Are e-cigarettes a gateway to smoking or a pathway to quitting?

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VERIFIABLE CPD PAPER

IN BRIEF

- Provides answers to the what, who, how, when and where questions regarding e-cigarettes to enable clinicians to offer broad advice to patients seeking medical advice regarding the use of e-cigs.
- Discusses whether e-cigs can be used as a smoking cessation tool or whether they renormalise smoking.
- Argues that patients should be cautious with e-cig use until evidence of safety is presented.

PRACTICE

Over recent years there has been a massive increase in the usage of electronic cigarettes (e-cigs) by the general public. There are mixed views regarding the safety and efficacy of e-cigs, even among healthcare professionals. While some individuals view e-cigs as a public health concern, others recommend them as a safe alternative to conventional cigarettes for smokers who are willing to quit. Since e-cigs are a new phenomena, many clinicians are unaware of their impact on users (known as vapers), who may seek medical advice regarding their use. This clinical review aims to educate healthcare professionals regarding the advantages and disadvantages of e-cigarettes and to discuss whether e-cigarettes help users quit smoking or whether they renormalise smoking. This article will describe the contents of e-cigs and how they are used, the history, advantages, disadvantages and then balance the positive and negative aspects of their use. Due to the lack of long-term follow up of the health effects of e-cigarettes, caution is advised with their use.

INTRODUCTION

The rapid rise of electronic cigarettes (e-cigs), also known as vape pens, e-hookas and hookah pens, has left legislators and policy makers struggling to keep up with developments in their sale and distribution to the general public. E-cigs can arguably be considered an emerging public health concern.[1,2] Additionally, many clinicians are not aware of the health effects on patients, who may seek medical advice regarding their use, and it is unclear to consumers what e-cigs contain (this differs by brand).

E-cigs are battery-operated devices with cartridges, generally containing a solution of a propylene gycol- or glycerin-based fluid, with flavourants, preservatives and nicotine at the desired amount (Table 1).[3–7] Puffing activates a heating element in an atomiser that vaporises the solution into an ultrafine particle vapour (also called plume, fog or aerosol) that is inhaled by the user (aka 'vaper') (Fig. 1).[6] No tobacco is burnt, hence the absence of smoke production. The purpose of this clinical review is to educate health professionals, policy makers and members of the public about the benefits and disadvantages of e-cigs based on findings from scientific literature and to discuss whether e-cigs are a smoking cessation aid or whether they renormalise smoking.

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METHODS

The authors come from dental, medical and surgical backgrounds and have produced this article using a multidisciplinary approach. In order to compile this article, a PubMed search was conducted with the keywords 'electronic cigarettes'. The reason for such a broad search was to gain a holistic view of the currently available literature on e-cigs. The entire PubMed database was searched for the most relevant results and over 80 articles were used to produce this clinical review. The selected articles have been scrutinised to exclude methodological flaws, severe conflicts of interests, inconsistencies and contradictions in results as such findings would undermine the validity. Excluding policy statements, no article older than 5 years was included in this article, which can be considered a weakness of this paper. The authors justify this by the fact that there is large volume of literature about this topic published each month and that much of the literature published in the last two years expands on previous work. Since e-cigs are new devices, there is a lack of long-term follow up regarding their health effects on users, hence no firm conclusions regarding the safety and efficacy of e-cigs can be made.

THE RISE OF E-CIGS AND LEGISLATION IN DIFFERENT COUNTRIES

E-cigs are mainly manufactured in China[7] but their use has spread around the world. Since they appeared in the USA in 2008, e-cigs currently generate $2 billion in sales annually and are expected to bypass conventional cigarettes in sales by 2024.[5] By January 2014, there were 466 e-cig brands (each with its own, mostly health-benefit promoting, website) and 7,764 unique flavours.[8]

In terms of legislation in different countries, there is great variability in how e-cigs may be marketed and sold. Brazil, Norway and Singapore have banned the sale and use of e-cigs,[9] while in Australia, the sale, possession and/or use of nicotine-containing e-cigs is illegal without a permit.[10] In the European Union, there is no harmonised legal framework and different Member States attribute a different legal status to e-cigs;[11] for example, Norway's ban compared to the liberal approach adopted by France that views restrictions on e-cigs to be counterproductive.[12] However, recent changes will make legislation on e-cigs more equivalent across the EU. In March 2014, the European Union Parliament decided that under the new terms of the EU Tobacco Products Directive, nicotine-containing devices not licenced as medicines (such as e-cigs) would

be prohibited, and such products would be required to carry health warnings, meet certain standards regarding purity and emissions, and be subject to restrictions on nicotine content. The suppliers would bear responsibility and liability for the safety of these products. It is anticipated that this directive will be implemented in the member states by 2016 and full compliance achieved by 2017.[13]

Despite the discrepancies in the regulation of e-cigs worldwide, many health organisations share a cautious approach to e-cigs. In 2010, based on several analyses, the WHO recommended a ban on disseminating information that suggests that electronic nicotine vaporisers are safer than conventional cigarettes or that they are an effective way of combating nicotine addiction, until appropriate evidence can be provided.[14] Statements[15–17] declare that e-cigs should be regulated as medicinal products with appropriate warnings of potential health effects given, particularly of toxicity risk in children.[18] At their 2014 annual meetings, the American Medical Association has called for stricter regulation of e-cigs meanwhile the British Medical Association doctors called for a ban on using e-cigs in public places.[19,20] In the UK, the policy regarding e-cigs is inconsistent across hospitals and a wider statement from the NHS is anticipatorily welcome.[21]

Although e-cigs have become popular with the general public, many people feel that e-cigs should be banned in various contexts. Half of the general population of Barcelona and more than a third of respondents to a US study do not support the use of e-cigs at indoor workplaces and public places.[22,23] Support for complete e-cig bans was strongest among older individuals, those with higher income, those who are married and former smoker respondents.[24]

Table 1 Examples of different e-cigs products available in the market. This table is reproduced, with kind permission, from Grana R, Benowitz N, Glantz S A. E-cigarettes: a scientific review. *Circulation* **2014; 129: 1972–1986[7]**

Product	Description	Some brands
Disposable e-cigarette 	Cigarette-shaped device consisting of a battery and a cartridge containing an atomiser to heat a solution (with or without nicotine). Not rechargeable or refillable and is intended to be discarded after product stops producing aerosol. Sometimes called ehookah.	NJOY OneJoy, Aer Disposable, Flavourvapes
Rechargeable e-cigarette 	Cigarette-shaped device consisting of a battery that connects to an atomiser used to heat a solution, typically containing nicotine. Often contains an element that regulates puff duration and/or how many puffs may be taken consecutively.	Blu, GreenSmoke, EonSmoke
Pen-style, medium-sized rechargeable e-cigarette 	Larger than a cigarette, often with a higher capacity battery, may contain a prefilled cartridge or a refillable cartridge (often called a clearomiser). These devices often come with a manual switch allowing the user to regulate length and frequency of puffs.	Vapour King Storm, Totally Wicked Tornado
Tank-style, large-sized rechargeable ecigarette 	Much larger than a cigarette with a higher capacity battery and typically contains a large refillable cartridge. Often contains manual switches and a battery casing for customising battery capacity. Can be easily modified.	Volcano Lavatube

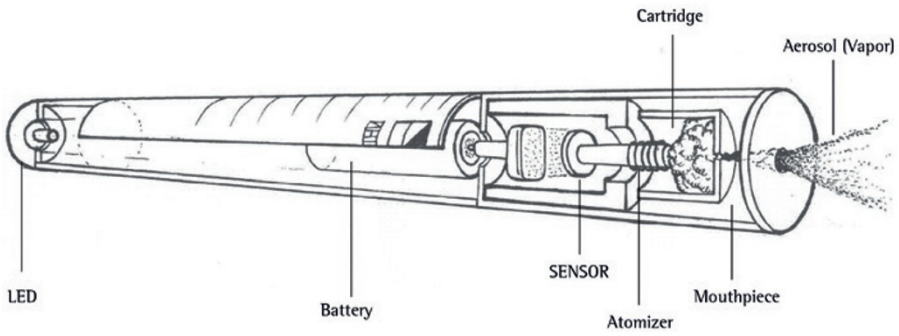

Fig. 1 The basic components of an e-cig– reproduced with permission from the *Brazilian Journal of Pulmonology* **(Knorst M M, Benedetto I G, Hoffmeister M C, Gazzana M B. The electronic cigarette: the new cigarette of the 21st century?** *J Bras Pneumol* **2014; 40: 564–573).**

THE RELATIONSHIP BETWEEN SMOKING AND VAPING

More than half (52%) of current or former smokers have tried e-cigs. The proportion of current vapers increased within the smoker population from 2.7% in 2010 to 6.7% in 2012 and further rising sixfold to 17.7% in 2014.[25–27] E-cigs are becoming increasingly popular among young adults, particularly men,[28–29] and their possession, similarly to conventional cigarettes, is highly influenced by parent and peer use.[30–33] These trends in use represent UK and US e-cig users. Although e-cigs were preferred to conventional cigarettes by smokers,[32,34] some smokers have started vaping concurrently with smoking,[35,36] and some have begun vaping exclusively and continue to do so.[37]

In light of these results, what is the appeal of e-cigs to conventional cigarette smokers? Hospitalised tobacco smokers expect fewer negative and positive outcomes from e-cigs *versus* conventional cigarettes, which suggests that e-cigs might be a viable, though imperfect, substitute to conventional cigarettes.[38] Vapers stated that e-cigs are popular because they are accessible, healthier than conventional cigarettes and more aesthetically pleasing,[33,39] but had some concerns about the possible toxicity and the future legal status of the devices.[40]

POSITIVES OF USING E-CIGS

In general, studies demonstrate that the health risks (including mental health effects) of e-cig vapour are likely to be smaller than those associated with conventional cigarettes and only few adverse effects were reported.[41,42] More recent generation devices appear to be more satisfying and are highly effective in reducing abstinence-induced cigarette craving and withdrawal symptoms to vapers.[43]

The most significant and clinically useful advantage of using e-cigs appears to be its use as a smoking cessation aid. E-cigs use can be considered modestly effective to help quit smoking.[41,44–46] In a randomised control trial, after 6 months of participation, verified participant abstinence to smoking was 7·3% with the use of nicotine e-cigs, 5·8% with patches, and 4·1% with placebo e-cigs.[47] Intensive users of e-cigs were six times as likely as non-users/triers to report that they

had quit smoking,[45] while vapers were generally more likely to report abstinence than those who used nicotine replacement therapies bought over-the-counter.[48] Fifteen puffs of an efficient e-cig delivers lower nicotine compared with smoking a conventional cigarette.[49] Those who switch from conventional to e-cigs report being less dependent on the latter[50,51] with a higher motivation to quit, higher quitting self-efficacy, and longer duration of smoking abstinence.[52] Increased duration of e-cig use was associated with fewer conventional cigarettes smoked per day in the short-term,[53] and overall, e-cig users tended to decrease the strength of nicotine in their e-cig products regardless of duration of use.[54]

Moreover, since e-cig vapours contain far fewer carcinogenic particles than conventional cigarettes, it was demonstrated[55] that vaping does not increase human total white blood cell count; rendering e-cigs with a lower risk of causing atherosclerosis and systemic inflammation. Vaping also decreases secondhand smoke exposure and is believed to have the potential to decrease incidence of respiratory illness/asthma, middle-ear disease, sudden infant death syndrome, and other diseases.[56]

It is stated that exposure to e-cig vapours results in far less toxicity than exposure to conventional cigarettes that initiate cytotoxicity and a pro-inflammatory profile.[58,59] A study's findings indicate that neither the e-cig liquids nor collected aerosols produce any meaningful toxic effects *in vitro*, in comparison to conventional cigarettes (which are proven to be cytotoxic and genotoxic).[59] E-cigs, especially nicotine-enriched types, produced lower particle matter levels than their conventional counterparts, and also notably lower levels than the nicotine-free e-cig counterparts.[60] Analysis shows that smoking delivers 1,500 times more harmful and potentially harmful constituents (for example, carbonyls, phenolics and benzene) compared to vaping aerosol in the air;[61] which means, unlike conventional cigarette smoke, exhaled e-cig aerosol is unvarying to bystanders' exposure for phenolics and carbonyls.[62]

NEGATIVES OF USING ECIGS

The main disadvantage of using e-cigs is the damage that can be caused by the e-cig emissions, both to human health and to the environment. While it has been argued that the emissions from e-cigs are less toxic than the emissions from conventional cigarettes, if all the emissions from e-cigs were exhaled, 25 times more exhaled particle matter would still be created than what exists in a typical urban environment,[42] increasing high particle dose in the respiratory system from 23% to 35% of the daily dose of a non-smoking individual.[63]

Nicotine acts as a gateway drug on the brain, and this effect is likely to occur whether the exposure is from smoking tobacco, passive tobacco smoke, or e-cigarettes[82]. Also, there have been reports that e-cigs produce many hazardous aerosol chemical compounds, especially carbonyl compounds such as formaldehyde, acetaldehyde, acrolein, and glyoxal, produced by higher e-cig battery voltages at temperatures of 150 °C.[64–67] When vaping, it is estimated that 20% to 27% of the e-cig-exclusive supersaturated propylene glycol (aka 1,2-propanediol) and vegetable glycerin-based liquid particles are inhaled through the lungs and become deposited into the circulatory system.[68] Additionally, heavy metals from the heating elements of the e-cig such as tin, nickel, and chromium can line pulmonary alveoli to form potential carcinogens once inhaled. Aerosolised nicotine seems capable of increasing the release of the inflammatory signalling molecule nitric oxide (NO) and can cause potential cardiovascular toxicity upon inhalation.[15,69] Furthermore, even though nicotine deposits and other residues concentrations are found to be lower in e-cig vapour than smoke, they can still accumulate on indoor surfaces and can be absorbed transdermally.[4,5,70–72] Within its limits, an *in vitro* study[73] demonstrated that menthol additives to e-cigs have a harmful effect on human periodontal ligament fibroblast proliferation. In one non-blinded study, the use of an e-cig with a nicotine cartridge for 5 minutes, compared to use without a cartridge, significantly increased total respiratory impedance, peripheral airway flow resistance, and oxidative stress; the clinical significance of these effects is not known.[74] Recent *in vitro* studies found that the cytotoxic effects of e-liquids were largely restricted to flavouring components that are increasing in diversity at a rapid rate.[75]

Furthermore, it is a frequent occurrence that consumers of e-cigs are not receiving correct information about the contents of e-cigs. Many e-cig samples lack or contain misleading information on the product and its ingredients, which raises safety and efficacy concerns for vapers.[76,77] E-cig fluid composition is not properly labelled: additives like nicotine and flavours vary between and within brands and contamination and impurities with various chemicals have been detected,[80,81] with nicotine content of the some liquids being variably 1.2-fold higher than claimed by the manufacturer.[80] A few e-cigs that had been declared 'free-of-nicotine' by the manufacturers, were identified to contain nicotine in the range of 0.115 µg/ml.[64] No amount of nicotine is known to be safe to take during pregnancy.

WEIGHING UP THE POSITIVES AND THE NEGATIVES

The main advantages of e-cigs are that they are less dangerous than conventional cigarettes (from what is currently known), that they cause less contamination to the environment and that they can help with smoking cessation. Each of these points will be discussed.

In terms of the negative health effects of e-cigs compared to conventional cigarettes, studies demonstrate that e-cigs contain substances (particularly flavourants) that may have cytotoxic effects on the respiratory and cardiovascular systems and may impair immunity. However, due to the lack of long-term follow up, these negative health effects are not proven and it is impossible to say for definite whether e-cigs would cause damage to the health of their users. Conventional cigarettes, on the other hand, have a proven track record of damaging human health. The smoking of conventional cigarettes causes over 100,000 deaths per year across the UK.[81]

While it is a valid argument that e-cigs cause less contamination to the environment, they still do cause contamination (which could be avoided if e-cigs were not used) and the widespread dissemination of e-cigs in society is an environmental concern.

Moreover, there is a large evidence base to support that the use of cigarettes has positive effects on smoking cessation as demonstrated earlier in this review. Therefore, the use of e-cigs as a smoking cessation aid may be useful and cost effective in a clinical setting. It is worth trying e-cigs as a smoking cessation aid as it appears to be effective in many users and the health service is suffering due to the burden of smoking. Smoking costs the NHS £2.7 billion each year, with costs to the wider UK economy of around £2.5 billion in sick leave and lost productivity.[81] However, if e-cigs are considered a pathway to quitting, they are by no means a safe alternative based on current knowledge.

CONCLUSIONS

The impressive rise of e-cigs in recent years should not be taken lightly, as the long-term health effects of their use are not yet known. The use of e-cigs may help motivated individuals who are serious about quitting conventional cigarettes to stop smoking and they have been demonstrated

to have positive effects as a smoking cessation aid in a large number of studies. However, for other individuals (especially those who only smoke e-cigs and those from younger generations), e-cigs can be considered to renormalise smoking and make smoking fashionable. We suggest a cautious approach to e-cigs until the long-term health effects have been thoroughly investigated. In the meantime, we also believe that an age limit should be applied to the sale of e-cigs worldwide, as there are concerns of toxicity to children. Pregnant women should also be advised against smoking nicotine-containing e-cigs.

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