



Research Office  
Legislative Council Secretariat

## Fact Sheet

# Health effects of e-cigarettes and heated tobacco products

FS09/17-18

## 1. Introduction

1.1 The past decade or so has seen an increase in the use of non-combustible electronic cigarettes ("e-cigarettes") and heated tobacco products ("HTPs"). E-cigarettes work by heating "e-liquid" to create vapour for users to inhale. E-liquid typically contains ingredients such as nicotine and propylene glycol/vegetable glycerine. HTPs use a battery-powered heating device to heat tobacco up to a temperature of 350°C.<sup>1</sup> This produces aerosol containing nicotine and other chemicals which are inhaled by the user through the mouth. The growing popularity of e-cigarettes and HTPs has provoked much discussion worldwide about their health effects and the need for regulation.

1.2 At its meeting on 21 May 2018, the Panel on Health Services requested the Research Office to study the health effects and regulation of e-cigarettes and HTPs. An information note, entitled *Regulation of e-cigarettes and heated tobacco products in selected places*, was issued earlier for the Panel meeting on 19 June 2018.<sup>2</sup> This fact sheet summarizes the findings of the research studies about the potential health effects and risks of e-cigarettes and HTPs.

## 2. Potential health effects and risks of e-cigarettes

2.1 A number of studies have been conducted on the potential health effects and risks of e-cigarettes, including the systematic reviews published by

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<sup>1</sup> In comparison, the tobacco of a conventional cigarette is burnt to 600°C when it is lit. See World Health Organization (2018).

<sup>2</sup> The meeting discussed, among other things, the legislative proposal to regulate e-cigarettes and other new tobacco products.

the World Health Organization ("WHO"), the National Academy of Sciences of the United States ("NAS")<sup>3</sup>, the European Union ("EU") and Public Health England ("PHE")<sup>4</sup>.

2.2 Systematic reviews employ a systematic method to identify and screen the relevant research studies on a clearly formulated question, and critically examine, synthesize and analyse the findings from the studies covered by the reviews. The nature of the afore-mentioned systematic reviews of e-cigarettes is briefly described as follows:

- (a) WHO issued ***A systematic review of health effects of electronic cigarettes*** in December 2015. The systematic review examined the **review results of 175 studies** published before 26 November 2015 on e-cigarettes of any topic relevant to health. The majority of the studies investigated the content of e-liquid and vapour, and/or performed experiments with cells, exposing them to e-liquid, vapour or extract of vapour<sup>5</sup>;
- (b) NAS published ***Public health consequences of e-cigarettes*** published in January 2018. The systematic review examined **over 800 peer-reviewed scientific studies** on e-cigarettes with respect to their key constituents, human health effects, and impact on the cessation of combustible tobacco cigarette (i.e. conventional cigarette) smoking<sup>6</sup>;
- (c) The EU adopted ***Study on the identification of potential risks to public health associated with the use of refillable electronic cigarettes and development of technical specifications for refill mechanisms*** in May 2016. The study was a **systematic review of a total of 319 publications** published between April 2015 and January 2016 about e-cigarettes and their potential risks<sup>7</sup>; and

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<sup>3</sup> Established by an Act of Congress in 1863, NAS is charged with providing advice to the government on matters related to science and technology. It is a private, non-profit society of distinguished scholars in the United States. See National Academy of Sciences (2018).

<sup>4</sup> PHE is an executive agency of the Department of Health and Social Care of the United Kingdom. It provides the government, the industry and the public with evidence-based scientific expertise and support. See GovUK (2018).

<sup>5</sup> See World Health Organization (2015).

<sup>6</sup> See National Academics of Sciences, Engineering and Medicine (2018).

<sup>7</sup> See European Commission (2016).

- (d) PHE published *Evidence review of e-cigarettes and heated tobacco products 2018* in February 2018. The systematic review examined the results of **1 070 peer-reviewed literature** on e-cigarettes published between 1 January 2015 and 18 August 2017. It was written by academics and medical experts<sup>8</sup> and summarized evidence to underpin the policy and regulation of e-cigarettes and HTPs.

2.3 Broadly speaking, the afore-mentioned systematic reviews focused on the effects of e-cigarettes on personal health in terms of the presence and amount of **harmful constituents** in the product and the corresponding **effect on human bodies**. They also examined the public health impacts with respect to the effectiveness of e-cigarettes in promoting **cessation of cigarette smoking** and the potential health risks from **passive exposure to vapour**.

### Harmful constituents

2.4 According to the WHO review, chemical constituents such as nicotine, metals, propylene glycol, glycerine, particles, tobacco-specific nitrosamines, carbonyls/carbonyl compounds, volatile organic compounds and polycyclic aromatic hydrocarbons were found in e-cigarettes.<sup>9</sup> These constituents are potentially harmful; e.g. nicotine causes dependence and addiction, and exposure to nicotine-containing aerosol from e-cigarettes likely elevated the cardiovascular disease risk in people with pre-existing cardiovascular disease(s).<sup>10</sup>

2.5 The NAS review also found nicotine in e-cigarettes and identified it as a potentially harmful constituent with known central and peripheral nervous system effects. However, the cardiovascular risk of nicotine in people without cardiovascular disease(s) is uncertain. The EU report found evidence of cytotoxic effects<sup>11</sup> of some e-liquids, especially when nicotine and flavour substances were present.

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<sup>8</sup> The authors of the review report included academics and medical experts from King's College London, UK Centre for Tobacco & Alcohol Studies, University of Stirling, Cancer Research UK, University of Nottingham, University College London and Queen Mary University of London. See Public Health England (2018).

<sup>9</sup> See World Health Organization (2015).

<sup>10</sup> See National Academies of Sciences, Engineering, and Medicine (2018).

<sup>11</sup> Cytotoxic effect is the result of destruction of healthy living cells due to toxicity. See Science Direct (2018).

2.6 As mentioned above, metals such as lead, chromium, tin, silver, nickel, copper, aluminium, cadmium and mercury were found in e-cigarette aerosol according to several studies included in the WHO review.<sup>12</sup> The PHE review considered that the levels of metals identified in e-cigarette aerosol did not give rise to any significant safety concerns.<sup>13</sup>

### Effects on human bodies

2.7 Conventional cigarettes pose serious risks to human health. Many of those health effects emerge only after decades of cigarette smoking. Unlike conventional cigarettes, e-cigarettes have been on the market since 2006.<sup>14</sup> As such, the afore-mentioned systematic reviews focused on examining the short-term exposure to e-cigarettes and summarizing the associated cardiovascular disease, cancer, respiratory diseases and other health symptoms observed on human bodies.

### *Cardiovascular disease*

2.8 According to some studies included in the WHO review, short-term vaping<sup>15</sup> could result in increased heart rate and an elevation in diastolic blood pressure.<sup>16</sup> The NAS review also showed that there was *substantial evidence*<sup>17</sup> for heart rate increasing shortly after nicotine intake from e-cigarettes. Likewise, the EU report indicated that the nicotine in e-cigarettes was sufficient to elevate the heart rate as well as systolic and diastolic blood pressure. It further suggested that exposure to nicotine might pose an additional risk to vulnerable population such as children, adolescents, and adults with certain comorbidity.

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<sup>12</sup> See World Health Organization (2015).

<sup>13</sup> See Public Health England (2018).

<sup>14</sup> E-cigarettes were invented in 2003 and entered the European and US markets in 2006. See Consumer Advocates for Smoke-free Alternatives Association (2018).

<sup>15</sup> The act of using an e-cigarette is something called "vaping".

<sup>16</sup> See World Health Organization (2015).

<sup>17</sup> As defined by NAS, "substantial evidence" means that there are several supportive findings from good-quality observational studies or controlled trials with few or no credible opposing findings. A firm conclusion can be made, and minor limitations to the evidence, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence. See National Academies of Sciences, Engineering, and Medicine (2018).

2.9 While reporting the short-term effects of e-cigarettes, the NAS review stated that there was insufficient evidence to conclude that e-cigarette use was associated with long-term changes in heart rate, blood pressure, and cardiac geometry and function. Furthermore, there was no available evidence to infer whether e-cigarette use was associated with clinical cardiovascular outcomes (e.g. coronary heart disease, stroke, and peripheral artery disease) and subclinical atherosclerosis (e.g. carotid intima-media thickness and coronary artery calcification). Similarly, the PHE review concluded that comparative risks of cardiovascular disease and lung disease in e-cigarette users had not been quantified, but they were likely to be also substantially below the risks of cigarette smoking.

### *Cancer*

2.10 The NAS review found substantial evidence of presence of chemicals such as formaldehyde and acrolein in e-cigarette aerosol that were capable of causing DNA damage and mutagenesis. This suggested the biological plausibility that long-term exposure to e-cigarette aerosol could increase the risk of cancer. Nevertheless, whether the levels of exposure were high enough to contribute to human carcinogenesis remain to be determined.

2.11 The WHO review found toxicant and carcinogen metabolites in urine of vapers, but the concentration of which was significantly lower than that of conventional cigarette smokers.<sup>18</sup> Meanwhile, the PHE review cited a study suggesting that the cancer potency of e-cigarette emissions was 0.4% of those of smoking.

### *Respiratory diseases*

2.12 The NAS review found *moderate evidence*<sup>19</sup> for increased cough and wheeze in adolescents who used e-cigarettes and an increase in asthma

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<sup>18</sup> According to WHO, the observation was made according to the findings of human experiments mostly based on very short-term exposure (e.g. vaping for a few minutes). The findings might not reflecting real-life exposure, thereby possibly underestimating negative long-term effects. See World Health Organization (2015).

<sup>19</sup> As defined by NAS, "moderate evidence" means that there are several supportive findings from fair-quality studies with few or no credible opposing findings. A general conclusion can be made, but limitations to the evidence, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence. See National Academies of Sciences, Engineering, and Medicine (2018).

exacerbations. However, there was *limited evidence*<sup>20</sup> for improvement in lung function and respiratory symptoms among adult smokers with asthma who switched to e-cigarettes completely or in part. In addition, limited evidence was identified for reduction of chronic obstructive pulmonary disease ("COPD") exacerbations among adult smokers with COPD who switched to e-cigarettes completely or in part.

2.13 According to WHO, propylene glycol and vegetable glycerine were two commonly used humectants in e-cigarettes functioning as solvents to produce aerosol to facilitate inhalation.<sup>21</sup> According to the EU report, exposure to mixtures containing propylene glycol might lead to respiratory symptoms as it may be rapidly absorbed during inhalation. The EU report also mentioned of recent studies which indicated that humectants in e-cigarettes might induce the release of cytokines and pro-inflammatory mediators and under certain conditions potentially caused irritation of the airways.<sup>22</sup> In contrast, the PHE review stated that among e-cigarette users, two studies of biomarker data for acrolein (a potent respiratory irritant) found levels of acrolein consistent with non-smoking levels.

### *Development of foetus and adolescent*

2.14 There have been concerns about the use of e-cigarettes by pregnant women and the role that nicotine might play in harming foetal development. According to the WHO review, foetal nicotine exposure might have long-term consequences for brain development of infants, potentially leading to learning and anxiety disorders.<sup>23</sup> Meanwhile, the PHE review cited animal research suggesting that foetal exposure to very high doses of nicotine had adverse consequences that were maintained through to adolescence, but the relevance for humans was unclear.<sup>24</sup>

2.15 As to the effects of nicotine on adolescent, the PHE review has made reference to a Royal College of Physicians report which stated that smoking in

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<sup>20</sup> As defined by NAS, "limited evidence" means that there are supportive findings from fair-quality studies or mixed findings with most favouring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors. See National Academies of Sciences, Engineering, and Medicine (2018).

<sup>21</sup> See World Health Organization (2017).

<sup>22</sup> See European Commission (2016).

<sup>23</sup> See World Health Organization (2016).

<sup>24</sup> See Public Health England (2018).

adolescence had been associated with cognitive and attentional deficits and suggested to impact mental health. Added to this, PHE concurred with a recommendation made by the United States Surgeon General<sup>25</sup> that the use of e-cigarettes by youth "should be avoided and actively discouraged". Earlier on, the United States Surgeon General issued a report in 2016 which gave a comprehensive review of the potential impact of nicotine on adolescent brains using human studies with smokers and animal studies.

### *Other disease symptoms*

2.16 According to the NAS review, there was substantial evidence that e-cigarette aerosol could induce acute endothelial cell dysfunction, promote formation of reactive oxygen species<sup>26</sup> and cause oxidative stress<sup>27</sup>. Similar observations on e-cigarette aerosol were found in the WHO review and the EU report. The former reported that "many studies have found stress and inflammation in cells exposed to e-cigarettes"<sup>28</sup>, whereas the latter recognized the evidence of potential risks of "oxidative stress, inflammation of the respiratory system and effects on blood glucose"<sup>29</sup>.

### Initiation and cessation of conventional cigarette smoking

2.17 According to the NAS report, there was substantial evidence that e-cigarettes used by youth and young adults increased their risk of using conventional cigarettes. There was also moderate evidence that e-cigarette use increased the frequency and intensity of subsequent conventional cigarette smoking among youth and young adult e-cigarette users who had ever used conventional cigarettes. On smoking cessation, the NAS report

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<sup>25</sup> The Surgeon General oversees the United States Public Health Service Commissioned Corps, a group of some 6 700 public health professionals working in the federal government. He or she is appointed by the President of the United States with advice and consent of the Senate. See Office of the Surgeon General (2018).

<sup>26</sup> A reactive oxygen species is a type of unstable molecule that contains oxygen and that easily reacts with other molecules in a cell. A build-up of reactive oxygen species in cells may cause damage to DNA, RNA, and proteins, and may cause cell death. See National Cancer Institute of the United States (2018).

<sup>27</sup> Oxidative stress is a condition in which antioxidant levels are lower than normal. See National Cancer Institute of the United States (2018).

<sup>28</sup> See World Health Organization (2015).

<sup>29</sup> See European Commission (2016).

concluded that there was some evidence, albeit limited, that e-cigarettes might effectively help people quit, especially if they contain nicotine.

2.18 The EU report made reference to the data collected from 28 EU member states in 2014 about the effectiveness of e-cigarettes in smoking cessation. The data showed that 49% of e-cigarette users reported that e-cigarettes had not helped them reduce or stop smoking tobacco, while 14% were able to quit completely, 13% succeeded initially but then relapsed, and 21% were able to reduce their tobacco use but not quit. The EU report also reported the analysis of five population studies which showed that e-cigarette use was associated with significantly lower odds of quitting cigarettes, indicating that e-cigarettes might pose a threat to smoking cessation attempts.<sup>30</sup>

2.19 The PHE report examined seven reviews about the effectiveness of e-cigarettes in smoking cessation and/or reduction. Among them, two found a positive effect, four found an inconclusive effect and one found a negative effect for using e-cigarettes on smoking cessation. As such, the PHE report could not come up with a conclusion and considered that further scientific trials of e-cigarettes were needed.<sup>31</sup>

### Passive exposure to vapour

2.20 According to the WHO review, bystanders exposed to vapour from e-cigarettes absorbed approximately as much nicotine as when exposed to smoke from conventional cigarettes. Human experimental studies showed that passive vaping<sup>32</sup> resulted in short-term lung obstruction and increased cotinine<sup>33</sup>, but it did not influence complete blood count<sup>34</sup> indices in smokers and never smokers.

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<sup>30</sup> See European Commission (2016).

<sup>31</sup> See Public Health England (2018).

<sup>32</sup> Passive vaping means breathing in the exhaled vapour from e-cigarettes.

<sup>33</sup> Cotinine is an alkaloid found in tobacco. It is the predominant metabolite of nicotine and used as a biomarker for exposure to tobacco smoke.

<sup>34</sup> A complete blood count is a measure of the number of red blood cells, white blood cells, and platelets in the blood, as well as the amount of hemoglobin (substance in the blood that carries oxygen) and the hematocrit (the amount of whole blood that is made up of red blood cells). The count is used to help detect certain illnesses including anemia, infection and leukemia. See National Cancer Institute of the United States (2018) and University of Rochester (2018).



2.21 In the EU report, e-cigarette emissions might be perceived as less harmful than cigarette smoke. Nevertheless, they produced similar aerosol and had similar particle deposition patterns in the lungs that might negatively affect lung function. An experimental study showed that exposure to second-hand vapour from e-cigarettes could cause short-term lung obstruction. Beyond laboratory experiments, concentration of airborne nicotine was found to be higher in homes where someone was using an e-cigarette compared to smoke-free homes.<sup>35</sup> The EU report also concluded that e-cigarettes would be a source of indoor air pollution<sup>36</sup>, hence exposure to these emissions in public places might potentially pose a risk to population health.

2.22 The PHE review showed that non-users might be exposed to nicotine vapour but the level of exposure was low, and exposure to other compounds also appeared very low, or at trace or non-detectable levels when compared with second-hand smoke. Therefore, it was unclear if any levels were sufficient to be of biological concern to humans.<sup>37</sup>

### 3. Potential health effects and risks of HTPs

3.1 HTPs are new to the market as they were first launched in Japan in 2014. There is currently limited number of studies on HTPs and many of them were funded by HTP manufacturers. Nevertheless, the PHE review covered 20 studies on HTPs, whereas the United States Food and Drug Administration ("FDA") issued a briefing document in January 2018 with review findings from five studies of HTPs.<sup>38</sup> The paragraphs below summarize the observations set out in the above two documents about the presence of **harmful constituents** on HTPs, the impacts of HTPs on **cessation of cigarette smoking**, and the health risks from **passive exposure to vapour**.

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<sup>35</sup> See European Commission (2016).

<sup>36</sup> The emissions contain harmful substances such as benzene, acetone, formaldehyde, acetaldehyde, acrolein, nicotine and nitrosamines, as well as high particle dose. See European Commission (2016).

<sup>37</sup> See Public Health England (2018).

<sup>38</sup> In 2016, an HTP manufacturer filed an application with FDA for approval to claim its HTP product as a modified risk tobacco product. As such, FDA prepared a briefing document as a reference paper for the Tobacco Products Scientific Advisory Committee, an advisory panel of FDA, to consider the application. The briefing document set out the results of scientific reviews published earlier and its own testing on the HTPs. See FDA (2018a).

## Harmful constituents

3.2 HTPs contain chemicals commonly found in conventional cigarettes, including nicotine, volatile organic compound, carbon monoxide and polycyclic aromatic hydrocarbons. FDA's testing confirmed lower levels of selected harmful and potentially harmful constituents such as carbon monoxide, heterocyclic amines, benzene, and toluene in the aerosol from an HTP compared with that from cigarette smoke.<sup>39</sup>

3.3 However, the PHE review found a much higher concentration of polycyclic aromatic hydrocarbons in HTPs relative to conventional cigarettes.<sup>40</sup> The review also disclosed that nicotine detected in aerosol from HTPs reached 70% to 84% of the nicotine detected in smoke from conventional cigarettes.

## Cessation of conventional cigarettes

3.4 According to FDA's briefing document, the prevalence of complete switching from conventional cigarettes to HTPs was low in the United States. Against this, there was a concern over what effect dual use of HTPs and conventional cigarettes would have on reducing health risks for tobacco-related diseases and reducing exposure to harmful and potentially harmful constituents as compared with complete switching.

3.5 FDA's briefing document also reported that HTP users were likely to reduce their cigarette consumption even if they continued to dual use. However, the health benefit of reducing cigarette consumption instead of quitting completely is unclear.

## Passive exposure to vapour

3.6 The PHE review cited an independent study result which showed that the tested HTPs generated four times lower levels of submicronic particles, an indicator of second-hand smoking, compared with environmental tobacco smoke from conventional cigarettes. Despite the lower levels of emissions, the study authors concluded that HTPs still posed health risks to users and bystanders.

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<sup>39</sup> See FDA (2018a).

<sup>40</sup> See Public Health England (2018).

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