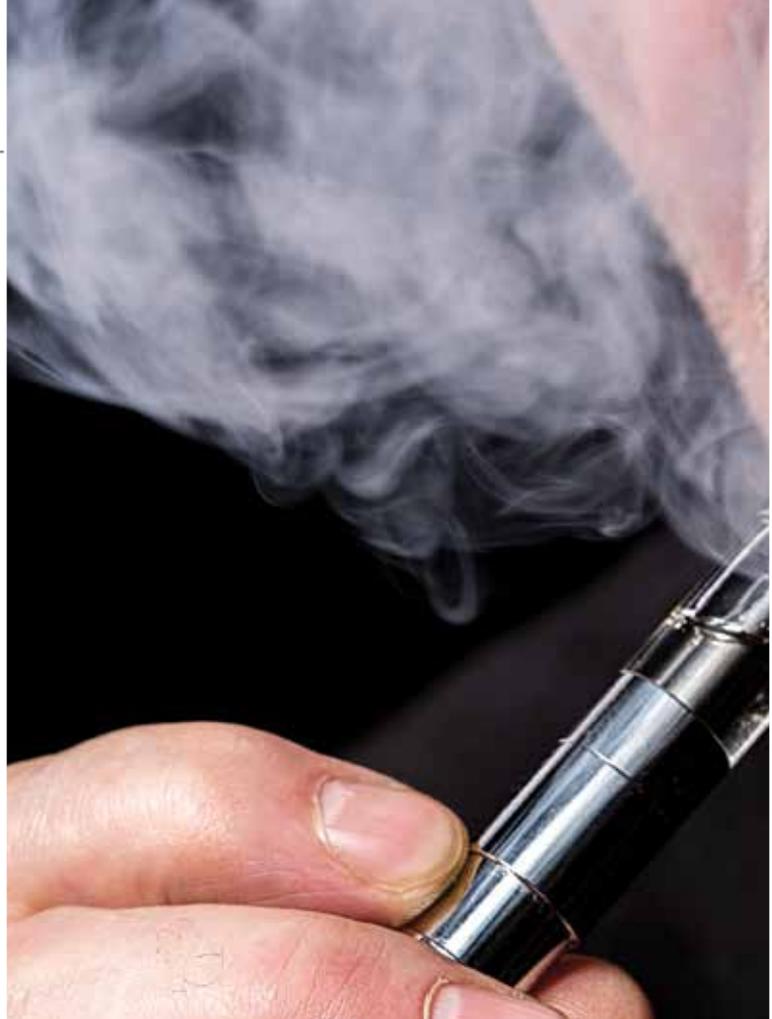


Electronic cigarettes

What should you tell your patients?

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Patients are increasingly asking their GPs about electronic cigarettes. Should they try them? Are they safe? Are they legal? GPs need to be ready to answer these questions.



KEY POINTS

- Electronic cigarettes (ECs) are battery-powered devices that create an aerosol of a liquid for inhalation; they can deliver effective nicotine doses and simulate the behaviour of smoking.
- Increasing numbers of tobacco smokers in Australia are using ECs to quit or reduce smoking.
- The limited evidence so far suggests that ECs may be effective smoking cessation aids; their use appears substantially safer than smoking, although there are no long-term safety data at present.
- ECs may have a therapeutic role for smokers who have been unsuccessful with or are intolerant of TGA-approved stop-smoking medications.
- ECs are likely to be most effective in conjunction with GP support and counselling and other antismoking therapies.
- Concerns that ECs may renormalise smoking and act as a gateway to smoking for young people can potentially be addressed by strong regulatory controls.

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Electronic cigarettes (ECs) are battery-powered devices that heat a liquid into an aerosol for inhalation and simulate the behaviour of smoking. ECs are mainly used in Australia and overseas by tobacco smokers to help them quit or reduce smoking.¹⁻³

Despite strict regulations in Australia, the use of ECs has grown dramatically over the past few years. Current EC use among smokers increased from 0.6% in 2010 to 6.6% in 2013.⁴ The latest National Drug Strategy Household Survey in 2013 found that one in seven smokers in Australia had used an EC in the previous 12 months, and 43% of these ECs contained nicotine.⁵

ECs are popular because, as well as delivering nicotine, they address the behavioural (handling), sensory ('throat hit', taste, inhaling and exhaling a visible 'smoke') and social components of the smoking ritual.⁶ Users rate ECs that contain nicotine as more satisfying than nicotine replacement therapy (NRT) and less harmful than smoking.² In England, ECs are now used more than NRT by smokers attempting to quit.⁷

However, many unanswered questions remain, and views about ECs are polarised. Some believe that ECs have a huge potential to improve public health and save millions of lives.⁸ Others are concerned that they could renormalise smoking, deter quitting and act as a gateway to smoking for young people.⁹ They point to the increasing control of ECs by multinational tobacco companies.

This article provides information for GPs who are faced with



reservoirs, which are refilled by the user.¹¹ More than 460 brands are available for sale on the Internet, and the technology is rapidly evolving.¹⁰

Nicotine delivery

Most ECs deliver lower doses of nicotine than tobacco smoking. However, with the right puffing technique, higher nicotine concentrations in e-liquids and evolving technical specifications of the devices, they can deliver as much, or potentially more, nicotine as regular cigarettes.¹² Later generation ECs deliver significantly more nicotine than early models because of larger atomisers, batteries and electronic circuitry for setting atomiser power.¹³

The delivery of nicotine increases with practice of use, with one study showing an 80% increase in overall nicotine intake over four weeks in EC-naïve users.¹⁴ Experienced vapers take longer and slower puffs to compensate for the less efficient nicotine delivery compared with combustible cigarettes.¹⁵

The speed of delivery of nicotine from ECs is much faster than from most forms of NRT but slower than from smoking, suggesting that some absorption is pulmonary as well as buccal.¹³ The evidence indicates that ECs may be less addictive than cigarettes.¹⁶

questions from patients about the use of ECs. We review the evidence for their effectiveness and the safety data for users and bystanders. We also discuss the legal and regulatory issues surrounding their use. Finally, we provide practical guidelines that GPs can use with patients who smoke and have failed to quit with first-line smoking cessation aids (e.g. NRT, varenicline) and are interested in using ECs in a quit attempt.

What are electronic cigarettes?

ECs essentially consist of a disposable or rechargeable lithium-ion battery, a heating element (atomiser) and a reservoir for the liquid ('e-liquid'). The e-liquid typically contains nicotine in varying strengths and flavourings dissolved in propylene glycol and/or vegetable glycerin. More than 7700 flavourings are available, including tobacco, menthol, fruit and confectionary flavours.¹⁰ Non-nicotine solutions and unflavoured liquids are also available.

The atomiser is activated when the user ('vaper') breathes in or presses a button, creating a fine mist that is inhaled from the mouthpiece. Some of the inhaled aerosol is exhaled as a visible mist.

The types of ECs available are shown in the Box.¹¹ Most users start with first-generation models that are designed to look like cigarettes and are sometimes referred to as 'cigalikes'. Some are disposable, and others use replaceable, prefilled cartridges of e-liquid attached to a rechargeable battery. Second- and third-generation models have more powerful batteries and larger

Effectiveness of electronic cigarettes

Smoking cessation

The limited evidence so far suggests that ECs may be effective in helping smokers to quit. A 2014 Cochrane review of two randomised controlled trials (RCTs) found that nicotine ECs doubled the quit rates compared with nicotine-free EC use, and the results were similar to the effect of NRT.¹⁷ However, the reviewers stressed that confidence in these results is low because of the small number of trials.

Both trials were conducted with low doses of nicotine in now obsolete early generation devices. However, recent studies have found that later generation models are more satisfying and can produce higher quit rates.^{13,18,19} A recent review of six studies (RCTs, prospective and cross-sectional studies) found that 18% of users reported smoking cessation after six months.²⁰

An observational study in England found that smokers who used ECs in a quit attempt were approximately 60% more likely to remain abstinent from cigarettes for at least a few months than those who try to quit unaided or by using an over-the-counter nicotine product.²¹

As expected, daily use of ECs appears to be more effective than intermittent or occasional use in helping smokers to quit.^{19,22} Daily use of later generation models appears more effective than similar use of early models.¹⁹

Numerous clinical trials and user surveys have found that nicotine ECs significantly reduce cravings to smoke and nicotine withdrawal symptoms.^{2,18,23,24} Non-nicotine models may also be

TYPES OF ELECTRONIC CIGARETTES AVAILABLE¹¹**First-generation 'cigalikes'**

- Resemble cigarettes
- Replaceable, pre-filled cartridge
- Low capacity rechargeable battery
- Single use, disposable models also available
- Airflow sensor activates the battery during puffing
- LED at the tip glows during inhalation

Second-generation 'tank' or 'eGo' models

- Large refillable reservoir (tank)
- Higher capacity battery
- User presses button to activate the battery during inhalation
- May have adjustable power output
- Deliver higher nicotine doses

Third-generation 'mods'

- Large refillable reservoir
- Higher capacity battery
- Replaceable components allowing user to modify to their preferences
- Electronic circuits, LED displays
- Adjustable power output
- Deliver higher nicotine doses and larger vapour volume

useful for some smokers, as they simulate smoking behaviour and provide sensory stimulation.^{20,23,24}

Smoking reduction

Clinical trials have shown that ECs can help smokers who are not intending to quit to substantially reduce cigarette consumption in the long term.^{24,25} Although the extent of the health benefit from 'dual use' of combustible and electronic cigarettes is not clear, many people report positive changes in symptoms, such as reduced shortness of breath, improved overall health, reduced smoker's cough,

increased sense of taste and smell and improved asthma and COPD control.^{24,26,27} A study of biomarkers among smokers who used EC to reduce rather than quit smoking found evidence of decreased toxicant exposure among these dual users.²⁸ However, as even low levels of smoking carry substantial risk, smokers should always be encouraged to quit smoking completely.

Harm reduction

Some tobacco smokers are either not willing or not able to stop using nicotine, even with approved therapies. Many experts believe

that huge public health benefits could be achieved if these tobacco smokers transfer their nicotine addiction to long-term EC use rather than continuing to smoke tobacco.²⁹ ECs provide nicotine without the products of combustion that cause most of the adverse health effects of smoking. Long-term use of nicotine can help prevent relapse to smoking and carries low risk, except in pregnancy, childhood and adolescence.³⁰⁻³²

Safety

The available toxicological, chemical and clinical evidence indicates that EC use is substantially safer than smoking.^{6,33,34} An international expert panel determined that ECs were at least 95% safer than combustible cigarettes, an assessment supported in a review for Public Health England.^{35,36}

As there is no combustion, the aerosol from ECs does not contain tar, carbon monoxide or most of the 7000 chemicals in tobacco smoke. It does contain nicotine, propylene glycol, vegetable glycerin and a variety of toxins that are formed during the heating process or from contamination of the nicotine solution. Nicotine causes dependence but otherwise has relatively minor adverse health effects in the doses used.^{30,31} Chronic exposure to propylene glycol in theatrical fogs has been reported to cause acute and chronic respiratory effects, including reduced lung function, and chronic indoor exposure in children may exacerbate rhinitis, asthma, eczema and allergic symptoms.³³ Glycerin appears to be nontoxic, but there is no available evidence on the potential health effects of long-term regular inhalation.³⁷

Some of the toxins and carcinogens found in tobacco smoke are also found in EC aerosols but at much lower levels. A study assessed EC aerosols for the four most important groups of toxic compounds present in tobacco smoke (carbonyl compounds, volatile organic compounds, tobacco-specific nitrosamines and metals) and found that their concentrations were between nine and 450 times lower in EC aerosols.³⁸ This has been confirmed by the

TABLE 1. POSSIBLE REGULATORY SOLUTIONS TO CONCERNS ABOUT ELECTRONIC CIGARETTES^{29,51-53}

Concern	Possible regulatory solution
Renormalising smoking	<ul style="list-style-type: none"> Ban on vaping in smoke-free places Restrictions or bans on advertising, as for tobacco
Gateway to smoking for younger people and nonsmokers	<ul style="list-style-type: none"> Ban sale to minors Ban flavours designed to appeal to youth Ban mass media advertising and restrict promotion to information provided to cigarette purchasers at time of purchase Restrict places of sale (e.g. licensed retailers) Require gatekeeper approval for purchasing (medical prescription or government licensing scheme) to restrict to adult smokers Label product with potential risks, including addiction
Inconsistent quality control	<ul style="list-style-type: none"> Develop and enforce manufacturing standards, including quality assurance certification for devices and e-liquids Require accurate labelling of ingredients in e-liquid Ongoing research on long-term safety
Accidental poisoning	<ul style="list-style-type: none"> Require child-resistant e-liquid containers Include safe storage and handling instructions on labels Educate public
Adverse effects of passive vaping	<ul style="list-style-type: none"> Ban vaping in smoke-free places, particularly indoor use Educate public to use outdoors only and to avoid use around children, pregnant women or susceptible individuals (e.g. those with cardiovascular disease)
Uncertainties about long-term safety	<ul style="list-style-type: none"> Discourage long-term use Educate public about uncertainties concerning long-term safety

finding of low levels of toxins and carcinogens in the urine of EC users compared with smokers.³⁹

Tobacco smoke contains particulate matter that is associated with cardiovascular and respiratory disease. ECs also release particulate matter, but there is considerable uncertainty about the potential health risk it poses.^{6,11}

Some flavourings used in ECs may be a health risk. Some sweet-flavoured e-liquids contain diacetyl and acetyl propionyl, which are associated with respiratory disease when inhaled.⁴⁰ Other flavourings have been associated with cytotoxic effects in in-vitro studies, but their clinical

significance is controversial.^{6,11}

The health effects of short-term EC use for smoking cessation appear to be minor.^{33,38} No serious adverse events have been reported in clinical trials of up to 24 months.²³⁻²⁵ Side effects reported in clinical trials and user surveys are generally mild and self-limiting and include mouth and throat irritation and dry cough.^{1,2,23,24}

No clinically significant adverse effects of ECs have been found on the blood count, lung function or cardiac function, although further research is needed.⁴¹⁻⁴³

The health effects of long-term EC use are unknown, but regular exposure over

many years is likely to increase the risk. However, based on what is known about EC aerosol composition and patterns of use, the risk is likely to be much lower than for cigarette smoking.^{6,17,33,34,36}

Passive vaping

A number of studies have assessed the impact of EC use on indoor air quality. The levels of toxins and nicotine detected are substantially lower from EC use than from cigarette smoking, and many experts think ECs are unlikely to cause significant harm to bystanders.^{33,36,44-47} However, others have expressed concerns about fine particulate matter in EC aerosols and exposure of children or pregnant women.^{11,46} Therefore, the safest recommendation is to avoid indoor use of ECs.

Legal status

In all Australian states it is illegal to possess or sell nicotine for use in ECs without approval, although it is not illegal to possess or use an EC without nicotine.⁴⁸ The sale of any device that 'is designed to resemble' a tobacco product is banned in South Australia, Western Australia and NSW, but it is unclear whether this applies to ECs that do not resemble cigarettes.⁴⁸ In spite of these restrictions, ECs and nicotine e-liquid are widely available over the Internet or 'under the counter'.

Patients can legally import nicotine solutions for a therapeutic purpose under the TGA personal importation scheme for unapproved therapeutic goods if they hold a prescription from an Australian medical practitioner. Three months' supply of nicotine can be imported at a time for personal use (www.tga.gov.au). Alternatively, local compounding pharmacies may be able to prepare a nicotine solution for individual patients in some circumstances.

Public health concerns and regulation

Some public health experts are sceptical of the health benefits of ECs and are concerned that they will lead to an overall

negative effect on public health.⁴⁹ For example, ECs may appeal to children and be a gateway to smoking. Another concern is that widespread use could renormalise a behaviour that resembles smoking and this could reverse decades of progress in tobacco control. Some believe that ECs will discourage smokers from quitting by encouraging 'dual use' (i.e. using ECs when smoking is not allowed and continuing to smoke when it is). There is also concern about the increasing control of ECs by multinational tobacco companies, which have an established history of deceit, manipulation and putting profit before health.⁹

Supporters of ECs argue that they have the potential to deliver substantial health gains if smokers who are otherwise unable to stop smoking use ECs to quit or replace cigarettes.⁸ Furthermore, some believe that if wisely regulated, ECs could make cigarettes obsolete.⁵⁰

We believe that the best solution is a carefully regulated middle path that maximises the potential benefits to smokers while minimising the risk of negative public health effects.⁵¹ Some possible regulations are listed in Table 1.^{29,51-53}

Guidelines for use of electronic cigarettes

NRT, varenicline and bupropion have been evaluated by Australian authorities for quality, safety and efficacy and are the recommended first-line medications for nicotine-dependent smokers wishing to quit.⁵⁴ However, for smokers who have failed to quit with these therapies, ECs may offer an alternative.^{36,55,56} Non-smokers should be discouraged from using ECs.

Counselling smokers

For those using ECs, the best results in attempting to quit are likely to be achieved with counselling and support from a GP and use in conjunction with other stop-smoking pharmacotherapies, such as nicotine patches or varenicline. The latter relieve background cravings whereas

TABLE 2. GUIDELINES FOR PRESCRIBING NICOTINE FOR ELECTRONIC CIGARETTES UNDER THE TGA PERSONAL IMPORTATION SCHEME

Nicotine-containing e-liquids for refillable tank models	
Nicotine concentration	<ul style="list-style-type: none"> • Most popular is 18 mg/mL • Others in common use are 24 mg/mL, 12 mg/mL, 6 mg/mL and nicotine-free
Solvent	<ul style="list-style-type: none"> • Nicotine is dissolved in propylene glycol (PG) and/or vegetable glycerin (VG) • Common PG to VG ratios are 70:30, 50:50 and 30:70, which have different qualities when vaped • More PG gives a stronger 'throat hit'; VG makes more mist and is sweeter
Flavouring	<ul style="list-style-type: none"> • Flavourings are potentially toxic and should be free of diacetyl and acetyl propionyl • Flavour-free solutions are safest
Volume	<ul style="list-style-type: none"> • Typically 2 to 5 mL per day • Up to 10 mL per day for some heavy users
Quantity	<ul style="list-style-type: none"> • A three-month supply per prescription • Up to 15 months' supply in a 12-month period*
Example of prescription	For user of 3 mL e-liquid per day: <ul style="list-style-type: none"> • Nicotine 18 mg/mL • 50% PG • 50% VG • Tobacco flavouring • Dispense 100 mL x 3
Nicotine-containing cartridges for cigalikes	
Quantity	<ul style="list-style-type: none"> • A three-month supply per prescription • Up to 15 months' supply in a 12-month period*
Example of prescription	For user of one cartridge per day: <ul style="list-style-type: none"> • Electronic cigarette cartridges • Nicotine 18 mg/mL • Dispense 90 cartridges

* Prescriptions to be written by a registered Australian medical practitioner and held by the patient (www.tga.gov.au).

ECs act more quickly and may be beneficial as a coping strategy for breakthrough cravings. ECs may be of special benefit for smokers for whom the hand-to-mouth ritual and sensory aspects of smoking are important.⁵⁷

It is important to inform smokers that ECs may help smokers to quit but that they are not yet established or regulated as smoking cessation aids. Also, the long-term adverse effects of ECs are

unknown, although they are highly likely to be less than the adverse effects of smoking. Smokers should be encouraged to use ECs in the short term; however, long-term use is preferable to relapsing to smoking.^{58,59}

Selecting an EC

Most users start with first-generation ECs (cigalikes), with or without nicotine. However, later generation EC models are

more effective at delivering nicotine and reducing cravings.^{13,18} Users of models with adjustable power should be advised to use low voltage settings as greater power output and temperatures can produce higher levels of toxins through the thermal breakdown of chemicals in the e-liquid.

The websites of some EC manufacturers provide information about quality assurance for their products, such as electrical safety standards or the absence of some of the more concerning hazardous substances, such as diacetyl. Patients can be encouraged to look for this type of information before purchase.

Nicotine delivery

Vaping requires a different puffing technique to smoking to achieve effective nicotine doses. Experienced vapers take longer and slower puffs than when smoking, to increase nicotine delivery and to overcome the higher draw resistance of ECs. Typical puff duration with an EC is 4 seconds, compared with about 2 seconds when smoking. A session of about 10 to 15 puffs is equivalent to smoking a cigarette.¹⁴

The most popular nicotine concentration in e-liquid is 18 mg/mL.^{1,2} However, some experimentation may be required to find the appropriate strength to manage nicotine cravings and urges. As with NRT, users can wean off ECs by progressively reducing the nicotine concentration (e.g. reducing to 12 mg/mL, then 6 mg/mL and finally nicotine-free solutions).

Satisfaction and nicotine delivery tend to increase with practice, and users should be encouraged to persevere for several weeks. Regular daily use is more likely to be effective than intermittent use.¹⁹

Handling and storage

ECs and e-liquids should be handled and stored carefully. Any spills should be immediately cleaned up with soapy water, as nicotine can be absorbed dermally. E-liquids should be kept in child-resistant bottles, stored out of reach of children and

disposed of carefully. The replacement cartridges of cigalikes can present a choking hazard to young children.

Prescribing e-liquid

Patients may request prescriptions to import nicotine-containing e-liquid under the TGA Personal Importation Scheme. This includes bulk supplies for refillable models and prefilled cartridges for cigalikes. Prescribing guidelines are presented in Table 2.

As with other prescription medicines, patients should be advised that a prescription for nicotine authorises only the person named on the prescription to use it. The patient should not supply nicotine solution to anyone else.

Conclusion

Electronic cigarettes may offer an alternative to smokers who have been unable to quit using the available first-line

therapies. Evidence for their effectiveness is growing, although more research is needed. The evidence so far indicates that ECs are substantially safer than smoking, but the long-term health effects are unknown. Although there are many unanswered questions about ECs, they may be a useful cessation option for some smokers, especially with the support and advice of GPs. **MT**

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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