

**As of October 2019:**

The RACP urges that all e-cigarette users exercise caution in light of the emerging international evidence of severe lung disease and a number of deaths which may be linked to e-cigarette use and seek medical advice for unexplained respiratory and gastrointestinal symptoms.

The RACP would like to remind the community that not smoking tobacco or vaping remain the safest options. If people wish to quit smoking, the RACP advocates for the proven and registered smoking cessation technologies, including pharmacotherapies, ahead of vaping. The College urges physicians to advise patients of all potential risks and benefits should patients wish to use e-cigarettes for smoking cessation.

The RACP acknowledges the advice provided by the [Australian Chief Medical Officer and State and Territory Chief Health Officers](#) and by the [New Zealand Ministry of Health](#).

**RACP Policy follows on next page**



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# **Policy on Electronic Cigarettes**

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## Preface

The Royal Australasian College of Physicians (RACP) represents physicians across a diverse range of disciplines, including addiction medicine, public health, oncology, thoracic medicine, cardiology, occupational and environmental medicine, internal medicine and paediatrics and child health.

Together with health professionals in other clinical disciplines, our physicians manage and treat patients with a range of health issues emanating from or exacerbated by smoking and the health impacts of addiction. In addition, they provide advice on and have leading roles in policies and initiatives to address and improve public health.

This document provides the position of the RACP on the emergence and rapidly increasing use of electronic cigarettes, their potential role in smoking cessation, the known health implications and the as yet unknown impacts on people's health – both for the individual and for the broader population.

This document is the result of in-depth review of the available evidence on e-cigarettes, and extensive consultation across and input from the RACP's many and diverse specialties to gain direct frontline clinical expertise and experience.

## Acknowledgements

The RACP would like to acknowledge and thank the members of the RACP e-cigarettes Reference Group that led the development of this document. We note that it is possible for differing views to be expressed on the basis of the same evidence and that therefore some of our recommendations do not represent the views of all Reference Group members. This document presents the position of the RACP and does not necessarily reflect each member's views in an individual capacity.

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# 1. Executive Summary

Over the last 20 years, national key tobacco control policies have resulted in a substantial decrease in smoking rates in Australia and New Zealand<sup>1</sup>. Key to this success has been the de-normalisation of smoking and thereby the changing of social norms, and raising the price of tobacco via increasing excise. Despite this however, tobacco use still accounts for a significant part of the burden of disease in both countries<sup>2</sup>. There also remains marked differences in smoking rates between population groups as well as a persistent correlation between smoking rates and low socioeconomic status<sup>3</sup>.

The advent a decade ago of electronic cigarettes (e-cigarettes) and their increasing popularity as a vehicle to deliver nicotine since, has raised discussions around their impacts on global tobacco control efforts and public health. Specifically, these discussions relate to their role in smoking cessation, their safety profile and long-term health effects, any impact on youth initiation of smoking and tobacco use, and net public health effects of e-cigarette use. The term 'e-cigarette' in this RACP document refers to electronic devices designed to deliver aerosol from a heated liquid into a person's lungs. The liquid (often called 'e-liquid') might or might not contain nicotine.

Around the world, divergent views are held by clinicians, health organisations, medical colleges, academics, local and national government authorities, and the general public. Some view e-cigarettes as a positive development in terms of either replacing tobacco cigarettes, as it is acknowledged that current data indicates they are less harmful, or in aiding smoking cessation. Others are concerned that e-cigarettes could prolong addiction to nicotine and/or smoking behaviour and also counteract the decades-long work that has shifted society's norms about smoking and helped reduce smoking rates. The divergence of opinion is not helped by the limited evidence available on the efficacy of e-cigarettes to help smokers quit and their long-term health effects.

This document provides an overview of the existing evidence, on which the development of the RACP policy on e-cigarettes was based. It covers the evidence on their potential risks and benefits, regulatory frameworks being taken nationally and internationally, and positions of other key health organisations on e-cigarettes. The development of this document has also been informed by the experience and expertise of RACP members, many of whose clinical practices and patients are being directly affected by these products. We note that this policy will be subject to review as appropriate if and when more decisive evidence emerges in some of the current areas of uncertainty regarding e-cigarettes'

## 2. RACP position and policy recommendations

This chapter sets out the RACP position and policy recommendations – for full references to the evidence supporting this, refer to Chapter 3.

The RACP is concerned there remains a lack of clear and robust evidence to inform policy makers, clinicians and the public about e-cigarettes. While there is some evidence that e-cigarettes may reduce the number of tobacco cigarettes smokers consume and that they are likely to be less harmful than tobacco cigarettes (due to lower level of potentially toxic substances in e-cigarettes compared with tobacco cigarettes), the evidence on their efficacy as aids in smoking cessation and their long-term health effects is either mixed or limited. There is also evidence indicating that their use affects the likelihood of youth initiating use of tobacco cigarettes. Based on the current evidence, at this point in time the net public health effect of e-cigarettes cannot be clarified with any degree of confidence.

The RACP acknowledges that e-cigarettes may have a potential role in tobacco harm reduction and smoking cessation for smokers unable or unwilling to quit. However, due to lack of long-term data and large population studies, e-cigarettes should be treated with caution. Users should be aware when using a nicotine-containing e-liquid that nicotine is highly addictive and a poison.

Any e-cigarette that claims therapeutic benefit (including smoking cessation) must undergo the appropriate regulatory approval pathway in order to be allowed to make such claims, by either the Australian Therapeutic Goods Administration or in New Zealand, Medsafe.

The RACP is of the view that e-cigarettes present no benefits and only potential harms to those who do not smoke, be they never smokers or former smokers. We are concerned that the use of e-cigarettes may increase the likelihood of tobacco smoking initiation, in particular among adolescents and young people, as indicated in some evidence. In view of this, the sale, supply, promotion and use of e-cigarettes must be effectively regulated and they should not be available to minors. E-cigarettes should be included within smoke-free environment legislation, primarily due to the potential harms from re-normalising smoking and the exposure to second-hand e-cigarette aerosol.

There is an urgent need for more studies into these products to provide a better understanding of their effectiveness for people trying to quit or reduce smoking, their potential harms both in terms of inhaling heated aerosols and in perpetuating addiction to nicotine at the individual and population levels, and of any impact on overall smoking rates and smoking initiation rates. The priority for funding studies must be for robust, randomised controlled trials and long duration prospective studies which are independent of vested interests.

Health professionals should be made aware that whilst there is some evidence that e-cigarettes can help in smoking cessation, there is little evidence about how their effectiveness compares with other available options. They should also be aware of the uncertainty about their safety profile. Careful clinical judgement should be applied when giving advice to patients.

The RACP is a strong advocate of smoking cessation. The evidence shows that smoking cessation (stopping smoking completely) is still the most effective way to reduce mortality and morbidity from tobacco-related diseases. All smokers should be encouraged and supported to quit smoking with the aid of either counselling or proven pharmacotherapy such as nicotine replacement therapy if required.

The rest of this section sets out more detailed recommendations aimed at improving the evidence base and e-cigarette regulation.

## 2.1 Improving the evidence base

There is a strong need to improve the evidence base on e-cigarettes, to properly inform the development of effective tobacco reduction and public health policy. It is crucial that this research and data collection include studies funded independently of vested interests and, where there are vested interests, that there is full and transparent disclosure of this. It is also vital that these studies take an international and long-term perspective.

**Recommendation 1** – All levels of government should co-operate to improve data collection on e-cigarette sales and use, together with the prevalence and characteristics of e-cigarette users by age groups, populations, and tobacco smoking status, to accurately estimate the population and group-specific effects. This can be achieved by adding in a few questions about e-cigarette use – such as experimentation and regular use – in the existing regular population surveys.

**Recommendation 2** – Funding for high quality research on the public health implications of e-cigarettes should be provided, particularly for high-quality randomised clinical trials and population-level studies. Studies should prioritise building evidence on the:

- Short- and long-term health effects of e-cigarettes, and of exposure to second-hand e-cigarette vapour,
- Efficacy of e-cigarettes as a smoking cessation aid,
- Impact on overall smoking rates and smoking initiation rates and the overall health of population, in particular on groups with higher levels of smoking or who have a greater risk of harm such as Aboriginal and Torres Strait Islander people and Māori,
- Extent and impact of dual-use of e-cigarettes and tobacco products; and
- Safety of inhaling flavouring chemicals used in e-cigarettes.

## 2.2 E-cigarette regulation

A national e-cigarette strategic framework, including policies and regulations, is crucial to ensure that we are able to build on the success of tobacco control initiatives. This is particularly important for Australia, due to its federal structure and the differences in how e-cigarettes are regulated across states and territories. A nationally defined and coordinated approach will allow for shared objectives and support coherence in policy measures.

**Recommendation 3**—The Australian and New Zealand governments should lead the development of national e-cigarette policies that are aligned with their tobacco control policies and are:

- Compatible with tobacco control policies articulated in the World Health Organization (WHO) mPOWER strategy<sup>i</sup>,
- Evidence-based, taking account of the WHO Framework Convention on Tobacco Control (FCTC),
- Subject to review in light of future research, and
- Configured to strike the appropriate balance between potential benefits of e-cigarettes and protection against potential harms they may cause to individuals and the broader population.

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<sup>i</sup> MPOWER is a policy package introduced by the WHO Framework Convention on Tobacco Control (FCTC) to help the country-level implementation of effective interventions to reduce the demand for tobacco.

Global tobacco companies, such as British American Tobacco, Imperial Tobacco, Reynolds American Inc. and Lorillard, have now either established or acquired e-cigarettes as part of their product line<sup>4</sup>. In light of this development, it is important for us to remain mindful of the tobacco industry's historical tactics and attempts to influence and resist tobacco control policy and that there are often major conflicts between the vested commercial interests of the tobacco industry and public health.

In the absence of evidence that allows the proper weighing of harms against benefits, the RACP supports appropriate regulatory controls on the sale, supply, use and promotion of e-cigarette devices, with a focus on youth protection.

**Recommendation 4** – E-cigarettes should not be allowed to be promoted in a way that encourages their uptake or smoking initiation. Their sale and supply to minors must be prohibited in all Australian states and territories and New Zealand.

**Recommendation 5** – The use of e-cigarettes should be banned in all areas that are designated to be smoke-free by Australia's state and territory laws and New Zealand's Smoke-Free Environments Act 1990 (SFEA).

**Recommendation 6** – Any therapeutic and toxicity claims made about e-cigarettes must be supported by transparent, high quality studies and have undergone the Therapeutic Goods Administration's or Medsafe's review processes and secured their approval.

**Recommendation 7** – E-cigarettes should be subject to Australia and New Zealand's excise tax, at a lower rate than that of tobacco cigarettes to discourage any e-cigarette users from switching to tobacco cigarettes. Effective regulation is needed on the quality control processes used to manufacture these products, and on their labelling requirements, to ensure consumers are appropriately protected.

**Recommendation 8** – E-cigarette products should be manufactured to suitable quality and safety standards and be subject to consumer law. Manufacturers must demonstrate the quality and safety of their e-cigarette products by providing evidence that national Good Manufacturing Practice (GMP) policies<sup>ii</sup> have been followed and that their products are safe for consumer use.

**Recommendation 9** – E-cigarette product packaging and labelling requirements should be implemented, including:

- Disclosure of all ingredients and their concentrations in e-liquids,
- Child-proof packaging standards to deter children's use and prevent accidental poisonings,
- Plain (standardised) packaging rules to reduce the appeal of e-cigarettes to youth; and
- Health warning labels.

### 3. Current Use

The use of e-cigarettes has grown markedly the world over since their commercial introduction in 2004. In 2015 alone, the global e-cigarette market amounted to roughly US\$10 billion; the United

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<sup>ii</sup> Good Manufacturing Practice (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards.



States accounted for more than half of these sales (56 per cent), followed by the United Kingdom (12 per cent)<sup>5</sup>. Increasing ever-use<sup>iii</sup> of e-cigarettes among adolescents and current and former smokers is evident, particularly in those countries with high volume of e-cigarette sales<sup>6</sup>. Data have shown that a large number of e-cigarette users are ‘dual users’, using e-cigarettes while concurrently smoking tobacco cigarettes<sup>7</sup>.

### 3.1 Australia and New Zealand

In Australia and New Zealand, only limited data are available on e-cigarette use by demographics and smoking status.

The Australian Institute for Health and Welfare (AIHW) reported on e-cigarettes for the first time in its 2013 National Drug Strategy Household Survey (NDSHS) finding that 14.8 per cent of the smoking population aged 14 or older had used e-cigarettes in the last 12 months<sup>8</sup>. Compared to smokers aged 60-69, younger smokers aged 18-24 were more likely to have tried e-cigarettes<sup>9</sup>. The 2016 NDSHS indicated that between 2013 and 2016, the rates of lifetime use (i.e. usage at least once within a person’s lifetime) of e-cigarettes increased remarkably across almost all age groups, although the majority of people who use them do not become habitual users<sup>10</sup>. The rate of experimentation was highest among smokers aged under 25, with 1 in 2 trying e-cigarettes in their lifetime. Approximately 31 per cent of current smokers had tried using e-cigarettes and only 4.4 per cent of current smokers continued to use them<sup>11</sup>.

At the state level, the 2014 New South Wales (NSW) Population Health Survey showed that 1.3 per cent of the adult population in NSW were current e-cigarette users, whilst at least 8.4 per cent of adults had ever used an e-cigarette<sup>12</sup>. Current smokers were 7.5 times more likely to be current e-cigarette users than non-smokers<sup>13</sup>. In Victoria, the proportion of Victorian adults who had used e-cigarettes increased from 1.8 per cent in 2011 to 7.3 per cent in 2013. The rates of e-cigarettes use was higher among smokers in younger age groups<sup>14</sup>.

In New Zealand, the Health Promotion Agency’s Health and Lifestyles Survey (HLS) reported that in 2014 13.1 per cent of individuals had ever used e-cigarettes, with only 1 per cent being monthly regular users<sup>15</sup>. Current smokers were reported to have the highest use of e-cigarettes. Among all current smokers surveyed, 49.9 per cent had ever used e-cigarettes<sup>16</sup>. The 2016 HLS found that the proportion of adults who had ever used e-cigarettes has increased to 17 per cent and of these, 16 per cent currently use them. Ever-use of e-cigarettes was higher among young people aged 15-34, compared with other age groups<sup>17</sup>.

### 3.2 Use in other countries

In the global context, systematic analysis is similarly hampered by a lack of data. However, the available data suggests that the uptake of e-cigarettes is most rapid in countries which have liberalised the e-cigarette market.

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<sup>iii</sup> In research studies of e-cigarettes, ever-use is typically assessed using the question, “Have you ever tried any of the following products, even just one time?” Respondents who select “electronic cigarettes or e-cigarettes” were considered ever-users of e-cigarettes.

In the United States (US), 3.5 per cent of adults were current e-cigarette users in 2015, with 58.8 per cent of them being current smokers, 29.8 per cent being former smokers and 11.4 per cent being never smokers<sup>18</sup>. Among young adults who currently used e-cigarettes, 40 per cent were never smokers<sup>19</sup>. Between 2011 and 2016, the level of e-cigarette use in the past 30 days among US high school students jumped from 1.5 per cent to 11.3 per cent, surpassing current use of every other tobacco product in this age group<sup>20</sup>.

In the United Kingdom (UK), a 2017 survey showed that the number of e-cigarette adult users has increased from 700,000 in 2012 to 2.9 million in 2017, representing 6 per cent of the population. Ex-smokers and current smokers account for a large proportion of the use; 52 per cent and 45 per cent respectively<sup>21</sup>. A 2016 national statistical report found that the percentage of high school students who had ever tried e-cigarettes exceeded that of tobacco cigarettes (22 per cent and 18 per cent respectively)<sup>22</sup>.

Similar patterns of e-cigarette use are observed in the European Union (EU). The proportion of ever e-cigarette users was 11.6% in 2014, up from 7.2% in 2012 in 27 EU countries analysed, and a 2014 survey showed that e-cigarette users in the EU were mainly current smokers, followed by ex-smokers<sup>23</sup>. Younger, current smokers or smokers who had tried to quit were more likely to use e-cigarettes<sup>24</sup>.

## 4. Potential risks and benefits of e-cigarettes

The evidence-base is currently not sufficient to properly inform the potential risks and benefits of e-cigarettes. The commonly discussed potential benefits of e-cigarettes include their role in tobacco harm reduction and tobacco smoking cessation, whilst concerns over their use are principally around health impacts on users and non-users, their gateway effect to tobacco, the renormalisation of smoking, and product safety.

To date, all the available studies assess short-term exposure, while the long-term health effects of e-cigarette use and exposure remains unknown.

A recent example of the lack of certainty regarding the risks and benefits of e-cigarettes is provided by the findings of the renowned National Academies of Sciences, Engineering and Medicine (NASEM) which in January 2018 published a comprehensive report on the [“Public Health Consequences of E-Cigarettes”<sup>25</sup>](#). Its core finding was that e-cigarettes may help adults to stop smoking but may lead children and young adults to start smoking. Overall it concluded that the net public health effect of e-cigarettes will depend on the relative magnitudes of three factors:

- Their impact on youth initiation of combustible products
- Their impact on adult cessation of combustible products and
- Their intrinsic toxicity.

Due to the limited number and quality of studies, there are limitations in understanding the potential health risks and benefits from the e-cigarette use on the individual and at the population level. Compounding the paucity of data and studies, the wide variety of e-cigarette devices and range of different constituents makes it difficult to draw definitive conclusions and to provide evidence-based policy and clinical recommendations. Notwithstanding these caveats, some provisional views based on the best available evidence to date are presented below.

### 4.1 Aid to smoking cessation

Opinions on the use of e-cigarettes as a smoking cessation aid differ, and existing evidence on their effectiveness in helping smokers reduce or completely quit smoking is mixed. Moreover, concern has been expressed that using e-cigarettes whilst continuing to smoke tobacco cigarettes (dual use) might mean individuals are less likely to try quitting smoking altogether.<sup>iv</sup>

A 2016 Cochrane systematic review with a meta-analysis of two randomised controlled trials (RCTs) revealed that, compared with placebo (i.e. non-nicotine) e-cigarettes, the use of nicotine-containing e-cigarettes is more likely to achieve six months' continuous abstinence from cigarette smoking, with no evidence of harm<sup>26</sup>. Due to the limited number of trials, the quality of this evidence was graded as low. A meta-analysis of 20 studies<sup>27</sup> (mostly non randomised cohort studies) indicated that, regardless

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<sup>iv</sup> See Yeh JS, Bullen C, Glantz SA. E-Cigarettes and Smoking Cessation. *New England Journal of Medicine*. 2016;374(22):2172-4 for a clinical vignette which illustrates the complexities clinicians must grapple with when considering e-cigarettes.

of interest in smoking cessation, the use of e-cigarettes reduced the likelihood of smokers quitting by 28 per cent, compared with smokers who did not use them.<sup>v</sup>

Another recent systematic review and meta-analysis included three randomised trials (including 1007 participants) and nine cohorts studies (including 13115 participants)<sup>28</sup>. It concluded that: "There is very limited evidence regarding the impact of e-cigarettes with or without nicotine on tobacco smoking cessation, reduction or adverse effects: data from RCTs are of low certainty and observational studies of very low certainty. The limitations of the cohort studies led us to a rating of very low-certainty evidence from which no credible inferences can be drawn."<sup>29</sup>

A longitudinal study in the UK reported a weak association between the use of e-cigarettes and smoking cessation, though their use was found to increase attempts to quit smoking and to reduce the number of cigarettes smoked per day<sup>30</sup>. Another longitudinal study in the US reported little difference in smoking cessation rates between short-term e-cigarette users and non-users, though it also found that long-term use of e-cigarettes resulted in a higher smoking cessation rate<sup>31</sup>. Furthermore, two prospective cohort studies found that the use of e-cigarettes alone increased the odds of abstinence from smoking<sup>32</sup>, with one of these studies also finding that while dual use did not increase abstinence, it may be helpful in reducing tobacco consumption<sup>33</sup>.

In terms of survey data, US population surveys identified that a statistically significant increase in the smoking cessation rate at the population level was associated with a substantial increase in e-cigarette use; e-cigarette users were more likely not only to attempt to quit smoking, but also to succeed in quitting, compared to non-users<sup>34</sup>. Similarly, a 2012/13 UK survey with one-year follow up showed that dual use of e-cigarettes on a daily basis increased the likelihood of attempting to quit and reducing smoking, but not the likelihood of smoking cessation, while non-daily use of e-cigarettes was not associated with any of these effects<sup>35</sup>.

With regard to the efficacy of e-cigarettes compared with nicotine replacement therapy (NRT), a few studies have reported that for smokers seeking to quit, nicotine-containing e-cigarettes can improve abstinence from tobacco at least as well as NRT<sup>36</sup>. A review undertaken in 2016 also reported that RCTs and population-based studies with more-precise evaluations find that e-cigarettes are at least as effective as NRT in assisting smokers to quit or to reduce their tobacco cigarette consumption<sup>37</sup>.

In summary, the limited evidence to date suggests that e-cigarettes might help some smokers reduce and quit tobacco smoking, but the robustness of the evidence is fairly low. The paucity of clear findings on the long-term impact and efficacy of e-cigarettes as an aid to quitting smoking leaves this open to question, and demonstrates the urgent need for more robust and thorough studies to fill the evidence gaps.

## 4.2 Harm reduction

E-cigarettes are seen by some as a viable harm reduction option for smokers who are unable to break their nicotine or smoking behaviour addiction. This is on the basis that combustion of e-cigarette liquids does not produce as many unsafe chemicals as tobacco and that therefore their use is less

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<sup>v</sup> However it is worth noting that this meta-analysis has some methodological limitations – in particular it accords the same weighting to non-randomised studies as it does to randomised studies.

harmful for smokers. The concept of 'harm minimisation' in the context of nicotine addiction focuses on removing the tobacco-related harms to smokers, rather than on people quitting nicotine completely<sup>38</sup>.

Some evidence suggests that there are immediate health benefits for individuals switching from tobacco smoking to e-cigarettes. A few studies found a significant reduction in smokers' levels of urinary metabolised acrolein and benzene as well as exhaled carbon monoxide after switching to e-cigarettes<sup>39</sup>. This finding suggests that switching from tobacco to e-cigarettes may be associated with a decline in exposure to selected toxicants and carcinogens otherwise present in tobacco cigarettes<sup>40</sup>.

A low-powered cross-sectional study showed that e-cigarette use may deliver similar nicotine levels as tobacco cigarettes and is also linked to reduced exposure to known tobacco-related carcinogens and toxins, but these benefits are not associated with dual use of e-cigarettes and tobacco cigarettes. It therefore suggests that the benefits of e-cigarettes can be realised provided there is full cessation of tobacco smoking<sup>41</sup>. A study comparing the risk of e-cigarettes and tobacco cigarettes based on the levels of the 12 most significant toxicants generated concludes with caution that the use of e-cigarettes presents a lower risk to health than tobacco smoking<sup>42</sup>.

Conversely other evidence shows that e-cigarette use is associated with health risks related to increased oxidative stress, induced by the toxic components and vaporisation<sup>43</sup>. A study in 2016 suggests that e-cigarettes are linked to an elevated risk of aortic stiffness and increased blood pressure in young smokers<sup>44</sup>. This is upheld by a 2017 review of eight studies, where some evidence was found showing a relation of e-cigarettes to cardiovascular risk<sup>45</sup>.

A systematic review of case reports found that e-cigarettes can have a negative impact on respiratory, gastrointestinal, cardiovascular, neurological and immune systems<sup>46</sup>. Experimental data suggest that e-cigarettes can induce lung inflammation, a hallmark for the development of lung cancer and chronic obstructive pulmonary disease (COPD), though much less than tobacco smoking<sup>47</sup>. Their use has a greater effect on reducing immune-related gene expression in nasal mucosa<sup>vi</sup> than tobacco smoking, particularly the expression of transcription factors, such as ERG1 (early growth response protein)<sup>48</sup>.

In terms of the health effects of reducing smoking, evidence suggests that the length of time that a person has smoked plays a larger role in determining morbidity and mortality rates than the number of cigarettes smoked per day<sup>49</sup>. A prospective cohort study found that heavy smokers who smoked 50 per cent fewer cigarettes per day did not lower their risk of premature death significantly. In other words, reduction in cigarette consumption is not proportionately associated with reduction in harm compared to quitting<sup>50</sup>. The result of this and another study therefore suggests that quitting tobacco smoking completely is more effective in reducing the risk of premature death from tobacco-related diseases than smoking less<sup>51</sup>.

Reinforcing the trend towards these highly equivocal findings on harm reduction from use of e-cigarettes, the recent NASEM report concludes that while "there is 'substantial' evidence that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organ systems, there is 'no available'

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<sup>vi</sup> immune-related gene expression in in nasal mucosa is a process where genetic instructions are used to synthesize gene products that are related to the immune system that is present in the tissues that line the nasal cavity.

evidence whether or not long-term e-cigarette use among smokers (dual use) changes morbidity or mortality compared with those who only smoke combustible tobacco cigarettes”<sup>52</sup>.

### 4.3 Nicotine dependence

E-cigarettes can be used as a means to deliver nicotine. There is evidence that e-cigarettes can deliver similarly rapid onset levels of nicotine as that obtained from tobacco cigarettes<sup>53</sup>.

Factors that can influence nicotine delivery from e-cigarettes include e-liquid components, device characteristics and use behaviour (e.g. a user’s puff volume, puffing rate, and depth of inhalation)<sup>54</sup>. However, the precise level of addictiveness of inhaled nicotine from e-cigarettes is less well studied<sup>55</sup>. One study concluded that nicotine-containing e-cigarettes are less addictive than tobacco cigarettes, and equally or less addictive than nicotine gum<sup>56</sup>. A recent US study examining the level of nicotine dependence among e-cigarette and tobacco cigarette users revealed that e-cigarette users experienced a remarkably longer time-to-first-use of the day and were less reliant on their respective devices than tobacco cigarette users<sup>57</sup>.

Though some studies suggested a single e-cigarette puff delivers lower nicotine level than a single tobacco cigarette puff, a review highlights that nicotine exposure is also determined by both experience in e-cigarette use and use behaviour<sup>58</sup>. Thus, e-cigarette devices are capable of delivering nicotine at levels that maintain nicotine dependence in experienced users due to adaptation of their use behaviours<sup>59</sup>.

### 4.4 E-cigarette aerosol

E-cigarettes are often depicted as producing non-toxic emissions that can be safely used indoors, but evidence suggests otherwise. Both the composition of e-liquids and e-cigarette device characteristics affect the toxicity of the aerosol.

E-cigarette liquids often contain a combination of propylene glycol, glycerol, and, optionally, nicotine and flavouring agents. However, in several studies and a review from the United States Food and Drug Administration (FDA), e-cigarette aerosols, cartridge, and refill liquids are found to contain an array of known human carcinogens and toxins<sup>60</sup>. The toxic chemicals identified include tobacco specific nitrosamines (TSNA), volatile organic compounds (VOCs), heavy metals, aromatic hydrocarbons (PAHs) as well as carcinogenic aldehyde and carbonyl compounds, all known to have adverse health effects<sup>61</sup>.

The safety of inhaling heated flavouring chemicals is unknown and has not been well studied. This makes high levels of flavouring chemicals contained in e-cigarettes a toxicological concern<sup>62</sup>. The Australian Government’s National Health and Medical Research Council (NHMRC) cautions that high doses of some flavour-chemicals may be safe for ingestion but unsafe when inhaled into the lungs<sup>63</sup>. A recent study found that the use of flavours in e-cigarettes may induce inhalation toxicity by causing inflammatory reactions in cells directly exposed to aerosols<sup>64</sup>. The toxicity profile of e-cigarettes is closely related to the concentration and number of flavours<sup>65</sup>.

Besides the constituents of e-liquids, the amount of aerosol produced from e-cigarettes also depends on the device and the battery output voltage being used<sup>66</sup>. There is a positive linear relationship between the voltage of the e-cigarette device and the total volume of aerosol generated<sup>67</sup>.

In terms of the effects of exposure to e-cigarette aerosols, there is evidence showing that it can raise the levels of cellular reactive oxygen species and cause notable DNA damage, which can subsequently give rise to tumour development and progression<sup>68</sup>. Despite this, two reviews found that aerosols produced by e-cigarettes do not contain as many toxic chemicals as those found in tobacco smoke and passive (i.e. second-hand) exposure to e-cigarette aerosol was less harmful than passive exposure to tobacco smoke<sup>69</sup>.

There are very few studies which have looked at the effects of e-cigarettes on air quality. Those available showed inconsistent scientific evidence on their potential to contaminate the environment due to lack of standardised methodology for conducting this research<sup>70</sup>. Some found that e-cigarettes generate a substantially lower level of particulate matter than tobacco cigarettes, while others found the same or slightly higher levels<sup>71</sup>. Moreover, a recent study found that short-term e-cigarette use (two hours) elevates the concentrations of particulate matter (PM 2.5), ultrafine-particulate matter and nicotine in the air and accumulation of nicotine on surfaces and clothing<sup>72</sup> which would have implications for risks associated with second-hand inhalation of these particles and dermal exposure to nicotine.

#### **4.5 Safety and quality of e-cigarette devices**

The market for e-cigarettes has expanded rapidly, and a broad range of e-cigarette brands and product models are available to consumers. However, there is little conclusive evidence available about their safety.

E-cigarettes are subject to differing quality control processes and labelling requirements, and there is a variation in the composition and concentrations of e-liquids, across and within brands<sup>73</sup>. There is evidence of false or misleading e-cigarette labels—some products do not clearly or accurately state the ingredients and their concentrations<sup>74</sup>. One study that analysed e-liquid samples found that up to 51 per cent mislabelled their nicotine levels, with one sample having a nicotine level 172 per cent higher than labelled<sup>75</sup>.

Further, a systematic review concluded that e-cigarette product labelling and packaging provided inadequate or misleading information about product contents, use and warnings<sup>76</sup>. In 2013, samples collected by the NSW Ministry of Health found that 70 per cent contained nicotine, despite nicotine-containing e-liquids being unauthorised for sale in all Australian states and territories<sup>77</sup>. This lack of quality control and product information has significant public safety implications.

In the past several years, the design of e-cigarette devices has evolved a great deal, but the risks inherent in their features remain. These risks include overheating and explosion of the batteries, e-liquid leaking, and operational risks (some modular devices are extremely complex to use)<sup>78</sup>. A number of accidents involving burns, fires and the explosion of devices have been reported, as a result of use in oxygen-rich environments or use while the battery was charging<sup>79</sup>. Some devices permit users to self-prepare or modify the e-liquid in a 'do-it-yourself' manner, thus the specific risks of a particular e-cigarette will depend on its characteristics and how it is used.

A report from the US Centres for Disease Control and Prevention showed that increased phone calls to US poisons control centres was attributable to e-cigarette use. Calls jumped from an average of one per month in September 2010 to 215 calls per month in February 2014, with 51 per cent of e-cigarette related phone calls concerning children between 0–5 years of age<sup>80</sup>. The calls relating to



children were primarily reporting ingestion of the e-liquid (68.9 per cent) and inhalation of the aerosol (16.8 per cent), as well as eye and skin irritation (14.4 per cent)<sup>81</sup>. This is in line with the findings of an EU study, where a total of 277 incidents related to e-cigarette use were reported across 10 EU Poison Centres between 2012 and 2015, with unintentional exposure to refill e-liquids mostly cited<sup>82</sup>.

## 4.6 Renormalising smoking

Many e-cigarette products are promoted in ways that glamorise smoking<sup>83</sup>. There are concerns that e-cigarette advertising and role-modelling could restore the social norms around smoking and undermine or even reverse the decades-long work to remove any positive associations with smoking. E-cigarette retail websites frequently make unsubstantiated claims about their products<sup>84</sup>. A 2011 study of 59 e-cigarette websites in the US reported<sup>85</sup>:

- 95 per cent made health-related claims
- 64 per cent had a smoking cessation-related claim
- 88 per cent stated that the product could be smoked anywhere
- 76 per cent claimed that the product does not produce second-hand smoke
- 93 per cent included claims that e-cigarettes were cheaper than cigarette smoking.

Adding to this, most websites offered candy, fruit, and coffee flavours and included youthful appeals such as images or claims of being glamorous, increased social status, enhanced social activity, romance, and use by celebrities<sup>86</sup>. A US study points out that direct e-cigarette marketing promotions is widespread and that there is a positive correlation between e-cigarette promotions and the prevalence and frequency of e-cigarette use<sup>87</sup>.

It has been estimated that e-cigarette advertising expenditure across media channels in the US tripled from \$6.4 million in 2011 to \$18.3 million in 2012<sup>88</sup>. Prior to any restrictions on the marketing of e-cigarettes coming into force, a wide range of advertising and marketing strategies were used to particularly target the youth market including:

- Television e-cigarette advertisements - in the US, youth exposure to television e-cigarette advertisements increased 256 per cent from 2011 to 2013<sup>89</sup>
- Product innovation - a wide range of choices of flavours, nicotine e-cigarette strengths, and modifiable designs are available for users<sup>90</sup>.
- Celebrity endorsements - images of celebrities such as Leonardo DiCaprio and Julia Louis-Dreyfus using e-cigarettes are widely circulated<sup>91</sup>.

Two studies have suggested that the visual imagery of e-cigarette use in product advertising increases daily smokers' urge to smoke tobacco cigarettes and may lead to more/increased smoking behaviour<sup>92</sup>. One of these studies also found that cues in advertising may undermine the abstinence efforts of former smokers<sup>93</sup>.

In terms of behavioural modelling, the effect on children and adolescents of seeing role models such as parents or celebrities using e-cigarettes has not been fully assessed. However, one study indicates that celebrity endorsements can impact greatly on e-cigarette uptake through enhancing positive attitudes towards them<sup>94</sup>. Additionally, in the context of tobacco smoking the role of environmental smoking (i.e. parent, sibling and peer smoking) has been identified as a critical element of children



and adolescents' susceptibility to smoking<sup>95</sup>. Role models can shape perceptions about the safety of tobacco smoking, lead to the development of favourable smoking-related cognitions among children and adolescents, and trigger an urge to smoke. These findings may well be extrapolated to the effect of role models in e-cigarette use.

#### **4.7 Recruitment of new tobacco smokers (Gateway effect)**

There is a growing body of evidence that indicates e-cigarette use among adolescents is associated with elevated risk of cigarette initiation<sup>96</sup>. This raises concerns that nicotine e-cigarettes could be used as a 'gateway' to establish addiction to nicotine and smoking behaviour, and so lead to new tobacco cigarette smokers<sup>97</sup>. The NASEM report concludes that "there is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults" and advises that close attention be paid to the effects of e-cigarettes use on initiation of tobacco use<sup>98</sup>.

A study based on the 2012-2013 US National Adult Tobacco Survey reported that young adults aged 18-29 who had never previously smoked but who used e-cigarettes were 2.4 times more open to tobacco cigarette smoking<sup>99</sup>. The rates of cigarette initiation among e-cigarette users reported are also high in a prospective cohort study – 6.17 times higher in comparison to never e-cigarette users<sup>100</sup>. Similarly, a 12 month prospective UK study involving 2836 adolescents also found a robust relationship between ever use of e-cigarettes and subsequent cigarette initiation<sup>101</sup>.

A longitudinal non-randomised study in the US has shown that high school students who had used e-cigarettes were more likely to report initiation of tobacco smoking over the next year than non-users<sup>102</sup>. This finding is corroborated by a study looking into the association between e-cigarette use and susceptibility to tobacco smoking among middle and high school students in Canada<sup>103</sup>.

A longitudinal study of 5 cohorts of Southern Californian adolescents attaining 12th grade in 1995, 1998, 2001, 2004, and 2014 indicated that tobacco use decreased in this population between 1995 and 2004. However, when the use of e-cigarettes was combined with the prevalence of current cigarette use in the 2014 data an overall increase was observed<sup>104</sup>. This increase suggests that e-cigarettes are also being taken up by adolescents who would not otherwise have initiated using tobacco products<sup>105</sup>. However, these studies stand in contrast to a 2017 UK study analysing five large-scale surveys with a total of 60,000 respondents aged 11-16, which shows e-cigarette experimentation does not cause young people to smoke<sup>106</sup>.

Tobacco use among adolescents is an important predictor of adult smoking; it is well known that individuals who start smoking early are more likely to continue smoking<sup>107</sup>. Data suggest that nicotine-containing e-cigarettes are increasingly being accessed and used by children and adolescents for experimentation purposes, with flavours cited as one of the top reasons for e-cigarette initiation<sup>108</sup>. Studies have shown that children develop nicotine dependence, even at low levels of consumption within days of starting to smoke<sup>109</sup>, and so the uptake of nicotine-containing e-cigarettes among children and adolescents is a cause for concern.

## 5. Regulatory framework for e-cigarettes

As with tobacco, regulation of e-cigarettes plays an important part in managing their availability and use. To date, a range of regulatory mechanisms have been utilised to control e-cigarettes including regulations related to access, usage, marketing, advertisement, packaging, and taxation<sup>110</sup>. Most are to prevent sales to minors and restrict their use in public places.

This snapshot of regulations in use across Australia and New Zealand can be expected to change over time. Appendix 3 summarises the different regulatory frameworks being implemented by the US, UK, and Canada.

### 5.1 Australia

In Australia, the laws governing the sale, supply and use of e-cigarettes is complex, partly related to the Federal and state/territory responsibilities and legislation that apply to tobacco products and pharmaceutical goods, and also because of the different approaches states and territories took to smoking regulation. This renders the regulation of e-cigarettes in Australia not clear-cut. As it stands, nicotine-containing e-cigarettes are illegal under Commonwealth, state and territory legislation, while non-nicotine containing e-cigarettes are legal and have been included into the majority of state tobacco control legislation to tighten their sale and promotion.

#### 5.1.1 Commonwealth Regulation

Nicotine is classified as either a Schedule 4 Prescription-only Medicine (S4) or a Schedule 7 Dangerous Poison (S7) under the Commonwealth Poisons Standard, with the exception of tobacco cigarettes and approved NRT<sup>111</sup>.

Nicotine containing e-cigarettes for therapeutic use falls within S4 classification, and the sale and advertising of such products is subject to approval by the Therapeutic Goods Administration (TGA)<sup>112</sup>. To date, there is no approved e-cigarette device or e-liquid for therapeutic use in the Australian Register of Therapeutics Goods.

Conversely, nicotine-containing e-liquids without a therapeutic claim is classified as a S7 Dangerous Poison (due to nicotine's classification). Their sale, supply and possession within Australia is prohibited and they cannot be legally bought in retail stores in Australia. Presently, the only avenues to access nicotine containing e-cigarettes are through two TGA schemes that allow the import of unapproved therapeutic goods<sup>113</sup>:

- TGA's [personal importation scheme](#) (PIS)<sup>vii</sup> - where an importer must hold a prescription from an Australian registered medical practitioner and the quantity imported must be no more than three months' supply at any one time and no more than 15 months' supply in a 12 month period.

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<sup>vii</sup> The Personal Importation Scheme permits an individual residing in Australia to have a therapeutic good sent to them from an overseas supplier through post or via an international courier; among other restrictions, the goods imported must be used by that individual or a member of his/her immediate family and must not be sold or supplied to any other person.

- TGA's [Special Access Scheme](#) (SAS) and [Authorised Prescriber](#) (AP) Scheme – where medical practitioners are required to apply to access the unapproved therapeutic goods on behalf of their patients.

How this personal importation scheme is monitored is very unclear. There are a number of websites where nicotine-containing e-liquids can be purchased online and the supply is posted from overseas; as explained in this example of text on one e-liquid online provider's [website](#) “*You might have heard that it is illegal to buy electronic nicotine cigarettes in Australia. Crikey! But this is not true. You CAN, in fact, buy e-cigarettes containing nicotine if you live in Australia. You just have to order them via international post under the following guidelines...*”<sup>viii</sup>

The Australian Standing Committee on Health, Aged Care and Sport recently completed its inquiry into the Use and Marketing of Electronic Cigarettes and Personal Vaporisers in Australia and recommended that a national approach be taken to the regulation of non-nicotine electronic cigarettes. It also recommends that the TGA continues to oversee the classification of nicotine and relevant exemptions, and the assessment of any electronic cigarette product as a therapeutic good<sup>114</sup>.

### 5.1.2 State and territory regulation

E-cigarette regulation at the state and territory level has been in a state of flux. All states and territories, except for the Northern Territory, have moved or are moving to regulate non-nicotine containing e-cigarettes, especially their sale, supply, promotion and use. By and large, youth protection is at the centre of the planned or enacted e-cigarette regulation.

Jurisdiction	Current Regulation
Queensland (QLD)	Effective from 1 January 2015, e-cigarettes (defined as a ‘personal vapouriser’) are included in its legislated definition of ‘smoking product’ and as such e-cigarettes will have the same restrictions on their point of sale, sale to minors, display, advertising, and promotion that apply for tobacco products <sup>115</sup> . Smoke-free requirements also extend to e-cigarettes – restricting their use in public areas, motor vehicles, hotels, clubs, businesses and restaurants <sup>116</sup> .
New South Wales (NSW)	In NSW, regulations on the sale and supply of e-cigarettes have come into force since late 2015. E-cigarettes and accessories <sup>ix</sup> have been included in the Public Health (Tobacco) Act 2008 as a discrete class from tobacco – banning their sales to minors; use of e-cigarettes in a car with a child present; and restricting display, advertising and promotion. NSW police have been authorised to seize electronic cigarettes from minors <sup>117</sup> . The NSW <i>Smoke-free Environment Act 2000</i> was amended in mid-April 2018 to prohibit the use of e-cigarettes in public

<sup>viii</sup> <https://veppociq.com/pages/electronic-cigarettes-with-nicotine-in-australia/> website accessed 23 January 2018

<sup>ix</sup> An e-cigarette accessory is defined to include a cartridge, capsule or other container designed to contain a liquid, aerosol, gas, vapour or other substance for use in an e-cigarette and a heating element designed for use in e-cigarettes.

	places and transport areas where smoking is banned. Moreover, e-cigarettes retailers are now required to notify the Health Secretary of their businesses <sup>118</sup> .
Australian Capital Territory (ACT)	The ACT government brought its territory laws in line with those of QLD and NSW in 2016, subjecting the sale and use of e-cigarettes to the same laws placed on tobacco cigarettes. The legislation prohibits the use of e-cigarettes in smoke-free areas, sales to under-18s, in-store and point-of-sale advertisements and displays. Sales by vending machine, promotions, inclusion in customer reward schemes, sponsorships and product giveaways are also banned <sup>119</sup> .
Victoria (VIC)	In mid-2016 the Victorian Government passed a Bill to amend the Tobacco Act 1987 to tighten controls on e-cigarettes, effective from August 2017. Under this amendment, e-cigarettes are treated as tobacco products, banning sales to minors and the use of e-cigarettes in smoke free areas <sup>120</sup> . However, a limited point of e-cigarette display is permitted in certified specialist e-cigarette retailing premises <sup>121</sup> .
Western Australia (WA)	There is currently no regulation specific to e-cigarettes in place in WA, but the <i>Tobacco Products Control Act 2006</i> disallows the sale and supply of e-cigarettes that resemble a tobacco product, irrespective of whether it contains nicotine or not. A ruling from the Supreme Court decision in 2014 also upheld this <sup>122</sup> . Additionally, the Education and Health Standing Committee put forward a report on <i>clearing the air on e-cigarette: factors regarding regulation that require consideration</i> in mid-2017, which was more of a discussion to prompt the WA government to consider how to cope with e-cigarettes into the future <sup>123</sup> .
South Australia (SA)	The SA Government has proposed to regulate e-cigarettes under <i>Tobacco Products Regulation Act 1997</i> and tabled the Tobacco Products Regulation (E-cigarette Regulation) Amendment Bill in Parliament in May 2017. The proposed changes include the prohibition of: <sup>124</sup> <ul style="list-style-type: none"> <li>• the sale of e-cigarettes to minors and by retail without a licence</li> <li>• the use of e-cigarettes in smoke-free areas</li> <li>• advertising and promotion of e-cigarettes</li> <li>• retail point of sale displays of e-cigarettes</li> <li>• indirect sales of e-cigarettes (such as internet sales)</li> <li>• the sale of e-cigarettes from temporary outlets, and vending machines.</li> </ul>
Tasmania (TAS)	There is currently no regulation on the availability and use of non-nicotine e-cigarettes in Tasmania, but the Tasmanian Government conducted a consultation on the proposed new regulatory framework for e-cigarettes in early 2017. The framework would introduce an e-cigarette retail licensing system, as well as a ban on sales to minors, the use of e-cigarettes in smoke free areas, and advertisement <sup>125</sup> .

Northern Territory (NT)	There is currently no regulation on the availability and use of non-nicotine e-cigarettes in NT. However, the NT legislation prevents the sale of e-cigarettes to children if they resemble tobacco products or are likely to encourage children to use them <sup>126</sup> .
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## 5.2 New Zealand

The Smoke-free Environments Act 1990 (SFEA) and the Medicines Act 1981 are the two primary pieces of legislation covering e-cigarettes. As of March 2017, the approach to e-cigarette regulation in New Zealand has undergone significant change. The New Zealand Government is planning to amend the Smoke-free Environments Act 1990 (SFEA) to legalise the sale and supply of nicotine containing e-cigarettes as consumer products, with some degree of controls. In addition to this, specific changes to the regulation of nicotine and non-nicotine containing e-cigarettes proposed by mid-2018 are as follows<sup>127</sup>:

- The sale of all e-cigarettes is restricted to people 18 years or over
- The sale of all e-cigarettes from the vending machines is prohibited except in R18 settings
- Broader advertising such as radio, TV and internet is prohibited
- Point-of-sale display for all retailers is permitted
- In-store display, promotion on the outside of the store, discount offers etc. in R18 retail settings is permitted
- Vaping is not allowed in workplaces and other areas designated to be smoke-free under the SFEA.
- The requirements for product safety will be set out

No amendments are planned to the Medicines Act 1981. E-cigarettes with a therapeutic claim, irrespective of whether they contain nicotine or not, will continue to be classified as medicines<sup>128</sup>. It is, therefore, illegal to sell and advertise any e-cigarette products with a therapeutic claim, without authorisation by MedSafe<sup>129</sup>. To date, no such therapeutic product has been submitted for approval under the Medicines Act<sup>130</sup>.

## 6. Conclusion

E-cigarettes are a new and evolving consumer product. The use of e-cigarettes has been widely discussed in public health and health policy domains, as to their role in smoking cessation, short- and long-term health effects, and the concerns they could undermine the gains made in tobacco control through a gateway effect or the renormalisation of smoking. Other issues include the quality and safety of e-cigarettes, and the impact of exposure to e-cigarette aerosol.

While most health experts recognise e-cigarette use as less harmful than tobacco smoking, the full extent of harm at the individual and population levels is not yet known and may not be evident for many years. The lack of clear and robust scientific evidence combined with divergent opinions among the medical profession on the role of e-cigarettes in tobacco control means that determining effective policy and regulation in this area is neither clear nor easy.

Governments have taken different approaches to regulating e-cigarettes. Both Australian and New Zealand governments recognise the potential risks of e-cigarettes to children and adolescents, as well as to the wider population, and regulate their promotion, sale and use. As of March 2017, New Zealand has legalised the sale of nicotine-containing e-cigarettes as consumer product, while Australia continues to ban the retail sale of nicotine containing e-liquids and retain the scheme allowing it to be imported for personal use.

However, until there is an adequate level of robust, comprehensive and independent data on which to base these vital and far-reaching policy decisions, the populations of Australia and New Zealand, and the policy makers attempting to make the right decisions on their behalf, are left unsure and uncertain of what is the best path to take. Given that the use of e-cigarettes is a new domain of research, further studies are needed to build a better understanding of their public health implications.

In the meantime, effective regulation must be enacted, monitored and enforced to prevent e-cigarettes' uptake by young people. It is vital that the rapid spread of e-cigarette use not undermine the decades-long battle against tobacco, smoking and addiction, and their accompanying devastation. However, it is just as important that any effective aid that helps people quit or reduce smoking is not lost.

## Appendix 1: Nicotine

Nicotine is the primary constituent in tobacco that causes compulsive use. To better manage nicotine addiction, understanding the basic mechanisms of nicotine is essential.

### Pharmacology of nicotine

Nicotine exerts its physiological effects by binding to nicotinic acetylcholine receptors (nAChRs) that are widely found in the peripheral and central nervous system. nAChRs located in the mesolimbic system of the brain are currently believed to be responsible for mediating nicotine addiction<sup>131</sup>. Activation of nAChRs stimulates the release of a variety of neurotransmitters. Of all neurotransmitters released, the elevated level of dopamine is crucial in inducing the reward pathway and in giving rise to the sensation of pleasure, while increasing the amount of glutamate complements and strengthens this pleasure sensation<sup>132</sup>.

In concrete terms, the modulation of the glutamatergic (excitatory) and dopaminergic (rewarding) neurotransmission in the midbrain contribute to the rewarding effects of nicotine, and synaptic plasticity in the nucleus accumbens, which is linked to learning and memory<sup>133</sup>. With long-term exposure to nicotine in the context of other facilitating factors, the brain reward system is altered and the number of nAChRs is increased. This results in the development of nicotine tolerance and the onset of nicotine addiction<sup>134</sup>.

In terms of its pharmacokinetics, nicotine is both lipid and water soluble and is thus readily absorbed through the skin, lungs, and the blood-brain barrier. The route of delivery is critical in the speed of nicotine delivery to the blood, and hence the brain<sup>135</sup>. The inhalational route is a very rapid means of delivering nicotine whereas absorption through the buccal mucosa is much slower (as in nicotine gum), and delivery through the skin (as in patches) is very slow.

### The addictive effects of nicotine

Nicotine itself is highly addictive, comparable to heroin and cocaine<sup>136</sup>. The speed of nicotine delivery to the brain and the dose delivered are important factors in initiating and maintaining dependence<sup>137</sup>. Cigarettes provide a rapid-onset method of nicotine delivery, allowing users to experience a rapid spike in plasma nicotine concentration<sup>138</sup>.

Smoking cessation is difficult due in large part to nicotine withdrawal symptoms. A broad spectrum of symptoms can present when a smoker ceases smoking abruptly or reduces the number of cigarettes smoked, such as mood changes, difficulty concentrating, and increased appetite. The development of withdrawal symptoms is strongly correlated with the degree of dependency<sup>139</sup>.

### The health impacts of nicotine

Nicotine exerts diverse effects on humans. The short and long-term effects of nicotine have mostly been studied in the context of tobacco smoking. Nicotine itself has been reported to have the following dose-dependent pharmacological effects:

- Catecholamine release

- Hemodynamic effects (increase in heart rate, transient increase in blood pressure vasoconstriction of coronary and other vascular beds)
- Effects on lipids
- Induction of insulin resistance
- Endothelial dysfunction
- Fetal teratogenicity
- Inhibition of apoptosis and enhanced angiogenesis (raising concerns about the development of cancer and heart disease)<sup>140</sup>

These pharmacological effects have health implications affecting some major organs such as the heart, lungs, and kidneys<sup>141</sup>. Research indicates that children and adolescents are more sensitive to the harmful effects of nicotine and the risk of nicotine addiction<sup>142</sup>. Nicotine exposure during periods of developmental vulnerability and pregnancy may disrupt the cognitive development of children and adolescents and elicit adverse fetal outcomes<sup>143</sup>.



## Appendix 2 – Regulatory framework for e-cigarettes in other countries

In the global context, the regulation of e-cigarettes in some countries has undergone developments, from patchy and non-existent to stricter rules, in order to tighten their sale and supply.

Jurisdiction	Current Regulatory Framework
United States (US)	<p>Prior to August 2016, e-cigarettes that were not marketed for therapeutic purposes were not under any body of federal regulation in the US. As of August 2016, the FDA extended its oversight to all tobacco products, including all electronic nicotine delivery systems<sup>144</sup>. This means e-cigarettes with nicotine are regulated in the same way as traditional tobacco products, including their manufacture, import, packaging, labelling, advertising, promotion, sale, and supply<sup>145</sup>. Under this new regulation, all electronic nicotine delivery systems have to undergo the FDA's review and evaluation, including their ingredients, product features, health risks and their attractiveness to minors and non-users. The regulations also prohibit the sale of nicotine containing e-cigarettes to minors in person or online, require health warnings on product packages and in advertisements, and ban their sale in vending machines<sup>146</sup>.</p> <p>As it stands, non-nicotine e-cigarette laws vary from state to state.</p> <p>E-cigarettes that are marketed for therapeutic purposes continue to be regulated by the FDA Center for Drug Evaluation and Research<sup>147</sup>.</p> <p>As of July 2017, the FDA proposed a plan to cut nicotine content in cigarettes to non-addictive levels.</p>
United Kingdom (UK)	<p>Under 2016 regulations, nicotine containing e-cigarettes are regulated either under the revised EU Tobacco Products Directive (TPD) as tobacco products or, if they are making a therapeutic claim, under the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) as medicines<sup>148</sup>.</p> <p>The revised EU TPD requires that all e-cigarette products sold fully meet the standards stipulated in the Tobacco and Related Products Regulations 2016, ensuring minimum standards for the safety quality of all e-cigarettes, promoting informed consumer choices and preventing youth initiation. Examples of specific rules include<sup>149</sup>:</p> <ul style="list-style-type: none"> <li>• the size of e-liquids must be no more than 2ml, with maximum nicotine strength capped at 20mg/ml</li> <li>• e-cigarettes must provide a nicotine dose in a consistent manner and be capable of being refilled without leaking out of the cartridge</li> <li>• sale to minors under 18 years old is prohibited</li> <li>• all packaging requires child-resistant caps and a health warning stating that 'this product contains nicotine which is a highly addictive substance'</li> </ul>

	No prohibition on the use of e-cigarettes in public places has been put in place <sup>150</sup> .
Canada	<p>Under the Canadian Food and Drugs Act, nicotine-containing e-cigarettes, with or without a therapeutic claim, are regulated as medicines. Authorisation is required prior to their importation, advertisement or sale in Canada. Non-nicotine e-cigarettes that do not make health claims are unregulated<sup>151</sup>.</p> <p>To date, no nicotine-containing e-cigarette product has so far received approval from Health Canada. Some provinces have put in place policies to restrict the sale, marketing and use of e-cigarettes with/without nicotine. For example, Nova Scotia has regulation banning the sales of e-cigarettes to persons under 19 years of age<sup>152</sup>. Despite this, reports highlight that e-cigarettes with or without nicotine are commonly accessible in Canada<sup>153</sup>.</p> <p>As of late 2016, the federal government of Canada proposed to amend the Tobacco Act to include e-cigarettes with or without nicotine as a discrete class of products, to render e-cigarettes less accessible to young people.</p>

## Appendix 3 – Positions of key health organisations on e-cigarettes

In midst of uncertainty about the risks and benefits of e-cigarettes, health organisations in Australia, New Zealand and internationally have expressed a broad spectrum of opinions about the access to and use of e-cigarettes.

### Health organisations in Australia and New Zealand

Organisation	Position
Australian Medical Association (AMA)	<p>The AMA advocates a cautious, evidence-based approach to the use of e-cigarettes<sup>154</sup>. Given that there is no evidence demonstrating the safety of vaping and the effectiveness of e-cigarettes in helping people quit, the AMA believes that e-cigarettes should not be allowed to become a socially acceptable alternative to smoking. The key recommendations in its position statement on <a href="#">Tobacco Smoking and E-cigarettes (dated Dec 2015)</a> were:</p> <ul style="list-style-type: none"> <li>• E-cigarettes be subjected to the same controls as tobacco cigarettes, which included restrictions on their sale, marketing, advertising and promotion.</li> <li>• E-cigarettes must not be marketed as cessation aids as such claims are not supported by evidence at this point in time.</li> </ul>
The Thoracic Society of Australia & New Zealand (TSANZ) and Lung Foundation Australia	<p>In mid-2017, the TSANZ and Lung Foundation made a <a href="#">joint submission</a> to the inquiry into the use and marketing of e-cigarettes in Australia. Both organisations oppose the liberalisation of e-cigarettes and the key reason for this is because the use of these devices causes injury to the lung. The submission states that “there is no reason to support an approach to regulating a product which causes ill health contains known carcinogens and other toxic compounds”. If these devices are to be used as a smoking cessation aid, they must undergo the TGA approval pathway.</p> <p>The TSANZ also states that there is no good public health claim for an unregulated approach to e-cigarettes and personal vaporisers. There is a strong case for a total ban on these products as they are currently available.</p>
The Royal Australian & New Zealand College of Psychiatrists (RANZCP)	<p>The RANZCP is supportive for the use of e-cigarettes, because of the stagnant smoking rates among severely mentally ill patients over the last 20 years. As stated in its 2017 <a href="#">submission</a> to the inquiry into the use and marketing of e-cigarettes in Australia, the RANZCP believes that the use of e-cigarettes is associated with harm reduction and reduction of some of the current health disparities experienced by people with mental illness. It also indicates its support for a comprehensive approach to tackle tobacco</p>

	related harm reduction and this should include the proportional regulation of e-cigarettes.
Royal Australasian College of Surgeons (RACS)	The <a href="#">RACS</a> does not support the use of e-cigarettes for either therapeutic or recreational purposes on account of inconclusive evidence of their effective use as a means for smoking cessation, health effects and impact on surgery. It also believes that same degree of caution for tobacco products should be applied to e-cigarettes and made several recommendations relating to restrictions on their sale, advertising, display, and use in public places, many of which are consistent with the findings of the South Australian Parliament Select Committee on E-Cigarettes.
Australia's National Health and Medical Research Council (NHMRC)	The updated <a href="#">statement on e-cigarettes</a> by the NHMRC in April 2017 states that the current evidence is insufficient to underpin claims that e-cigarettes aid smokers to quit and are a safe alternative to tobacco smoking. Future research is required to evaluate their safety, quality and efficacy. In the interim, the NHMRC recommends that health authorities and policy-makers should mitigate their potential harms and protect vulnerable population groups.
Lung Foundation Australia	In its <a href="#">position statement</a> on e-cigarettes dated June 2014, the Lung Foundation Australia considered the current evidence base to be insufficient to recommend the use of e-cigarettes over current therapeutic modalities to help quit smoking. They advocate for regulation on access to e-cigarettes with or without nicotine.
Cancer Council Australia & Heart Foundation	A 2014 <a href="#">joint position statement</a> between the Cancer Council Australia and the Heart Foundation advised extreme caution on e-cigarettes; both organisations support a ban on their sale (apart from TGA approved products) and promotion and the use of e-cigarettes in smoke-free areas.
Public Health Association Australia, (PHAA)	As indicated in its <a href="#">statement</a> on e-cigarettes, the PHAA supports the advice of the World Health Organization (WHO) that the regulation of e-cigarettes should be evidence-based and in line with the FCTC. In light of this, e-cigarettes should be subjected to existing tobacco control policies, that is – prohibiting all forms of their advertising and promotion and unproven health claims and applying smoke-free measures to e-cigarettes.
Stroke Foundation	The Stroke Foundation does not support the use of e-cigarettes on the basis that there is insufficient evidence of the use of e-cigarettes as a smoking cessation aid but increasing evidence pointing to e-cigarette use linked to the smoking initiation in young people, as stipulated in its <a href="#">e-cigarettes policy position paper</a> .

Australian Council on Smoking and Health (ACOSH)	It its 2017 submission to the inquiry into the use and marketing of e-cigarettes in Australia, <a href="#">ACOSH</a> recommends against the supply and use of e-cigarettes in Australia in view of current evidence base, except for TGA approved e-cigarette products for therapeutic use. It also strongly recommends the development of specific regulatory standards concerning e-cigarettes in Australia.
Australian Dental Association (ADA)	In its <a href="#">submission</a> to the inquiry into the use and marketing of e-cigarettes in Australia, the ADA urges the government extend regulations in effect governing the use, manufacturing and marketing of tobacco products to e-cigarettes and asserts that the discussion between practitioners and patients about the use of e-cigarettes should only be taking place after all other avenues were explored.
Cancer Society of New Zealand	The Cancer Society of New Zealand released a <a href="#">position statement</a> in 2014, emphasising that evidence is required to confirm the role of e-cigarettes in tobacco harm reduction at the individual and population levels before advocating for their widespread promotion. Its position was reiterated in its <a href="#">submission</a> to NZ Ministry of Health’s consultation on policy options for regulation of e-cigarettes, recommending that the status-quo is an appropriate policy option.

## International health organisations

Organisation	Position
WHO Framework Convention on Tobacco Control (FCTC) <sup>x</sup>	The World Health Organization (WHO) prepared a <a href="#">report on Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS)</a> in 2016 for the Conference of the Parties (COP) to the WHO FCTC. The report emphasised that the potential role for e-cigarettes in tobacco control was still a subject of debate. The magnitude of health risks associated with e-cigarettes was assessed as likely to be lesser as compared to tobacco cigarettes, but there was a dearth of evidence to quantify the relative risk between e-cigarettes and tobacco cigarettes. It has advocated for measures to safeguard public health, prevent the proliferation of tobacco addiction problems and protect tobacco control efforts.

<sup>x</sup> The WHO Framework Convention on Tobacco Control (FCTC), a legally binding instrument, sets the global tobacco control policies, practices and strategies to combat the cause of tobacco epidemic. The Conference of the Parties (COP) is the governing body of the FCTC and is composed of 180 Parties. Many have set implementation targets in accordance with the obligations of the convention.

<p>National Academies of Sciences, Engineering and Medicine (NASEM)</p>	<p>The NASEM published a report on the <a href="#">Public Health Consequences of E-cigarettes</a> in January 2018 after assessing the available evidence on health effects, harm reduction, smoking cessation, and gateway effects related to e-cigarette use. The key conclusions from its report are as follows:</p> <ul style="list-style-type: none"> <li>• Overall, there is limited evidence that e-cigarettes may be effective aids to promote smoking cessation</li> <li>• There is substantial evidence that e-cigarette use is associated with reduced exposure to potentially toxic substances, compared with tobacco cigarettes.</li> <li>• There is moderate evidence that the use of e-cigarettes is associated with increased chances of smoking cessation, albeit the overall evidence from observational studies is mixed.</li> <li>• There is substantial evidence that the use of e-cigarettes will increase the likelihood of youth initiating use of tobacco smoking.</li> <li>• There is conclusive evidence that most e-cigarettes contain and generate potentially hazardous substances.</li> </ul>
<p>Royal College of Physicians (RCP), UK</p>	<p>The RCP's 2016 <a href="#">Nicotine without smoke: tobacco harm reduction report</a> asserts that e-cigarettes are likely to have a role in smoking cessation and their use neither serves as a gateway to smoking nor renormalises smoking. Smokers should therefore be encouraged to use e-cigarettes as a substitute for smoking. The report also suggests a balanced approach to e-cigarette regulation.</p>
<p>American College of Physicians (ACP), US</p>	<p>The ACP supports the regulation and taxation of e-cigarettes. In its 2015 <a href="#">policy position paper</a>, the ACP recommended that e-cigarette promotion, advertising and marketing be subjected to the same restrictions as tobacco products. Furthermore, vaping in public places and the use of flavouring in e-cigarette products should be prohibited. The paper called for anti-smoking educational campaigns to be conducted in schools and advertised via social media. The potential risks of e-cigarettes should also be included as part of youth tobacco prevention efforts.</p>
<p>Royal College of General Practitioners (RCGP), UK</p>	<p>The <a href="#">RCGP Position Statement on the use of non-combustible inhaled tobacco products (E-Cigarettes)</a> released in 2016 aligns with that of Public Health England. The RCGP recommends that all General Practitioners (GPs) should provide advice on the relative risks of smoking and e-cigarette use and support the use of e-cigarettes in circumstances where conventional smoking cessation options fail to help smokers quit tobacco smoking. The RCGP states that e-cigarettes are a low-cost device to reduce tobacco smoking, in particular for vulnerable population groups and GPs should actively engage with smokers who want to use e-cigarettes to quit smoking.</p>

Public Health England (PHE), UK	The PHE's <a href="#">expert independent evidence review</a> in 2015 concluded that e-cigarettes are 95 per cent less harmful than normal cigarettes. No evidence was found showing that the use of e-cigarettes among children or non-smokers would lead to tobacco smoking.
UK Faculty of Public Health (FPH), UK	In July 2016, the UK FPH and PHE together with a number of health organisations released a <a href="#">statement on e-cigarettes</a> . This stated that e-cigarettes are markedly less harmful than tobacco smoking, but continued research into their long-term effects is required. Using local stop smoking services is still the most effective method to quit smoking.
Cancer Research UK	<a href="#">Cancer Research UK</a> endorses a light touch regulation of e-cigarettes, so that their potential to help people quit smoking could be maximised, while the risks of unintended consequences such as promotion of smoking could be minimised. It concludes there is insufficient evidence to support an indoor ban on e-cigarettes.
British Medical Association (BMA)	In its 2017 <a href="#">position statement</a> , the BMA recognises that e-cigarettes have the potential to helping achieve a tobacco-free society. On this basis, the BMA supports an e-cigarette regulatory framework that seeks to minimise the potential harms while maximising their potential for reducing tobacco-related harm. This framework should focus on: <ul style="list-style-type: none"> <li>• Ensuring products are safe and effective;</li> <li>• Protecting children and young people; and</li> <li>• Research to inform future regulatory and policy approaches, in particular the impact of e-cigarettes uses on smoking behaviours and the health impact of e-cigarettes use.</li> </ul>
American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO)	In a 2015 <a href="#">joint policy statement</a> , the AACR and ASCO expressed their support for the regulation of all e-cigarettes that meet the statutory definition of tobacco products by the FDA and for taxing e-cigarettes. All e-cigarette products should be required to register with the FDA, with their ingredient lists clearly specified. Additional regulations recommended were: the requirement of warning and safety labels and childproof packaging, the restriction of youth focused marketing and advertising, the prohibition of the use of e-cigarettes in public places, and the prohibition of the use of flavouring agents. All data related to electronic nicotine delivery systems (ENDS) composition, use and health effects should be fully and publicly disclosed.
American Cancer Society (ACS)	In its 2018 <a href="#">position statement</a> , the ACS concludes that the current generation of e-cigarettes are less harmful than tobacco cigarettes, but their long-term health effects are so far unknown. The effects of all tobacco products need to be closely monitored. It recommends that public health policies such as taxation, and raising the minimum age of purchase to 21 be

	implemented to prevent the initiation and use of all tobacco products including e-cigarettes. Only FDA-approved cessation aids should be advised by clinicians to their patients and for individuals who will not attempt to quit smoking, the least harmful tobacco products should be used.
American Lung Association (ALA)	ALA expressed its concerns about the increasing popularity of e-cigarettes in the US market in its <a href="#">statement on e-cigarettes</a> dated 2015. Other concerns listed were the potential health consequences of e-cigarettes and unproven therapeutic claims as well as e-cigarettes becoming a gateway to regular cigarettes in young people.
Surgeon General, US	The Surgeon General's 2016 report on <a href="#">E-Cigarette Use Among Youth and Young Adults</a> concluded there was a need to implement evidence-based mechanisms to prevent e-cigarette use among youth and young people. The Report recommended that the manufacturing, marketing and distribution of e-cigarettes should be regulated at the country level, and highlighted the importance of addressing the unintended consequences that e-cigarettes may bring as well as research and evaluation gaps.
Canadian Medical Association (CMA), Canada	The <a href="#">CMA</a> supports a ban on the sale of nicotine containing e-cigarettes, given a lack of solid evidence on the harms and benefits of e-cigarette use. As such, they have called for ongoing research into this area. The CMA has taken the perspective that the sale of e-cigarettes without nicotine should not be permitted to Canadians younger than the minimum age for tobacco consumption (Provinces vary between 18 and 19).
Heart and Stroke Foundation, Canada	In its 2016 <a href="#">e-cigarettes in Canada position statement</a> , the Heart and Stroke Foundation calls on the Canadian federal, provincial and municipal governments to regulate all e-cigarettes. The specific policies that should be quickly implemented include: prohibition of e-cigarette sales to minors and use in public spaces; prohibition of the sale of e-liquid flavours that are attractive to youth and adolescents; and regulation of e-cigarette product to minimise toxic additives advertising and promotion.



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