

# E-cigarettes: a guide for eye care practitioners

**Dr Rohit Narayan** takes a look at the latest evidence concerning e-cigarette use, either as a means to aid smoking cessation or as a potential threat to ocular and systemic health when used recreationally

Conventional cigarettes use does appear to be falling. However, since their introduction in 2003, e-cigarettes are giving concern to a range of clinicians. There appears to be two schools of thought: one of harm minimization, with considerable support from national organisations, such as Public Health England (PHE), that insist that e-cigarettes are 'at least 95% safer than cigarettes';<sup>1</sup> the other is more precautionary and supported by the European Respiratory Society<sup>2</sup> and the Federation of International Respiratory Societies<sup>3</sup> among others,<sup>4</sup> coming out strongly against their use. Additionally, there is disagreement on the potential impact on adolescents, creating a further global divide on policy.<sup>5</sup>

E-cigarettes deliver nicotine by vaporising propylene glycol/vegetable glycerine, nicotine, and flavourings.<sup>6</sup> The nicotine hit induces pleasure, reduces stress and anxiety, and causes addiction.<sup>7</sup> E-cigarette technology and designs have evolved<sup>8</sup> and have been the subject of a growing body of research focused on the chemical makeup and risk analysis of chemicals, metals, and particulates found in e-cigarette liquids and vapor.

In this article I address the following question: Are e-cigarettes the health benefit that their supporters suggest, or an emerging and sinister threat to health?<sup>9,10</sup>

## HARM REDUCTION?

How safe are e-cigarettes? The fact they do not produce either tar or carbon monoxide is better than cigarette smoke.<sup>9</sup> There is, however, growing evidence of their health risks,<sup>11</sup> coupled to the fact they contain nicotine, an addictive drug.<sup>12</sup>

The dangers of nicotine exposure among the young has been highlighted in a recent US Surgeon General advisory document (2018) where nicotine exposure during adolescence can impact learning, memory and attention, and brain development.<sup>13,14,15</sup>

Nicotine exposure from e-cigarettes is not the only concern. There are thousands of different combinations of compounds and flavourings that can be vaped. Very few of have been studied and regulation is limited. Those that have appear to have their own adverse effects and should not be considered watered down versions of tobacco.<sup>16</sup> Some studies found vape liquids contained substances that have some level of hazard/risk of danger<sup>17</sup> and breach the European Tobacco Products Directive (ETPD), pro-

hibiting the addition of compounds which pose a risk to human health, either when heated or not (only nicotine is excepted).<sup>18</sup>

Vape fluids have different effects to those of tobacco smoke on lung tissue and specifically cause marked biological changes to the bronchial epithelium.<sup>6</sup> These changes are not harmless and are linked to the development of chronic obstructive pulmonary disease (COPD),<sup>6</sup> as well as having an association with myocardial infarction.<sup>11</sup>

Those in favour of a more liberal regulatory approach on vaping acknowledge that the long-term safety of this addiction is not known. This is concerning given that the effects of second hand tobacco smoke are still emerging, taking decades to manifest.<sup>9</sup> An example of this is a recent study where an increased risk of death from COPD was found in non-smoking adults who were exposed to second hand tobacco smoke in childhood.<sup>19</sup> The discovery of these associations after many decades of being exposed to second hand tobacco smoke means that it will be very many years before we can determine whether passive exposure to vaping is safe.<sup>9</sup> Indeed, although research is limited, the evidence is that second hand exposure to vaping emissions is not safe.<sup>20,21,22</sup>

There is particular concern about the now widely cited claim by Public Health England (PHE) that e-cigarettes are '95% safer' than traditional cigarettes. This figure is based not on empirical data but on a meeting of individuals, whose report conceded that the evidence was insufficient to reach a robust conclusion.<sup>23</sup> The PHE's view is far from universally accepted in the UK,<sup>24</sup> where the National Institute for Health and Clinical Excellence (NICE), which evaluates evidence on effectiveness of treatments, does not recommend them as cessation aids.<sup>25</sup> The claim is also viewed with scepticism abroad,<sup>26</sup> with concerns expressed of this apparent 'evidence-deficient' endorsement<sup>27</sup> determining public policy in the UK.<sup>24</sup> Some toxicologists consider the Public Health England's promotion of e-cigarettes as 'a reckless and irresponsible decision',<sup>28</sup> and some respiratory experts express concerns that continuing with the current PHE approach risks 'a further epidemic of devastating lung disease for today's children.'<sup>9</sup>

## GATEWAY OR ROAD BLOCK?

There is a marked difference of opinion regarding whether the use of e-cigarettes by young people serves as a gateway to tobacco smoking rather than a means of cessation.<sup>9</sup> Recent reports from →

**FIGURE 1** The impact of nicotine addiction, particularly in the young, cannot be underestimated (image courtesy of J Green)



the UK<sup>29</sup> and USA<sup>30</sup> highlight these opposing views. The US report cites 'there is substantial evidence' of a gateway effect, whereas the UK report concludes 'e-cigarettes are attracting very few young people who have never smoked into regular use.'

Looking at the literature, the argument against a gateway runs that vaping has been rising while smoking continues to fall.<sup>31</sup> So, vaping cannot be causing any significant degree of increased harmful smoking among adolescents.<sup>32</sup> In truth, declining trends of smoking among youth were apparent well before the introduction of e-cigarettes.<sup>33,34</sup> A recent study that analysed data from nine clinical trials, taking into account a variety of risk factors, concluded that the odds of subsequent cigarette smoking by non-smokers who had any experience of vaping more than tripled compared with those with no vaping experience.<sup>35</sup>

Those who do not support the gateway effect suggest that people switching from e-cigarettes to traditional tobacco share common risk factors.<sup>31</sup> Interestingly, several longitudinal studies have reported the strongest association between e-cigarette use and smoking initiation among youth with the lowest risk of smoking.<sup>36,37</sup> More concerning are studies that show that a third of youth who start with e-cigarettes have risk profiles that make them unlikely to start with cigarettes.<sup>38</sup> Another argument supporting vaping often put forward concerns the a natural propensity for some people to smoke; or, to put it another way, 'kids who will smoke, will smoke'. If this were true, how then do we explain the dramatic falls in uptake that have been seen in countries that have robust, comprehensive tobacco control programmes?

Critics of the idea that there is a gateway effect also state that studies proving a gateway effect often fail to discriminate between experimentation and regular use, and some researchers question whether a single puff or occasional e-cigarette use can lead to regular smoking.<sup>39</sup> In reality, every regular smoker started with a 'simple puff,' nearly always in their youth,<sup>38</sup> typically progressing through more regular use to daily smoking. It has been recently reported that over two-thirds of smokers who tried as little as a single puff became, for a time, regular smokers.<sup>40</sup>

## NICOTINE

The impact of nicotine addiction, particularly in the young, cannot be underestimated (figure 1). A 'sleeping effect' exists, whereby initial exposure to nicotine lead to a vulnerability to future smoking for three or more subsequent years.<sup>41</sup> The 'neurobiological insult' of nicotine was recently highlighted in the US Surgeon General's report on the potential risks of nicotine and electronic

**FIGURE 2** An early cigarette-like e-cigarette



cigarettes to youth.<sup>42</sup> Indeed, this stated that 'The first symptoms of nicotine dependence can appear within days to weeks of the onset of occasional use, often before the onset of daily smoking.'<sup>43</sup>

There does not appear to be a minimum nicotine dose or duration of use as a prerequisite for symptoms to appear.<sup>44</sup> In some cases, even smoking on a monthly basis greatly increases the likelihood of developing dependence in a younger person.<sup>45</sup> In keeping with the theme of addiction, the US Surgeon General raised the concern that nicotine in adolescence can also increase the risk of future addiction to other drugs.<sup>15</sup> Bearing this in mind, it is alarming that e-cigarettes are becoming a known, viable, illicit drug delivery system. Some studies, citing survey respondents, found more than a third were actively using their vaping device to inhale recreational drugs.<sup>15,46</sup>

Given the addictive potential of nicotine, it is worrying that a reported 90% of vape shops are selling products to adults who have never smoked or vaped, and therefore breaching the code of conduct that applies to these businesses.<sup>47</sup>

There is growing evidence that, for many young people, the first contact with nicotine is in the form of e-cigarettes<sup>48</sup> and that their use is strongly associated with a subsequent progression to tobacco products.<sup>49</sup> Some clinicians feel that the debate around 'safety or gateway' misses the fundamental question of whether it is desirable that young people should be exposed to nicotine, a known drug of addiction, at all. They instead advocate stressing the need to get across the message that nicotine is a dangerous drug of addiction, and that young people must be warned of the adverse consequences, and protected as far as possible therefrom.<sup>9</sup> Some suggest adopting regulations that apply to tobacco should be applied to e-cigarettes, including those relating to advertising, packaging and taxation, where possible. The only justification for their use is when aligned with nicotine patches and gum for the specific purpose of smoking cessation.<sup>9</sup>

## CESSATION

Does the use of e-cigarettes help adult smokers give up conventional tobacco products? Research into the concentration of nicotine deliverable in e-cigarettes does suggest that, for adult smokers trying to stop, e-cigarettes can be an effective tool.<sup>50,51,52</sup>

Adapting the speed of nicotine delivery from e-cigarettes may assist smokers in fully switching away from conventional cigarettes.<sup>53</sup> Other nicotine replacement therapies (NRTs), such as nicotine gums, patches and inhalators, deliver nicotine much more slowly and at lower doses than conventional cigarettes.<sup>54</sup>

The form of nicotine used plays an important role.

# CONTINUING EDUCATION

Conventional e-liquid – termed freebase nicotine – is more volatile and likely to be deposited in the oral cavity/upper respiratory tract. This results in a slower absorption profile, more closely resembling that of an NRT than that of a conventional cigarette.<sup>55</sup>

The need for more effective and appealing e-cigarette products, to provide satisfying alternatives to smoking, has led to the recent development and marketing of e-liquids containing nicotine salts. Nicotine salts are formed by the reaction of nicotine with a suitable acid and are less volatile than freebase nicotine.<sup>56</sup> More of the nicotine (in salt form) reaches the alveoli of the lung for pulmonary absorption, replicating a cigarette-like nicotine delivery in the lung. The implication is that nicotine salt inhalation devices should enable the adult smoker to get the same nicotine ‘hit’ and therefore make them more appealing products for adult smokers who are switching from cigarettes to vapour products. This is in line with public health recommendations in the UK.<sup>51</sup>

The e-cigarette active ingredient concentration generally advocated is 40mg nicotine lactate, which has the closest nicotine uptake profile to that of a conventional cigarette, resulting in greater user satisfaction and less desire to continue to smoke as before. However, this concentration of product would not be permitted in the European Union. Both Public Health England and the Royal College of Physicians have stated that the cap on nicotine concentrations imposed by the ETPD may limit the effectiveness of e-cigarettes as a smoking substitute, particularly for heavier smokers.<sup>57,58</sup>

Increasing the nicotine strength of liquids with nicotine lactate formulations and suitable flavour options that can be legally marketed to smokers may maximise the public health potential of e-cigarettes.<sup>50</sup>

## EVIDENCE OF EFFECTIVENESS

Once again there is no general policy consensus regarding the effectiveness of e-cigarettes in smoking cessation. A recent US report states ‘there is insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or other smoking cessation treatments.’<sup>23</sup> The view of PHE is to recommend that ‘e-cigarette use, alone or in combination with licensed medication and behavioural support from a Stop Smoking Service, appears to be helpful in the short term.’<sup>29</sup>

The rationale that e-cigarettes have the potential to increase cessation rates is not necessarily backed up clinically, with much of the available evidence actually suggesting a reduction in cessation rates.<sup>59</sup> Where evidence does exist, it is not convincing.<sup>60</sup> and

indeed in a recent trial, paying people to stop smoking was the only effective strategy.<sup>61</sup> A meta-analysis actually revealed that e-cigarettes were associated with less quitting among smokers.<sup>62</sup>

## COMMERCIAL PRESSURES

It is accepted that NRT plays an important role in tobacco cessation, especially when combined with counselling.<sup>63</sup> ‘Big tobacco’ – corporations that profit from the sale of tobacco – has had an interest in NRT for many decades, adopting the approach that suggests ‘if anyone is going to take away our business it should be us.’<sup>64</sup> On the other hand, many health practitioners, researchers, and policy makers instead view e-cigarettes as a disruptive technology<sup>65</sup> that would compete with the established multinational cigarette company brands. By 2014, all the major multinational tobacco companies had entered the e-cigarette market. They did so either by buying existing e-cigarette companies or by developing their own products.<sup>66</sup> The most recent offering currently proving very popular in the US is the JUUL manufactured and sold by a private firm that has recently received major investment from the tobacco industry.<sup>67</sup>

As the major tobacco companies have moved into, and increasingly dominated, the e-cigarette market, they have also appeared to dominate the political and policy-making environment, just as they did shape conventional cigarette policy in the past.<sup>68,69</sup>

Different countries around the world have reacted in a variety of ways to the introduction of e-cigarettes in their markets, ranging from no regulations to a ban on e-cigarettes.

## THE EUROPEAN RESPONSE; THE TPD

The Tobacco Products Directive provides a regulatory framework for e-cigarettes throughout the EU.<sup>70</sup> The TPD recognises the harm reduction potential of the products, but also acknowledges the existing uncertainties resulting from gaps in knowledge and contradictory scientific views.<sup>71,72</sup>

The main objective of the TPD is to coordinate the national laws of EU Member States concerning the manufacture, presentation, and sale of tobacco and related products, taking into account the need to guarantee the highest levels of health protection. The TPD does not, however, strive for the full harmonisation of the e-cigarette market, and certain aspects are decided at national level.

The majority of member states prohibit the use of e-cigarettes in public places and have introduced age restrictions on the purchase of e-cigarettes. Of interest is the decision to restrict domestic advertising and sponsorship activities. The notable →



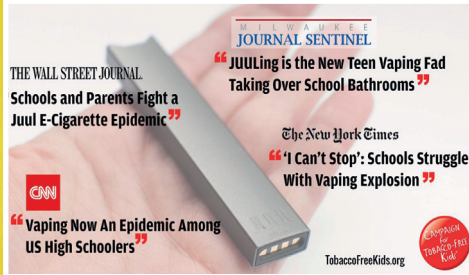
**FIGURE 3** Tank-style e-cigarette (image courtesy of J Green)



**FIGURE 4** The JUUL showing main unit (left) and the JUULpod which contains the e-liquid and serves as a mouthpiece (right)



FIGURE 5 Concern in the US is rising



exception to this is, surprisingly, in the UK.<sup>73</sup>

The most important differences between member states are the various restrictions on the use of flavours. Some countries have, or are considering, adopting a ban on all but tobacco flavoured e-liquids. This would be in line with the FDA recommendations to ban flavoured e-liquids at grocery stores and gas stations in the US.<sup>74</sup>

**GOVERNMENT VERSUS COMMERCE**

Concerns exist over the apparently ambiguous role of the tobacco industry in government-approved cessation schemes which calls into question the ethics of profiting from an addiction and its treatment.<sup>75</sup> The tobacco industry's role has been seen by some as transitioning from the cigarette business into the nicotine business, renormalizing the industry and nicotine use<sup>76,77</sup> while at the same time legitimising the company role as both partner and producer of innovative nicotine products. This has been described as the 'pharmaceuticalisation' of the tobacco industry.<sup>76</sup> A good example of this was the approval in 2015 for British American Tobacco (BAT) to receive a medical licence for its e-cigarette (e-Voke).<sup>78</sup> Furthermore, the availability of e-cigarettes on the NHS has been supported by PHE,<sup>79</sup> although this is not the view of the current NICE guidelines.<sup>80</sup>

FIGURE 6 Example of advertising aimed at younger people



The global cigarette market was worth US\$888 bn in 2018 and projected to reach a value of US\$1,124bn by 2024.<sup>81</sup> This represents an attractive potential tax revenue stream for governments. Included in this has been a dramatic rise in the popularity of e-cigarettes.<sup>82</sup> It is now estimated that there are 35 million e-cigarette users globally (including heat-not-burn tobacco products).<sup>83</sup> The e-cigarette industry in isolation is predicted to grow by 22% annually, and be worth \$50bn by 2025.<sup>84</sup> This is three times more than the global contact lens market in the same time frame.<sup>85</sup>

**MARKETING STRATEGY**

There are concerns about the enormous resources being used by the tobacco industry to promote e cigarettes by changing the message to one of 'lifestyle choice' rather than as a means of cessation.<sup>9</sup> One only has to compare vaping marketing with that of nicotine patches and gum.<sup>24</sup>

As an example, consider the recent introduction of the JUUL, marketed as the iPhone of e-cigarettes. E-cigarette devices have

evolved substantially over recent years,<sup>86</sup> from the early-generation cigarette-like e-cigarettes (figure 2) to more advanced modifiable tank style e-cigarettes<sup>87</sup> (figure 3) and now to the emergence in 2015 of sophisticated, sleekly designed, discreet high-tech devices like JUUL (figure 4).<sup>88</sup>

The JUUL has two basic components: the device, being a flat, rectangular, portable e-cigarette fashioned to look like a computer USB drive<sup>89</sup> which includes a temperature regulation system and a battery that is rechargeable at a USB port.<sup>90</sup> The second part is the e-liquid cartridge, or 'JUULpod,' which also serves as the mouthpiece.<sup>86</sup> JUUL is manufactured to be a closed or non-modifiable system.<sup>91</sup>

The JUUL's popularity, having almost 75% of the US e-cigarette market,<sup>92</sup> is due in part to its trendy, discreet design and youth-friendly flavours, such as apple, berry, mango and crème brûlée. It uses a proprietary e-liquid formula (JUUL salts), based on nicotine salts rather than free-based nicotine, and one pod equates to the nicotine in a pack of cigarettes.<sup>93</sup> Consequently, JUUL is said to create an experience more like combustible cigarette smoking than that found with other e-cigarettes on the market.<sup>88,89</sup> This is an attribute that appeals to both young and adult smokers.<sup>90</sup>

Since the cornerstone of the strategy of the tobacco industry has been to market to the youth,<sup>94</sup> it should not be surprising that the e-cigarette uptake of this group in the US has reached alarming levels, with over 20% of high school (secondary school-age) students, some 3.6 million people, currently using e-cigarettes.<sup>95</sup> This, coupled with a general acceptance of the gateway effect in the US, has resulted in the US surgeon general recently publishing an advisory document on e-cigarettes (and JUUL specifically) warning of the dangers of vaping, now epidemic among the youth (figure 5).<sup>15</sup>

Over 70% of e-cigarette business is conducted online,<sup>96</sup> with most existing e-cigarette companies operating websites or other web-based selling systems.<sup>98</sup> There appears to be a distancing of products away from tobacco<sup>98</sup> by e-cigarette manufacturers, by using a variety of techniques such as changing the terminology used to 'vaping' as opposed to smoking (figure 6).<sup>82</sup> The aesthetic appeal is being promoted, including attractiveness, coolness, colours, and innovative packaging and flavour variations. In addition, there is also evidence of celebrity endorsements and sports sponsorship.<sup>99</sup>

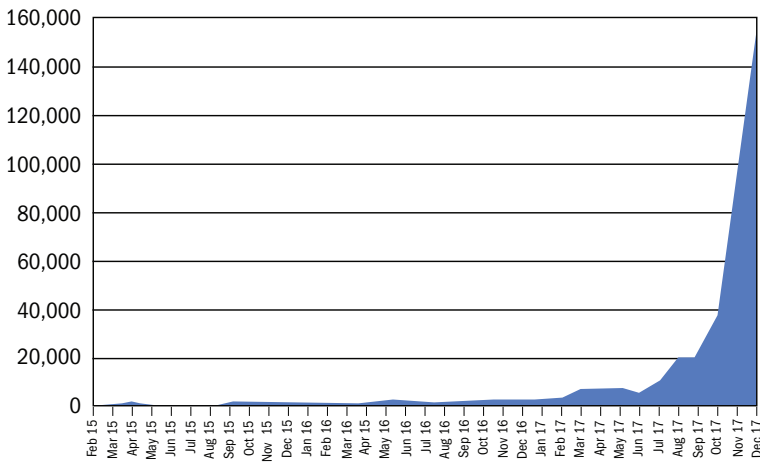
Social media has become a powerful tool for spreading the pro-vaping message by the vaping industry and its advocates (figure 7). Research into the success of JUUL's have concluded that social media activities were highly correlated retail sales. Targeted cross-platform social media campaigns, with little investment, can have substantial influence on people's attitudes, beliefs and behaviours related to these products.<sup>86</sup> There is little in the way of the public health field reflecting the clinical point of view in ongoing social media dialogues. This highlights the need for public health bodies to interact with the public to actively influence social media conversations and create a more balanced discussion.<sup>82</sup>

**WHY SHOULD ECPS BE AWARE?**

Though the evidence base regarding the ocular impact of e-cigarettes is far from comprehensive, an increasing number of reports suggest a strong association between the use of vaping and direct adverse effect, mainly through ocular surface disease, and indirect impact, particularly through the impact upon cardiovascular health of inhaled chemicals.

There is currently little research regarding the ocular impact of e-cigarettes,<sup>100</sup> although some professional bodies have produced →

**FIGURE 7** Number of JUUL related tweets on Twitter 2015-17<sup>86</sup>



patient leaflets<sup>101</sup> highlighting the public health dangers of smoking and e-cigarettes.

Of the research that is available, the direct ocular impact of e-cigarette's appears to be at the ocular surface. The vapour contains potentially toxic chemical, such as acrolein and formaldehyde which can cause ocular irritation and dry eye.<sup>102-104</sup>

Other effects on the eye are more related to the influence of nicotine and include:

- The speeding up of diabetic retinal changes<sup>105</sup>
- Playing a role in diabetic macular oedema development<sup>106</sup>
- Reduction in blood flow in microvascular beds and contributing to macular degeneration<sup>107</sup>

**CONCLUSION**

E-cigarettes are one of the most controversial issues in public health today. Although they are less harmful than smoking, there is disagreement on the level of risk reduction, as they are not absolutely harmless. It will take years to generate final conclusions about the clinical effects of switching from tobacco to e-cigarette use. More research is needed into the interactions between smoking and e-cigarette use in adolescents and to examine whether e-cigarettes are a source of harm or harm reduction in this population.<sup>9</sup>

Given what we know about the ocular impact of conventional smoking upon systemic and ocular health, it is important for all eye care practitioners to keep up to date in this area so as to be better able to offer appropriate advice to both existing smokers, vapers and those who may express a concern or interest. ●

**Dr Rohit Narayan is a therapeutic optometrist based in the Midlands.**

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