

Electronic cigarettes



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Electronic cigarettes

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This briefing has been written because many stop smoking services are struggling to decide what role they have in relation to electronic cigarettes, and how they should respond to enquiries about them from smokers. There is also debate about the future licencing of electronic cigarettes and whether they offer an opportunity to make significant public health improvements or not.

Executive summary

- Electronic cigarettes are devices that deliver nicotine by heating and vapourising a solution that typically contains nicotine, propylene glycol and/or glycerol, and flavourings
- Electronic cigarette use is increasing in smokers wanting to quit but particularly among smokers who want to reduce the health risks of smoking or to save money
- Electronic cigarettes are not currently licensed for smoking cessation; they do have to comply with consumer protection legislation
- The quality of electronic cigarettes is improving. With experience, users can achieve overall blood nicotine levels similar to those achieved with smoking conventional cigarettes; although it takes longer to reach these levels and they still receive less nicotine per puffing session
- Electronic cigarettes can reduce urges to smoke and can help smokers quit, although these data are not as robust as those for licensed stop smoking medicines
- Data from one good quality randomised controlled trial show that electronic cigarettes were as effective as nicotine patches in helping people stop smoking for six months, when used in combination with minimal support from a trained practitioner
- Short-term exposure to electronic cigarettes appears to be associated with few serious risks. Mouth and throat irritation are the most commonly reported symptoms and these appear to subside over time. There are no high quality safety data regarding long-term electronic cigarette use but there is no a-priori reason to expect that such use may pose risks anywhere near the risks associated with smoking
- Low levels of toxicants and carcinogens have been detected in electronic cigarette liquid and vapour although these are much lower than those found in conventional cigarette smoke and are not considered to pose any passive inhalation risk

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- Concurrent (dual) use of conventional cigarettes and electronic cigarettes has been associated with greater motivation to quit, and to a reduction of smoke intake from regular cigarettes. This may be associated with health benefits, although the extent of any such benefits remains to be determined
- There are currently no robust data to support the concern that the existence of electronic cigarettes might 'normalise' smoking and increase use of conventional cigarettes

Recommendations for practice

1. Be open to electronic cigarette use in people keen to try them; especially in those that have tried, but not succeeded, in stopping smoking with the use of licensed stop smoking medicines
2. Provide advice on electronic cigarettes that includes:
 - Electronic cigarettes can provide some of the nicotine that would have otherwise been obtained from smoking regular cigarettes
 - Electronic cigarettes are not a magic cure, but some people find them helpful for quitting, cutting down their nicotine intake and managing temporary abstinence
 - There is a wide range of electronic cigarettes available and clients may need to try various brands, flavours and nicotine dosages before they find a brand that they like
 - Electronic cigarette use is not exactly like smoking and users may need to experiment and learn to use them effectively (e.g. longer 'drags' are required and a number of short puffs may be needed initially to activate the 'vapouriser' and improve nicotine delivery)
 - Although some health risks from electronic cigarette use may yet emerge, these are likely to be, at worst, only a small fraction of the risks of smoking. This is because electronic cigarettes do not contain combustion chemicals which cause lung and heart disease and cancer
3. Multi-session behavioural support, as provided by trained stop smoking practitioners, is likely to improve the efficacy of electronic cigarettes in the same way such support markedly increases the efficacy of NRT
4. Stop smoking services can provide behavioural support to clients who are using electronic cigarettes and can include these clients in their national data returns.* As with other unlicensed nicotine containing products, the stop smoking service cannot provide or prescribe them until such time as there are licensed options available
5. If a client being seen at a stop smoking service is using an electronic cigarette but also wants to use NRT, then it is OK for them to use the two in conjunction. They do not need to have stopped using the electronic cigarette before they can use NRT

* providing they adhere to the national data definitions in the service and monitoring guidance, which are based upon the Russell Standard: <http://www.ncsct.co.uk/usr/pub/assessing-smoking-cessation-performance-in-nhs-stop-smoking-services-the-russell-standard-clinical.pdf>

Electronic cigarettes

Introduction

There is currently much debate within the tobacco control and public health community over whether electronic cigarettes should be subjected to medicines regulation or left as a consumer product where it is already subject to consumer protection legislation.

There is also debate as to whether electronic cigarettes should be recommended to people who want to quit smoking, and whether electronic cigarettes should be recommended to smokers as a means of harm reduction.

This briefing summarises the evidence and the recommendations for practice made on the previous page are drawn from this current knowledge.

Background

Electronic cigarettes are devices that deliver nicotine to the user by heating and vapourising a solution that typically contains nicotine, propylene glycol and/or glycerol, plus flavours. As there is no combustion involved with the operation of electronic cigarettes, there is no smoke and no other harmful products of combustion, such as tar and carbon monoxide.

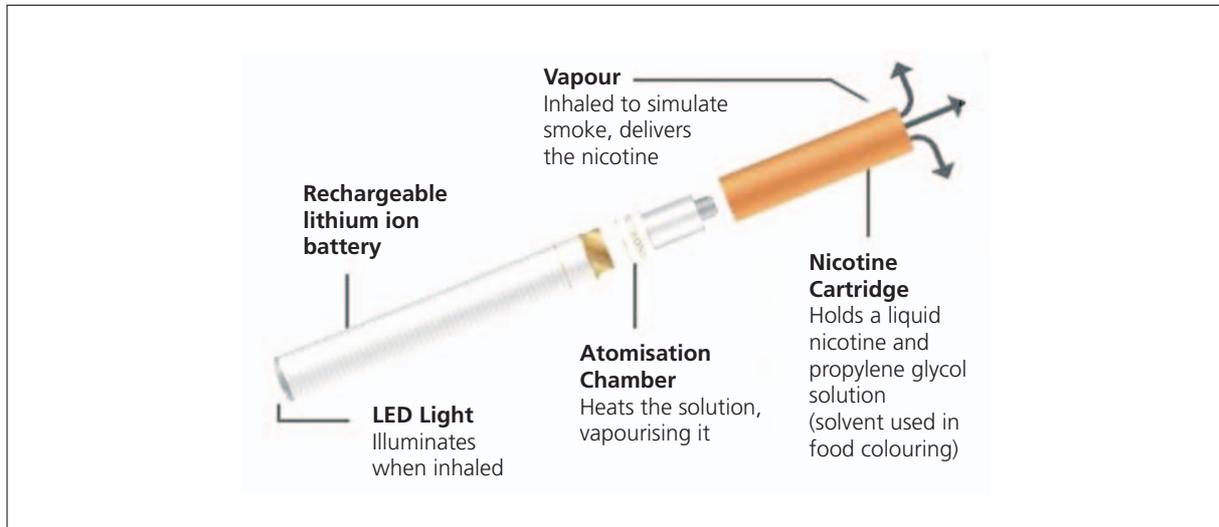
The development of the first electronic cigarette is generally attributed to Hon Lik at the Chinese company Ruyan in 2004¹; they appeared on the UK market a few years later.

Electronic cigarettes generally consist of a battery, a vapourising chamber and electronic cigarette liquid. The liquid can be contained in sealed cartridges or can be added to a tank system. Some electronic cigarettes use 'cartomisers' that combine the vapourising system and electronic cigarette liquid in a single unit.

The 'first generation' electronic cigarettes are typically designed to look like a cigarette and generally use cartomisers. When the user takes a puff (or presses a button on some models) a heating coil is activated and subsequently vapourises the electronic cigarette liquid creating a mist (or vapour) that can be inhaled. Many first generation models have a LED on the end of the device that also glows when a puff is taken.

Electronic cigarettes

Figure 1: Example of a 'first generation' electronic cigarette



The 'second generation' electronic cigarette look less like a regular cigarette and usually contain a 'tank' that the user fills with their choice of electronic cigarette liquid; in which they can decide upon flavours and strength (nicotine concentration typically ranging from 0 to 24mg/ml). There appears to be a trend towards more experienced electronic cigarette users ('vapers') preferring newer generation electronic cigarettes (often called personal vapourisers). These bear little resemblance to cigarettes and can be used with a range of atomisers, cartomisers, and tank systems giving the user a greater range of choice. These systems typically use larger batteries with adjustable power settings and replaceable coils and wicks.

Figure 2: Example of a 'second generation' electronic cigarette



Electronic cigarettes

Recently we have seen the emergence of 'third generation' electronic cigarette devices that allow the user to adjust the voltage applied to the atomiser (often referred to as 'variable voltage devices') using a control unit that can be set to different modes. The atomisers usually sit in the fluid and use different types of coils or wicks that can be replaced. Some come with 'puff counters' or downloadable software so the user can program their own voltage level and monitor their patterns of use.

Figure 3: Examples of 'third generation' electronic cigarette



Electronic cigarettes have been developed as a 'lifestyle' or consumer product, and not as a medicine. Regulatory authorities in some countries have ruled that, as they contain nicotine, electronic cigarettes automatically fall under medicines regulation.^{e.g.2} The UK Medicine and Healthcare Products Regulatory Agency (MHRA) ruled in June 2013 that electronic cigarette manufacturers would need to obtain a license to sell electronic cigarettes by 2017.

In contrast to this (and superseding the MHRA ruling), in December 2013 the European Parliament rejected a proposal to license all electronic cigarettes as medicines. However, a European directive in February 2014 introduced rules that included: maximum nicotine concentrations of 20mg/ml, limits on the size of tanks (to contain a maximum of 2ml electronic cigarette liquid), limits on containers of nicotine liquid (a maximum 10ml), ingredient quality and consistent delivery levels. There will also be new packaging and labelling requirements, plus existing rules for cross-border advertising and promotion of tobacco products will also apply to electronic cigarettes. These rules will come into force in May 2016.

Electronic cigarettes

Prevalence and epidemiology

Awareness of electronic cigarettes is high, especially among current and ex-smokers, in countries where electronic cigarettes are sold.³ In the UK, use by smokers increased from 2.7% in 2010 to 6.7% in 2012.⁴ By 2013 11% of smokers reported ever using electronic cigarettes.⁵ Similar increases have been seen in the USA (e.g. 0.6% in 2009 to 2.7% in 2010,⁶ and to 6.2% in 2011⁷).

In many of these surveys 'ever use' includes people that have a single try, but data suggest that around a third of people who reported ever using them are current users,⁴ and some 10–15% can be expected to become daily users.^{8,9}

The most recent UK data show that 15% of smokers surveyed are currently using electronic cigarettes.¹⁰

Young people are also experimenting with electronic cigarettes. For example in Poland in 2010–2011, 23.5% of 15–19 year olds surveyed reported any use of electronic cigarettes.¹¹ In the USA electronic cigarette use had increased from 1.4% to 2.7% and 4.7% to 10.0% in middle school and high school students respectively, between 2011 and 2012. Although this sounds alarming, most use occurred in adolescents who were also smoking. The Polish study found that 3% of never smokers reported using electronic cigarettes, and in the US study 0.5% and 0.7% of middle and high school students who had never smoked conventional cigarettes had tried electronic cigarettes.¹²

These surveys did not assess daily use and so only show the prevalence of experimentation. Studies that have assessed daily electronic cigarette use in never smokers^{5,8,13} however show no evidence of progression from experimentation to daily electronic cigarette use.

A 2013 survey by Action on Smoking and Health (ASH)¹⁴ showed that 11% of 16–18 year olds who *had heard of electronic cigarettes* had "tried electronic cigarettes once or twice"; only 1% used electronic cigarettes more than once a week. Among young people who had *never smoked*, 1% had "tried electronic cigarettes once or twice", 0% report continued electronic cigarette use and 0% expect to try an e-cigarette soon.

There is a concern that electronic cigarette use may act as a gateway to tobacco use,^{15,16} but to date there is no evidence to support this. However it is reported that adolescents who smoke who had tried electronic cigarettes are more likely to intend to quit smoking.¹⁷

Overall, electronic cigarette users are more likely to be current smokers than ex-smokers.^{4,18} They tend to be younger, better educated and from higher socioeconomic groups than non-users.^{7,19,20} The most commonly reported reasons for using electronic cigarettes include seeing them as a safer and cheaper alternative to smoked tobacco, helping to manage urges to smoke and other tobacco withdrawal symptoms, and assisting with quitting.^{21,22,3}

Electronic cigarettes

What is in electronic cigarette fluid and vapour?

Electronic cigarette liquid contains various concentrations of nicotine. The liquid is often labelled as weight (mg) per millilitre, or as a percentage of volume. Sometime a descriptive label is used, e.g. high or extra high strength. A concentration of 18mg/ml is most commonly used;^{21 23} electronic cigarette liquid is currently available in strengths ranging from 0mg/ml to 36mg/ml, although it is soon to be limited to a maximum of 20mg/ml under EU ruling.

In a study of five popular brands of electronic cigarette available in the UK, brands labelled as containing 18–24mg nicotine contained 12.8–33.0mg nicotine.²⁴

In terms of nicotine in vapour, approximately 15 x 70ml puffs are needed to deliver up to 1mg nicotine.²⁴ This is less than a typical conventional cigarette, where an average of 12 x 46ml puffs are needed to deliver 1.5 to 2.6mg of nicotine²⁵

A number of toxicants have been found in electronic cigarette liquid and vapour. An early FDA report also found the presence of diethylene glycol (a toxin at high doses) in electronic cigarette fluid,²⁶ but at very low levels and has not been found since.^{27 28} Toxicants including acrolein and acetaldehyde,²⁹ metal and silicate particles,³⁰ and tobacco-specific nitrosamines (TSNAs)^{31 26 32} have also been found. However, as some experts have highlighted these are either at lower levels than seen in cigarette smoke or at levels that are not associated with health risk.^{33–35}

Quality control

There has been criticism of the quality of electronic cigarettes and devices have been reported to leak and malfunction.^{18 36}

There is concern that labelling may not be accurate and indeed there have been reports of cartridges labelled as 'no nicotine', containing nicotine.^{26 37} However, more recent data suggest that quality controls are improving and there is relatively good consistency in labelling the nicotine content of electronic cigarette liquid.^{24 27 38}

Whilst there is a need for quality production of electronic cigarette liquid, labelling the nicotine concentration may be as unhelpful as nicotine labelling on regular cigarettes. This is because it is only the nicotine contained in the mist, or vapour, that can be absorbed and the labelling of cartridge content has little relationship to nicotine levels in vapour.^{24 39} Other factors such as heating of the liquid and how the user puffs on the electronic cigarette also have a role to play. Electronic cigarettes usually require more 'suck' than regular cigarettes.⁴⁰ The puff duration associated with electronic cigarette use is typically longer than smoking conventional cigarettes (e.g. 2.4 seconds for conventional cigarettes versus 4.3 seconds for electronic cigarettes).⁴¹

Electronic cigarettes

Do electronic cigarettes deliver nicotine to the user?

The first studies showed that electronic cigarette use produced very little increase in blood nicotine levels.^{42–44} For example, Bullen et al (2010) showed that electronic cigarettes produced a maximum blood nicotine concentration of 1.3 ng/ml, compared to 13.4 ng/ml achieved with smoking a regular cigarette. The maximum blood nicotine concentration achieved with the Nicorette® nicotine inhalator was 2.1 ng/ml.⁴²

More recent studies have demonstrated, however, that electronic cigarette use can result in blood nicotine levels that are similar to those seen with oral NRT products (e.g. 4–6ng/ml)^{45,46} but achieved significantly faster (e.g. peak blood nicotine levels are reached within five minutes after starting to use it⁴⁷).

Higher peak blood concentrations have been found in experienced electronic cigarette users, e.g. 13–14 ng/ml after an hour of ad lib use,^{48,49} which is similar to the changes seen after smoking a conventional cigarette.⁵⁰ The finding that electronic cigarette users can have similar levels of cotinine in saliva as regular smokers also supports this.^{51,52} However electronic cigarettes still delivery nicotine slower than conventional cigarettes.⁵³

Do electronic cigarettes alleviate withdrawal symptoms?

Electronic cigarette use can reduce urges to smoking in inexperienced users,^{42–44,46,54,55} as well as in those that have had some practice in using electronic cigarettes⁴⁵ and in experienced users.^{48,49}

In studies that used a non-nicotine electronic cigarette control^{42,54,55} both nicotine and non-nicotine electronic cigarette use reduced urges to smoke, however the reduction was larger with nicotine-containing electronic cigarette use.

The acute effect on other withdrawal symptoms is less pronounced with studies finding little or no significant effect,^{42–45} or only showing an effect in subgroups.⁵⁴

Electronic cigarettes

Do electronic cigarettes help people reduce or quit smoking?

Results from surveys show that electronic cigarette users report that the devices help them to either quit or cut down smoking.^{4 18 22 23 56} However, the respondents are often a self-selected group and not necessarily representative of all electronic cigarette users.

More robust survey data collected from cohorts of smokers followed up over time present mixed results. One showed that among people who were using electronic cigarettes and smoking at baseline, 46% had stopped smoking conventional cigarettes at one-year follow-up.⁵⁷ Another found that in a sample of UK smokers who were trying to stop smoking, those using electronic cigarettes were more likely to quit smoking than those who used NRT.⁵⁸ Others have found that electronic cigarette users are no more likely to quit smoking than non-electronic cigarette users;³ one study suggests that they may be less likely to quit than non-electronic cigarette users.⁵⁹ However, the last study⁵⁹ did not control for potential confounding factors (e.g. compared to non-electronic cigarette users, electronic cigarette users were more likely to have previous unsuccessful quit attempts, and to live with others who smoke).

A small number of prospective cohort studies have described the effect of electronic cigarette use in smokers who were not ready to quit smoking.⁶⁰⁻⁶² In one, 40 highly dependent middle-aged smokers were provided with electronic cigarettes for up to six months. Abstinence rates at six and 18 months were 23% and 15% respectively. Two years after enrolment, 13% achieved at least six months of CO validated abstinence from conventional cigarettes and 28% had achieved a sustained $\geq 50\%$ reduction from baseline cigarette consumption.^{60 61} Another tested the same approach with 14 smokers with schizophrenia⁶² and reported 14% 30-day CO validated abstinence rates at one-year.

To date there have been two randomised controlled trials that have examined the effects of electronic cigarette use in people who did,⁶³ and did not,⁶⁴ want to quit.

In the study examining the effect of electronic cigarette use (two different doses for 12 weeks) compared to non-nicotine electronic cigarettes, in 300 smokers not intending to quit, biochemically validated six-month abstinence rates at one-year follow-up were 13%, 9% and 4% in the three groups (differences were not significantly different).⁶⁴ There was no significant difference between the three groups in the proportion of participants that achieved $\geq 50\%$ cigarette reduction. Unfortunately the study was underpowered (i.e. it did not have enough subjects to be able to detect a statistically significant difference between groups) and lacked a 'no-electronic cigarette' group, which makes the results only tentative. In addition, the brand of electronic cigarette used in this study had poor nicotine delivery, often malfunctioned, and was subsequently discontinued.

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In the smoking cessation study⁶³ comparing nicotine-containing electronic cigarettes with 21 mg nicotine patches and with non-nicotine electronic cigarettes, participants were provided with a referral to telephone quitline but with no face-to-face contact. In this minimal support context, there were no significant differences in validated continuous abstinence at six months (7.3% nicotine electronic cigarette, 5.8% nicotine patch, and 4.1% non-nicotine electronic cigarette). Significantly higher self-reported smoking reduction, and higher user endorsements, were observed for the participants who received nicotine electronic cigarettes relative to those who received nicotine patch. Again the study was underpowered and used electronic cigarettes with low nicotine delivery.

Are there any adverse effects on health of electronic cigarettes?

There has been considerable debate about the safety of these devices. Although electronic cigarettes have not been proved harmless, they are generally considered significantly less harmful than smoking.²⁹

Electronic cigarettes primarily deliver two substances (1) nicotine and (2) the vapour, which is usually formed from propylene glycol or glycerol and often contains flavourings.

Regarding the safety of nicotine, there is good evidence from the use of NRT that nicotine is associated with few health risks in smokers. There is general agreement among experts that it is not nicotine that causes the adverse health effects associated with smoking. However there are some data, for example, that suggest that nicotine might have adverse effects in pregnancy.⁶⁵

Some commentators have raised concerns over the potential for nicotine poisoning with electronic cigarettes, especially in children. Cases of poisoning have been reported in the scientific literature, both accidental in a child⁶⁶ and intentional in adults;⁶⁷ all recovered without any lasting illness.

It is often quoted that a dose of 60mg of nicotine is lethal in adults, but the source of this information appears to come from rather dubious experiments undertaken in the late 19th century, and the actual lethal dose is likely to be much higher.⁶⁸ Nonetheless, nicotine is a substance that needs to be kept out of the reach of children, and electronic cigarette liquid should be stored in childproof containers.

Regarding propylene glycol (PG), the US Food and Drug Administration has classified PG as an additive that is "generally recognized as safe" and it has been used as an excipient in some old and new pulmonary inhalation devices,^{69 70} as well as in food and cosmetics. Mild adverse effects (e.g. throat irritation) have been documented.⁷¹ Although the short term risks of inhaled PG are likely to be low, data concerning long-term health risks of repeated exposure are lacking.

Electronic cigarettes

A number of studies have reported on acute effects of electronic cigarettes. No adverse effects of short-term electronic cigarette use has been found on haematological or blood chemistry parameters, nor cardiovascular function in smokers or ex-smokers.^{72–75} The exception is that electronic cigarette use increases heart rate after overnight abstinence,^{46 48} but this is to be expected. Two studies examined acute effects of electronic cigarette use on respiratory function. One reported a small, and not clinically relevant, increase in airways resistance post-electronic cigarette use.⁷⁶ The other showed no significant adverse effect of electronic cigarettes on lung function.⁵² By comparison, smoking a conventional cigarette was associated with a significant reduction in FEV1/FVC, a measure of lung function.

Second hand electronic cigarette vapour can expose non-users to nicotine,^{52 77} and other toxicants but this exposure is some 10 times less than conventional cigarettes⁷⁷ and unlikely to have any adverse health effects.³⁴

Electronic cigarette studies have collected information on adverse events (AEs). None of the experimental^{42–46 48 49 52 54 55} or prospective follow-up studies^{61 62} reported serious adverse events (SAEs). Any AEs were largely mild to moderate and included symptoms such as mouth and throat irritation and dry cough, similar to those reported in user surveys.^{18 21–23}

No significant difference in the frequency of AEs between electronic cigarette and control groups (non-nicotine electronic cigarettes or patch) were observed in the two randomised trials of electronic cigarettes.^{63 64} No AEs were rated as serious in one study,⁶⁴ and in the other SAEs did not differ between groups and were deemed to be unrelated to the study products.⁶³

The most commonly reported symptoms by electronic cigarette users in online forums are effects on the mouth and throat; some potentially more serious, although less common, AEs such as increased blood pressure have been documented.⁷⁸ The FDA Centre for Tobacco Products (CTP) also recorded three serious AEs due to electronic cigarettes; two were second-degree facial burns cause by electronic cigarette exploding and an infant death caused by choking on an electronic cigarette cartridge.⁷⁹

Three case reports of serious adverse events associated with electronic cigarette use have been published. Two were respiratory illnesses (lipoid pneumonia⁸⁰ and acute eosinophilic pneumonitis⁸¹) and the other cardiac (acute asymptomatic atrial fibrillation⁸²); in all cases the problems resolved when electronic cigarette use ceased.

Note

The main limitation we have faced in drafting this briefing is the lack of reliable and good quality evidence in the literature, especially on the subject of cessation, which is the main driver for public health interventions.

In addition, the review is limited by the fact that there is no singular electronic cigarette product. Many different forms exist, each with their own technology, delivery and nicotine concentrations – not to mention the difference between how people use these devices.

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