettes result in the variability in how e-cigarettes heat and convert nicotine solution to an aerosol (57). Consequently, the levels of nicotine and other chemicals delivered are different. These four studies have used different concentrations of nicotine either in the cartridges or the e-liquids that are filled in the tank of the e-cigarettes which may also result in the different levels of nicotine in the vapor released. Out of these four studies, studies by Schober et al. (24), Bush and Goniewicz (51) and O’Connell et al. (49) stated the nicotine concentration used of 18 mg/mL, 10–15 mg/mL, and 16 mg/mL, respectively. Another factor may be due to the sensitivity of the methodologies employed in determining the levels on IAQ parameters of the respective studies. As the detection of IAQ parameters can be measured using different selections of measurement tools and the equipment for analysis may be different in terms of its limit of detection (LOD), this may be one of the factors of the differences concentration measured between each study.

Two of the reviewed studies incorporated additional measures in which they included biomarkers of exposure (24, 50) among their research parameters. These studies focused on the exposure to nicotine and other VOCs by measuring the level of cotinine as well as mercapturic acid in biological samples. Mercapturic acids are formed mainly through the metabolism of VOCs via the glutathione pathway. VOCs and/or their metabolites can react with glutathione, and undergo further metabolism to form mercapturic acids before being removed from the blood by the kidneys and excreted into urine (58, 59). The assessment of biomarkers adds a degree of strength to a study in which it helps to provide an objective confirmation of the actual exposure experienced by the respondents. For instance, the level of cotinine present in urine may be helpful in determining the smoking status of the respondents as well as to confirm that the respondents were actually exposed to nicotine in indoor air. Apart from that, it helps to control the extent of conclusions made by such studies (60). In studies where no biomarkers of exposure are involved, the exposures were normally being assumed by the researchers, thus leading to either overestimation or underestimation of the actual exposures. The assessment of biomarkers of exposure towards the chemicals or pollutants of interest will avoid any misleading conclusions made by such research. An aspect of a biomarker of exposure that needs to be controlled/understood in establishing a relationship with the source of exposure is that exposure can occur via other sources. For example, exposure to nicotine may as well occur through dietary intake (52). Consumption of plants from the family Solanaceae such as potatoes, cauliflowers, eggplants and green tomatoes which naturally contain small amounts of nicotine may contribute to the levels of cotinine especially in urine samples (61, 62). The study by Schober and colleagues showed significant difference of urinary cotinine between those exposed to nicotine smoking compared to non-nicotine smoking (24). However, no significant difference of urinary cotinine was observed between the non-users living in homes with e-cigarettes users compared to non-users living in control homes in the study by Ballbè et al. (50). The inconsistencies between these studies may be due to external exposure to nicotine such as second-hand smoke from conventional cigarettes or the small number of study samples involved.

These are the studies available so far that focused on the effects of e-cigarette emissions on the indoor air quality in which human volunteers were asked to vape and where the exhaled vapors released into the specified indoor spaces (rooms or homes) were measured. Limited studies have been done using human volunteers especially in terms of asking them to vape for several reasons. Firstly, ethical clearance of such research is difficult to attain due to stringent ethical application processes which are mainly concerned with the issues of safety arising from the participation of volunteers as there are risks of explosion, leakage or overheating of the devices which might occur during the course of the fieldwork (63–65). In order to recruit human samples in any scientific studies, volunteers need to be informed clearly in terms of the possible health or safety risks that they may experience during or after joining the study (60). As there is not enough data so far to rule out the definite risks that may arise due to e-cigarette use, the information related to the potential health or safety risks remains unclear and are thus unable to be given to the respondents. Thus, the mandatory requirement of the application for ethical approval for such research is difficult to satisfy. Secondly, as human samples are recruited in this kind of study, they are subject to vary in terms of the individual retention to nicotine (66, 67). Different individuals may inhale the vapors deeper than others resulting in different levels of the contents of vapors exhaled into the indoor air (68). Apart from that, there is no standard guideline on how study using this kind of method should be conducted. For instance, the size of the experiment rooms, the numbers of e-cigarette users per session and the methodologies employed should
be at least similar for enabling the findings of the studies to be comparable and meaningful especially in providing scientific evidence for the implementation of regulation on e-cigarette usage in indoor settings or in public places.

This paper only reviewed four articles that fulfilled the inclusion criteria set for this review. As such, the conclusions were based only on the evidence gathered from these studies alone. Thus, the results of this review should be interpreted with caution. The four selected studies have used an older generation of e-cigarettes in which these devices may have been developed with less consideration in terms of its safety features or the amount of the vapors released. As suggested by Farsalinos et al. (69) there is a continuous improvement in the design, properties and safety features of the e-cigarettes parts, with new-generation atomizers featuring Pyrex glass and stainless steel structures substituting plastics and other metals. As the engineering technology in the fabrication of e-cigarette devices is now developing, it has been argued that there is a potential for a better reduction of unwanted and/or high levels of chemicals in e-cigarette vapors (31, 70, 71). The materials used in creating components of e-cigarettes have been shown to determine the constituents of the vapors such as the contents of heavy metal (31, 38).

It has been reported that for each month, there is a net increase of 10.5 e-cigarette brands and 242 new flavors of the e-liquids on the market (72). Historically, the market was highly fragmented and largely dominated by small players but started in 2013, large manufacturers such as Altria (Philip Morris), R.J. Reynolds and Lorillard increasingly entered the market with their own products and bought already established brands (2). This rapid production of new products has made it hard for the concerned stakeholders such as researchers in the public health field and policy makers to ensure that the products introduced to the public are safe for the users and non-users who are involuntarily exposed to e-cigarette vapors. Thus, it should be the responsibility of the manufacturers of these products to scientifically prove their products are safe for human use and to include any potential harm that may be experienced by the users. For instance, manufacturers or distributors of cosmetic products are legally responsible for ensuring that their products are safe when consumers use it according to the directions in the labeling or in the customary or expected way (73). Manufacturers may also need to conduct toxicological testing to determine the safety of each ingredient and the finished product. Animal testing is not a specific requirement for marketing a cosmetic; however, it is important for all tests to be scientifically sound. Manufacturers of pharmaceutical products have been reported to spend significant resources to carry out laboratory experiments or animal testing in order to prove the safety of a newly developed product for human consumption prior to it being commercialized. On average, approximately US$800 million was spent in 2003 by pharmaceutical companies in order to bring one new drug to the market (74). With the rapid rising of costs for research and development in drug industries particularly in the cost of clinical trials, the average funds required had swelled to US$1.7 billion in 2009 (75). Although these are examples for pharmaceutical drugs, the use of e-cigarettes for therapeutic purposes needs to be proven as safe for human consumption. These costs needs to be borne by the manufacturers of the e-cigarettes to ensure the safety aspects of their products and any safety claims should be supported with scientific evidence.

Although there is no solid conclusion which can be drawn from the current knowledge available from these four studies, it is proven that there is a potential exposure towards the known and still unknown contents of the e-cigarette vapors. Thus, the claims made by the manufacturers and retailers as well as the mind-set of the users that e-cigarettes only release harmless water vapors have been shown as fallible. The fact that the exposure towards the vapors released even at low levels is likely to be experienced by other susceptible populations and healthy non-users; as such the usage of e-cigarettes in the presence of such populations needs to be regulated in countries where no restrictions are present.

Conclusion

From all the studies on the contents of e-cigarette vapors, there are a few parameters that are consistently found in e-cigarette vapors namely; nicotine, propylene glycols and PAHs. However, there are wide variations in terms of the levels between the studies. This may be due to the different methodology used in such studies such as numbers of volunteers recruited, size of the indoor settings, the method used for measuring the contents of e-cigarette emission in indoors and the sensitivity of the analysis equipment used. The evidence shown rejects the claims by manufacturers, retailers and users that e-cigarette vapors consist of only water vapors. The exposure among susceptible groups of population such as children, asthma patients, the elderly, pregnant women and healthy non-users in prolonged exposure have the possibility to be a health concern. More studies are needed on IAQ exposure related to e-cigarette usage in natural settings that mimic actual vaping scenarios. Keeping
with the standards in the production of consumer goods, the duty in proving safety claims of the e-cigarettes lies with the manufacturers. As such, safety claims which are backed up with concrete and reliable scientific evidence will help to avoid any false safety claims of the products in the market and to reduce any unwanted exposure to potential health hazard chemicals released from the use of e-cigarettes.

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