Nicotine vaping products as a harm reduction tool among smokers: review of evidence and implication for pharmacy practice

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Introduction

Smoking cessation is one of the most important and cost-effective preventive health measures to reduce the risk of premature mortality and morbidity. However, some smokers find stopping smoking very difficult despite repeated attempts ('hardcore smokers'), even with approved pharmacological cessation aids^{1,2}. Although studies indicate that the proportion of smokers with hardcore attributes are low in Australia, the proportion of hardcore smokers has increased among people from low socioeconomic backgrounds³. Conventional approaches to assist smoking cessation typically involve a relatively short treatment period of 12-26 weeks with approved smoking cessation medicines (varenicline, bupropion or nicotine replacement therapy) combined with behavioural counselling⁴. Non-pharmacological methods are also widely used (counselling alone and "cold turkey"). However, some smokers are turning to non-conventional approaches, such as the use of nicotine vaping products (NVPs) to quit smoking⁵.

Nicotine is a naturally occurring alkaloid found in tobacco. While it is a highly addictive substance, exposure to low concentrations of nicotine in the absence of tobacco smoke, such as in nicotine replacement therapies (NRT), is not associated with any increase in the risk of heart attack, stroke or death⁶. Concerns have been raised that long-term NRT use may increase cancer risk⁷ but while the data on the long-term nicotine or NRT use is insufficient, experimental studies largely indicate that nicotine alone is not carcinogenic^{8,9}. While there are strong concerns about the safety of nicotine exposure during pregnancy and its potential effects on fetal development and neonatal well-being^{10,11}, there is a general consensus that maternal use of NRT in pregnancy is safer for the fetus than continued smoking¹². While completely stopping the use of nicotine in any form is the best decision a smoker can take, continuing to use nicotine in a substantially less harmful product, such as NRT or NVPs provides an opportunity to reduce smoking-related death and disease for smokers who are unable to achieve abstinence from nicotine. With the growing popularity of NVPs as a way to quit smoking, pharmacy staff are regularly being asked by smokers for evidence-based advice about them¹³. This commentary summarises the current evidence surrounding the safety and efficacy of NVPs and provides a guide for pharmacy staff on discussions with customers regarding NVPs.

What are NVPs?

NVPs (also known as e-cigarettes, electronic nicotine delivery systems or personal vaporisers) are battery powered devices with chamber for holding the liquid, a mouthpiece, a battery and a heating coil that heats a liquid solution (known as e-liquid) into an aerosol mist (colloquially known as vapour) that is inhaled in a manner that resembles smoking. The two most common solvents used are propylene glycol and glycerol or a combination of the two. Glycerol produces a more visible cloud than propylene glycol, while propylene glycol produces a greater ‘throat hit’ that some smokers enjoy, and is better at carrying flavours than glycerol. NVPs can either contain a variable concentration of nicotine (typically ranging from 3 to 20 mg/ml) or be nicotine-free. Some small devices that have lower battery power, such as pod devices, use a higher nicotine concentration (up to 59 mg/mL¹⁴) to compensate for lower vapour production. The level of nicotine and other chemicals that users (known as vapers) are exposed to varies considerably across different generations and brands of vaping devices and e-liquid and is also affected by how the device is used (power settings, puff topography etc.)¹⁵. First-generation NVPs are the prototype products containing low-capacity batteries and pre-filled cartridges. They are less efficient in delivering nicotine compared to the newer generation re-fillable vaping devices (tank models) which generally contain an integrated atomizer and high-performance battery. Pod devices are a relatively new design. These sometimes look like a USB drive. The use of nicotine salts rather than ‘freebase’ nicotine is also a new innovation that has accompanied the introduction of pod systems. Nicotine salts, which have nicotine in a protonated form, reduces the rough throat hit associated with nicotine inhalation, allowing a higher concentration of nicotine to be inhaled than with nicotine in the basic or unionised ‘freebase’ form.

Trends in NVP use

There has been a rapid increase in NVP use globally since their introduction into the market in the mid-2000s. The uptake of NVPs varies considerably between countries, with a rapid uptake evident in countries that have allowed them to be sold with nicotine as consumer products¹⁶. Data regarding trends on the use of NVPs are limited in Australia. The Australian Institute of Health and Welfare (AIHW) included questions regarding NVP use in the National Drug Strategy Household Survey in 2013 and 2016. The results suggest that current use of NVPs in Australia was very low among the general population (people aged 14 or older) with only 1.2% reporting current use of NVPs¹⁷. However, the use of NVPs among smokers in Australia significantly

increased between 2013 and 2016, with approximately one third of smokers (31%) having ever tried NVPs and 4.4% currently using them¹⁷.

Can NVPs be a tool to quit smoking?

Although there has been an increase in our understanding of NVPs in recent years, the current evidence base for the efficacy of NVPs in smoking cessation is limited. A number of systematic reviews and meta-analyses have been published in recent years that summarise findings from randomized controlled trials, prospective cohort and cross-sectional studies (Table 1).

Table 1. A summary of recent systematic reviews on the role of NVPs in smoking cessation

Study (author, year)*	Type of study included	Conclusion/main finding
Hartman-Boyce, 2016 ¹⁸	3 RCTs and 21 cohort studies	Nicotine containing NVPs result in a higher and statistically significant smoking abstinence rate compared with non-nicotine containing NVPs.
Malas et al., 2016 ¹⁹	62 articles with various study designs	While most of the studies demonstrated an association between NVP use and smoking cessation and/or reduction, the overall quality of the current studies is low or very low.
El Dib, 2017 ²⁰	3 RCTs and 9 prospective cohort studies	<p><i>RCTs:</i> Nicotine-containing NVPs result in a non-significant increase in smoking cessation compared with non-nicotine NVPs.</p> <p><i>Cohort studies:</i> A possible reduction in quit rates with the use of NVPs compared with no use of NVPs.</p> <p>The overall quality of evidence was judged to be of ‘low certainty’ or ‘very low certainty’</p>

Findings from the above comprehensive reviews¹⁸⁻²⁰ concluded that although the evidence suggests a higher smoking abstinence rate with nicotine containing NVPs compared with NVPs without nicotine, the current body of scientific evidence needs strengthening to draw robust conclusions about the effectiveness of NVPs as a smoking cessation aid. Similarly, scientific reports commissioned by notable health bodies have come to similar conclusions²¹⁻²³. However, the current body of evidence is increasing^{24,25}. In January 2019, Hajek and colleagues published an RCT that evaluated the effectiveness of NVPs for smoking cessation (sustained and

biochemically validated abstinence for 1 year) compared with NRTs. Both groups (a total of 886 participants) were also provided with behavioural support for at least 4 weeks. After 1 year of follow up, NVPs were found to be nearly twice as effective as NRTs for smoking cessation (18% vs 9.9%; relative risk: 1.83; 95% CI: 1.30-2.58; p -value <0.001)²⁴. Similarly, a recent RCT conducted by Walker et al (2019) concluded that combining nicotine containing NVPs with nicotine patches can lead to ‘a modest improvement in smoking cessation’ compared to patches alone or combination of patches and NVPs without nicotine²⁵.

What evidence is there about the safety of NVPs?

Continuum of risk

A number of evidence reviews now confirm that people who vape instead of smoking are exposed to fewer ‘harmful and potentially harmful chemicals’ (HPHC)^{21,26}. The relative harm of nicotine containing products were estimated by Nutt et al.²⁷ using a multi-criteria decision analysis (MCDA) model. Abrams and colleagues²⁸ adopted the data from Nutt et al. and classified various types of nicotine products into ‘no harm’ (no use), ‘much less harm’ (smokeless tobacco, NRTs and e-cigarettes) and ‘extreme toxicity’ (combustible tobacco). Accordingly, while ‘no use’ of any nicotine containing products is the most desirable outcome to reduce harm, the use of NVPs is estimated to represent less than 5% of the harm compared to using combustible tobacco products. While the Nutt et al. study was widely criticised on the basis of limited evidence, reliance on consensus of selected participants and potential conflicts of interest of some participants²⁹, other studies using different approaches have come to similar conclusions, that vaping is much lower risk than smoking^{26,30}. A review of the evidence commissioned by Public Health England (PHE) citing 415 publications, which was updated in 2018, reaffirmed its previous estimate that NVPs are likely to be about 95% safer than conventional cigarettes and encouraged smokers to switch from smoking to vaping based on the relative levels of HPHCs in the emissions of NVPs compared to cigarettes, and observed reductions in biomarkers among smokers who switched²³. While there is ongoing debate about the accuracy of this estimate, a consensus report from the National Academies of Sciences, Engineering, and Medicine (NASEM), concluded that “there is conclusive evidence that completely substituting NVPs for combustible tobacco cigarettes reduces users’ exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes”²¹.

Stephens (2017) modelled and compared the cancer potencies of various nicotine-delivering aerosols and concluded that NVPs result in emissions with much less carcinogenic potency than tobacco smoke if used under typical use device settings, liquid formulation and vaping behaviour³⁰. Figure 1 summarises nicotine containing products along the continuum of risk Reproduced from McNeill and Munafò, 2012³¹

Figure 1. Nicotine containing products along the continuum of risk.

Short and long-term health risks

The Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO) recently conducted a scientific review into the use and health impacts of NVPs and concluded that even though there is evidence that substituting NVPs for conventional cigarettes among smokers results in health improvement, the use of NVPs has independent health risks, the magnitude of which are not yet determined²². There is evidence that NVPs contain and emit potentially toxic substances in addition to nicotine²¹, but toxicological studies show that the content and concentration of these

harmful chemicals in the vapour and body fluids are far less in NVPs than in combustible cigarettes under usual use conditions³². The NASEM report concluded that there is a lack of evidence on whether NVP use is associated with clinical cardiovascular outcomes²¹. However, a recently published RCT showed that smokers demonstrated a significant improvement in vascular health within 1 month of switching from smoking to vaping³³.

There is a certain lack of long-term studies to provide information regarding the effect of NVPs on the development and/or exacerbation of conditions such as cancer, cardiovascular and respiratory diseases. A recent review conducted to evaluate the respiratory effects of NVPs concluded that the current evidence base is insufficient to determine whether the respiratory health effects of NVPs are less than those of combustible tobacco products³⁴. Similarly, the CSIRO report concluded that although NVP aerosols contain and emit some carcinogenic compounds and metabolites, there is insufficient evidence regarding the risk of cancer from the levels found in the NVP aerosol²².

Other potential health risks related to NVPs include battery related injuries (overheating, fire and explosions) and poisoning from accidental e-liquid ingestion in children, which have been reported in the literature and mainstream media³⁵. The risk of nicotine toxicity and accidental poisoning among children from e-liquid ingestion can be reduced by implementing legislation requiring the use of child-resistant containers, warning labels and by educating the public to store nicotine e-liquid away from children, similar to other potentially dangerous household products and medicines.

Health officials in the USA including the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) are investigating an outbreak of lung illnesses associated with the use of vaping products. During 2019, about 2,700 cases of vaping product use associated lung injury and 60 deaths have been reported to CDC³⁶. The lung damage is due to a chemical injury, but the exact chemical that has caused the injuries has not been confirmed. The investigators have narrowed the products involved to illicit vaping products containing tetrahydrocannabinol (THC), with a “cutting agent”, vitamin E acetate, strongly implicated. The FDA and CDC have warned consumers to stop using THC vaping products, particularly those obtained from ‘informal’ sources³⁷. While inhaling vitamin E acetate oil may be a direct cause of lung injury and could

plausibly cause conditions such as lipoid pneumonia, which some outbreak patients have been diagnosed with, this agent does not fit with the full range of lung conditions diagnosed as part of the outbreak. A current theory is that another chemical has formed from the vitamin E acetate which has caused the lung damage observed. As vitamin E acetate is not added to nicotine vaping products, which unlike THC vaping products require a water-soluble solvent rather than an oil-based one, these do not appear to be involved in the outbreak³⁸.

Estimating the possible health outcomes of NVP use

Due to this being a relatively new product, the risks and/or overall population health gain from the long-term use of NVPs are uncertain. Thus, public health researchers have estimated the possible health outcomes using hypothetical scenario-based modelling^{39,40}. One study conducted using a decision-theoretic model projected an overall reduction of 21% in smoking related mortality and reduction of 20% in life years lost as a result of NVP use⁴⁰. The authors pointed out that the overall health gains or harm from NVP use depend on the magnitude of health risks of NVPs compared with combustible tobacco cigarettes and rates of NVP uptake by never smokers⁴⁰. A similar modelling study conducted to estimate the health effects of NVP sales in the USA and UK reported that a scenario in which NVP use rises only among current youth or adult smokers interested in quitting had overall population-level health gains regardless of associated health costs³⁹. In the report commissioned by NASEM, modelling taking into consideration a variety of possible assumptions concludes that NVP use represents a net public health gain under the most likely scenarios²¹. The net public health gain or loss from NVP use, however, will ultimately be contingent on who uses them and how they are used, for example, how many smokers fully switch to NVPs and how many non-smoking youths engage in persistent long-term use. These outcomes can be influenced by the regulatory framework that is adopted, with the highest benefit likely to be realised when NVPs are regulated in a way that will discourage access to and uptake by youth and non-smokers while encouraging smokers to switch to them³⁹.

Current debates and controversies surrounding NVPs

Potential role of NVPs in tobacco harm reduction

The concept of harm reduction has been embraced by the public health community and implemented with great success within the areas of alcohol, illicit drug use and sexual health. Harm reduction strategies are those that focus on reduction of harm without necessarily requiring complete abstinence. Examples include needle exchange programs to curtail the spread of blood-borne viruses among intravenous drug users, substituting methadone for heroin dependence, and encouraging the use of condoms to prevent sexually transmitted diseases⁴¹. Pharmacists have played a critical role in delivering these harm reduction interventions. However, harm reduction interventions for tobacco smokers has been controversial, with current approaches to reducing tobacco-related disease focussed on the complete cessation of nicotine use⁴². Opponents of tobacco harm reduction often cite historical examples of purported tobacco harm reduction alternatives such as filtered, low-tar and low nicotine yield cigarettes, which were part of the tobacco industry's manoeuvres to encourage continued smoking using an allegedly safer tobacco product instead of quitting⁴³. These products were eventually shown to be equally as harmful as conventional cigarettes. On the other hand, advocates of tobacco harm reduction cite the role Swedish snus has played in reducing tobacco-related death and disease in Sweden by displacing cigarettes as an example of positive population health outcomes through product substitution⁴⁴. Snus, a Swedish moist tobacco product that is used orally, has much lower health risk compared to smoking cigarettes due to its low carcinogen content and absence of respiratory risks^{45,46}. Smoking prevalence among Swedish men was only 8% in 2016, which is the lowest smoking rate in Europe⁴⁷. The tobacco-related mortality among Swedish male smokers is also among one of the lowest in Europe, despite the high prevalence of snus use (18% in 2016)^{47,48}. In contrast, death rates among Swedish women, few of whom use snus, was comparable with the mortality rate of European women⁴⁸, indicating the role snus has played in reducing tobacco related harm among Swedish men.

In England, the concept of tobacco harm reduction is endorsed by the government and peak health bodies such as the Royal College of Physicians²⁶, and is integrated into the National Institute for Health and Care Excellence's (NICE) smoking cessation guidelines as an alternative approach to support unwilling or hard-to-quit smokers to improve their health⁴⁹. These approaches include long-term use of approved nicotine replacement therapies, but also unlicensed substitutes such as NVPs. The UK's National Centre for Smoking Cessation and Training released a briefing for stop smoking services and online training for healthcare professionals on how to incorporate NVPs into

smoking cessation clinical practice^{50,51}. Similarly, the government in New Zealand acknowledged the potential role of NVPs to reduce tobacco related harm and has encouraged smokers to switch to vaping if they find it difficult to quit by other means⁵². In Australia, the Royal College of General Practitioner's guideline for supporting smoking cessation, which was updated on January 2020, recommended the use of NVPs as 'a reasonable intervention' for people who are motivated, but are unable to quit smoking and have brought up NVP usage with their healthcare providers.⁴

Gateway effect and renormalisation of smoking

One of the major health concerns voiced by NVP critics is the potential influence NVPs have on recruiting new cigarette smokers ('gateway effect'), particularly among young people, and its potential effect on weakening tobacco control efforts, and re-normalising smoking. There is no clear and agreed definition for "gateway" in the scientific literature. Generally, the gateway hypothesis could be described in relation to NVPs as a theory of causality by which the use of NVPs has a risk-enhancing effect (by acting as a catalyst) for initiating combustible tobacco use⁵³. It posits that non-smokers who use NVPs will eventually switch to conventional cigarettes due to perceived advantages such as fast response rate and more satisfactory level of nicotine from cigarettes compared with NVPs.

A number of studies have attempted to document the possible relationship between NVP use and willingness to smoke, initiation of smoking and escalation of cigarette use. Findings from systematic reviews and meta-analyses suggest that the likelihood of intention to use and initiation of cigarette smoking is high among adolescents who use NVPs^{54,55}. The recent review of scientific studies commissioned by NASEM also concluded that "there is substantial evidence that e-cigarette use increases the risk of ever using combustible tobacco cigarettes among youth and young adults"²¹. However, the current body of scientific evidence to support the "gateway" claim is widely contested. Firstly, the methodological approaches and thus the credibility of findings from these studies is widely challenged due to the difficulty of establishing a cause-effect relationship in the presence of many confounders. A plausible alternative explanation is that the majority of young people using NVPs would have gone on to use tobacco products regardless because they were already at high risk of smoking from the outset. This is known as the common liability theory⁵⁶. Etter (2017) elaborated on the common liability to addiction in relation to NVPs

as “adolescents with a liability to try nicotine will initially use the product that is most easily available, most heavily advertised, about which they are most curious or for which peer pressure to use is highest”⁵³. Unlike the gateway theory, which can only explain the temporal ordering of behaviours (vaping and smoking), common liability to addiction (i.e. nicotine addiction) embraces other biobehavioural factors that contribute to the development of the behaviour (vaping or smoking) such as genetic vulnerability, personality traits (i.e. risk-taking, rebellious) and risk factors associated with nicotine use (such as mental health and having family members/friends who smoke)⁵⁶. Secondly, other lines of evidence cast doubt on the overall applicability of the gateway theory in informing public health policy and practice. For example, adolescent smoking has declined rapidly in the US while adolescent NVP use has increased⁵⁷.

Although sale to minors (less than 18 years old) is now prohibited in most countries, the potential of youth uptake of NVPs is one of the major public health concerns about these products⁵⁸. The prevalence of youth NVP use differs considerably across countries and smoking status. The 2016 US Surgeon General’s report stated that NVPs were “the most commonly used tobacco product among youth, surpassing conventional cigarettes”⁵⁹ and the FDA Commissioner announced that there are “clear signs that youth use of NVPs has reached an epidemic proportion”⁶⁰. In contrast, youth NVP use in the UK has remained low despite a high prevalence of vaping among adults⁶¹.

Prolonged dual use and discouragement from cessation efforts

Prolonged dual use (concomitant use of NVPs and conventional cigarettes) and discouragement from smoking cessation is another concern raised by those critical of NVP use⁶². It has been argued that smokers who become dual users could represent ‘missed opportunities’ for quitting smoking altogether, as some of these smokers could have stopped smoking completely had they not started vaping. Rather, the use of NVPs maintains their addiction to nicotine and thus deters them from quitting and a number of cross-sectional studies are cited to support these claims. However, it is difficult to infer a behavioural phenomenon behind dual use based on findings from cross-sectional studies since the study design fails to differentiate smokers who are engaging in long-term dual use from those who are using NVPs for smoking reduction, smoking cessation or smokers who are just experimenting with NVPs. Currently, there is a lack of credible scientific evidence from robust methodological designs to prove the claim that NVP use discourages smokers from cessation

efforts. In fact, findings from the few available longitudinal studies suggest that the rate of cessation and quit attempts among smokers who use NVPs has increased over time⁶³⁻⁶⁵.

How are NVPs regulated in Australia?

The question of how to regulate NVPs is a major source of debate in many countries and continues to divide the public health community. Australia is an example of a highly restrictive regulatory environment for NVPs and the regulatory approach differs significantly from other developed countries such as the US, UK, Canada and New Zealand. The regulation of NVPs in Australia encompasses national tobacco control laws, the therapeutic goods administration (TGA), consumer protection legislation, and the state-based drugs and poisons regulations⁶⁶. Nicotine is classified in the Poison Standard as Schedule 7 (a dangerous poison) except when for human or animal therapeutic use. When for human therapeutic use, nicotine is in Schedule 4 (therapeutic substances that can be obtained from a pharmacist only on prescription from an authorized prescriber) except when in preparations for oromucosal or transdermal use such as nicotine patches, gum or mouth sprays, which are unscheduled and can be sold by general retailers⁶⁷.

In general, therapeutic goods must be approved by the TGA and included on the Australian Register of Therapeutic Goods (ARTG) before being supplied in Australia. So far, there are no NVPs or nicotine liquid refill products listed on the ARTG⁶⁶. Therefore, while approved NRT products can be sold in a range of commercial outlets including pharmacies, supermarkets and petrol stations, vaping products containing nicotine are illegal to sell⁶⁶. However, according to the TGA, Australians can access nicotine for use in NVPs for a therapeutic purpose (e.g. quitting smoking) via one of the legal pathways for accessing unapproved therapeutic goods, if the person holds a valid medical prescription. These pathways include personal importation of up to three months' supply from overseas, the Special Access Scheme and the Authorised Prescriber Scheme⁶⁶. Pharmacists in Australia may also be able to supply liquid nicotine legally for smoking cessation by extemporaneously compounding the liquid for the individual patient on prescription⁶⁸. Due to the complex nature of the current regulatory landscape, there is widespread public confusion about the legal status of NVPs⁶⁹.

In general, it is legal to use a vaping device that does not contain nicotine anywhere that smoking is allowed and most jurisdictions (except Western Australia) allow these nicotine-free products to

be sold under similar conditions to combustible cigarettes (e.g. bans on sales to people aged under 18, retail display bans etc)⁶⁶. In some jurisdictions, it is an offence to sell any products that resemble tobacco products. While the majority of these jurisdictions (Queensland, New South Wales and South Australia) exclude NVPs from the definition of ‘products that resemble cigarettes’, the Western Australian government currently considers sale of vaping products (with or without nicotine) a breach of this legislation regardless of whether the device visually resembles a cigarette or not.

Implication for pharmacy practice

Pharmacists, being one of the most easily accessible health professionals in the community, are uniquely positioned to educate patients on the health risks of smoking and the benefits of a smoke-free life. With the growing popularity and use of NVPs as a way to quit smoking, pharmacy staff are likely to receive more inquiries from smokers for evidence-based advice about NVPs. In a recent survey conducted among pharmacy staff in Brisbane, more than 1 in 3 pharmacy staff (39%) had been asked about “e-cigarettes” by their customers¹³ and nearly all of the pharmacy staff (91%) reported that they felt uninformed and needed more information regarding the safety, efficacy and regulation of NVPs. The Pharmacy Board of Australia states that the sale of tobacco products is regarded as unprofessional conduct, but has not provided advice on the sale of NVPs⁷⁰. The Pharmacy Guild of Australia⁷¹ stated in 2015 that promoting, stocking, and/or supplying NVPs in pharmacies is against its Quality Care Pharmacy Program (QCPP) requirements, which indicates that cigarettes, tobacco or smoking-related products or implements should not be sold or promoted. However, there are no clear guidelines or policy statements provided by any of the professional organisations for pharmacists on how pharmacy staff should handle customer enquiries about NVPs or on dispensing prescriptions for nicotine solution for use in NVPs as a cessation aid. Therefore, based on the scientific evidence presented herein, in Table 2 we provide a summary of key points that pharmacy staff can use when discussing NVPs with their customers.

Table 2. A guide for pharmacy staff on discussions with customers regarding NVPs, 2020

Questions	Guide for counselling
General	<p>At all times, counsel the patient on the benefits of smoking cessation and the full range of options available to help them.</p> <p>First line treatment for smoking cessation is behavioural counselling accessible for free via Quitline combined with TGA-approved smoking cessation products such as NRTs, bupropion and varenicline.</p>
Are NVPs less harmful than combustible cigarettes?	The long-term health risk of NVPs is not yet established and there may be some risks associated with NVP use. However, evidence strongly indicates that these products are less harmful compared to combustible tobacco cigarettes and offer smokers the opportunity to reduce tobacco-related harm, if they are unwilling or unable to quit smoking by other methods. Under no circumstances should smoking be considered less harmful than vaping.
What are the ingredients of NVPs?	NVPs contain a variable concentration of nicotine (typically ranging from 3 to 20 mg/ml), and can also be used without nicotine as a behavioural replacement for smoking. Other main ingredients are propylene glycol, glycerin, water and flavourings.
Can NVPs be used to quit and/or cut down smoking?	<p>The current literature regarding the efficacy of NVPs in smoking cessation is not conclusive. However, the evidence base is growing with RCTs indicating NVPs are equally or more effective than NRTs for smoking cessation.</p> <p>For unwilling or hard-to-quit smokers, NVPs could be a viable tobacco harm reduction tool due to the fact that vaping is significantly less harmful than smoking.</p>
Is it safe to use NVPs long term?	Due to being a relatively new product, the risks from long-term use of NVPs are uncertain and not fully quantified. However, vaping is likely to be much less harmful than long-term use of smoked tobacco. The lowest risk option is to use NVPs for a limited time until the former smoker is confident they can stop without relapsing to smoking.
Are nicotine containing NVPs associated with the recent outbreak of lung injuries in the USA?	Illicit vaping products containing THC with vitamin E acetate, <i>not</i> licit NVPs, are strongly implicated in the recent outbreak of vaping product use-associated lung injury. Vitamin E acetate is not present in licit NVPs available on the market.
Is it safe to use NVPs during pregnancy?	<p>TGA-approved NRTs are safe to use during pregnancy and are effective for quitting especially if combined with behavioural counselling.</p> <p>Although little research has been conducted around the safety of NVPs in pregnancy, they are likely to be lower risk for the mother and baby than continuing to use smoked tobacco.</p>
Can NVPs and cigarettes be used together?	It is important that smokers using NVPs are encouraged to stop smoking completely rather than using NVPs as a partial substitute. Even low level smoking

	<p>still confers substantial health risk. Dual use of both cigarettes and NVPs is unlikely to confer greater health risk than smoking alone, but there may be little health benefit from NVP use without stopping smoking. Those finding it difficult to stop smoking altogether may benefit from trying a higher dose of nicotine and increasing the frequency of vaping. Vaping less than daily is unlikely to be sufficient for successful smoking cessation. Some vapers find experimenting with different devices and liquids help them to find a product that works best for them.</p> <p>Stopping NVP use once they are confident of not relapsing to smoking will also minimize any residual health risks associated with vaping.</p>
Is it legal to use nicotine containing NVPs in Australia?	<p>Currently, nicotine is classified as a ‘dangerous poison’ (schedule 7) unless used to help quit smoking in which case it is a ‘prescription only medicine’ (schedule 4). Vaping products containing nicotine are illegal to sell in all States and Territories unless approved by the TGA or supplied via a pathway for accessing unapproved therapeutic goods. Smokers can import nicotine liquid for use as a smoking cessation aid if they have a medical prescription.</p> <p>In most jurisdictions, it is legal to use a vaporising device that does not contain nicotine anywhere that smoking is allowed. Use with nicotine requires a medical prescription.</p> <p>In Western Australia, it is an offence to sell any products that look like tobacco products. This includes NVPs with or without nicotine.</p>
How can I get nicotine liquid for use in NVPs as a cessation aid?	<p>In Australia, a valid prescription from a registered medical practitioner is needed for legal access to nicotine for use in NVPs.</p> <p>These legal pathways are: (1) personal importation of up to three months’ supply from overseas; (2) the Special Access Scheme (SAS); (3) Authorised Prescriber Scheme (APS), and (4) via compounding pharmacies. While writing a prescription for nicotine via SAS and APS has considerable paperwork for doctors, the personal importation and extemporaneous compounding are less onerous routes for supply.</p>
Can I vape in smoke-free areas?	In most jurisdictions, vaping is not allowed in places where smoking is prohibited. If in doubt it is best to follow the same restrictions as for smoking.
Safety precautions	<p>NVP users should be advised to store nicotine e-liquid out of reach of children and use containers with child-resistant closures to prevent possible accidental poisoning. Even refill liquids labelled as nicotine-free should be stored this way as some may have been mislabelled.</p> <p>The following preventive measures can be taken to avoid potential battery explosion: (1) use NVPs with inbuilt safety features; (2) avoid overcharging (such as overnight charging); (3) avoid putting batteries in a pocket with other metal objects; (4) replace damaged (or wet) batteries; (5) use only the charger supplied with the device and (7) do not try to modify the device.</p>

Conclusion

While evidence on the safety and efficacy of NVPs is emerging, evidence suggests that they are less harmful compared to combustible cigarettes and offer smokers the opportunity to reduce tobacco-related harm. For unwilling or hard-to-quit smokers, NVPs are a viable cessation or harm reduction tool. The maximum benefit from using NVPs as a harm reduction tool, however, will only be realised if smokers completely stop smoking rather than using NVPs as a partial substitute, because even low level smoking still confers substantial health risk. Moreover, NVPs should be used for a limited time until the former smoker is confident they can stop without relapsing to smoking. Vaping devices should not be used for delivering other substances such as THC. Pharmacy staff, as a trusted source of health information, need to keep abreast of the currently growing body of literature in order to provide current and evidence-based information for patients.

References

1. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev*. 2010;12.
2. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2012;11(11).
3. Clare P, Bradford D, Courtney RJ, Martire K, Mattick RP. The relationship between socioeconomic status and 'hardcore' smoking over time—greater accumulation of hardened smokers in low-SES than high-SES smokers. *Tob Control*. 2014;23(e2):e133-e138.
4. The Royal Australian College of General Practitioners. *Supporting smoking cessation: A guide for health professionals*. Second ed. East Melbourne, Vic: RACGP; 2019.
5. Bonevski B, Borland R, Paul CL, et al. No smoker left behind: it's time to tackle tobacco in Australian priority populations. *Med J Aust*. 2017;207(4):141-142.
6. Hubbard R, Lewis S, Smith C, et al. Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death. *Tob Control*. 2005;14(6):416-421.
7. Stepanov I, Carmella SG, Han S, et al. Evidence for endogenous formation of N'-nitrosonornicotine in some long-term nicotine patch users. *Nicotine Tob Res*. 2009;11(1):99-105.
8. Shields PG. Long-term nicotine replacement therapy: cancer risk in context. *Cancer Prev Res*. 2011;4(11):1719-1723.
9. Hecht SS. Tobacco carcinogens, their biomarkers and tobacco-induced cancer. *Nat Rev Cancer*. 2003;3(10):733-744.
10. Holbrook BD. The effects of nicotine on human fetal development. *Birth Defect Res C*. 2016;108(2):181-192.
11. Bruin JE, Gerstein HC, Holloway AC. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. *Toxicol Sci*. 2010;116(2):364-374.
12. Diamanti A, Papadakis S, Schoretsaniti S, et al. Smoking cessation in pregnancy: An update for maternity care practitioners. *Tob Induc Dis*. 2019;17(August):57.

13. Erku DA, Gartner CE, Do JT, Morphet K, Steadman KJ. Electronic nicotine delivery systems (e-cigarettes) as a smoking cessation aid: A survey among pharmacy staff in Queensland, Australia. *Addict Behav.* 2019;91:227-233.
14. Jackler RK, Ramamurthi D. Nicotine arms race: JUUL and the high-nicotine product market. *Tob Control.* 2019;28(6):623-628.
15. DeVito EE, Krishnan-Sarin S. E-cigarettes: impact of E-liquid components and device characteristics on nicotine exposure. *Curr Neuropsychopharmacol.* 2018;16(4):438-459.
16. Yong H-H, Borland R, Balmford J, et al. Trends in e-cigarette awareness, trial, and use under the different regulatory environments of Australia and the United Kingdom. *Nicotine Tob Res.* 2014;17(10):1203-1211.
17. Chan G, Leung J, Gartner C, Yong H-H, Borland R, Hall W. Correlates of electronic cigarette use in the general population and among smokers in Australia—Findings from a nationally representative survey. *Addict Behav.* 2019;95:6-10.
18. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev.* 2016;14(9):CD010216.
19. Malas M, van der Tempel J, Schwartz R, et al. Electronic cigarettes for smoking cessation: a systematic review. *Nicotine Tob Res.* 2016;18(10):1926-1936.
20. El Dib R, Suzumura EA, Akl EA, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: a systematic review and meta-analysis. *BMJ Open.* 2017;7(2):e012680.
21. National Academies of Sciences Engineering and Medicine. *Public Health Consequences of E-Cigarettes.* Washington DC: The National Academies Press; 2018.
22. Byrne S, Brindal E, Williams G, et al. *E-cigarettes, smoking and health, A Literature Review Update.* CSIRO, Australia;2018.
23. McNeill A, Brose LS, Calder R, Bauld L, Robson D. *Evidence review of ecigarettes and heated tobacco products 2018. A report commissioned by Public Health England.* London: Public Health England; 2018.
24. Hajek P, Phillips-Waller A, Przulj D et al. A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy. *N Engl J Med.* 2019;380:629-637.
25. Walker N, Parag V, Verbiest M, Laking G, Laugesen M, Bullen C. Nicotine patches used in combination with e-cigarettes (with and without nicotine) for smoking cessation: a pragmatic, randomised trial. *Lancet Respir Med.* 2019;8(1):54-64.
26. Royal College of Physicians. *Nicotine without smoke—tobacco harm reduction.* London: RCP; 2016.
27. Nutt DJ, Phillips LD, Balfour D, et al. Estimating the harms of nicotine-containing products using the MCDA approach. *Eur Addict Res.* 2014;20(5):218-225.
28. Abrams DB, Glasser AM, Pearson JL, Villanti AC, Collins LK, Niaura RS. Harm minimization and tobacco control: reframing societal views of nicotine use to rapidly save lives. *Annu Rev Public Health.* 2018;39:193-213.
29. Polosa R. E-cigarettes: Public Health England's evidence based confusion? *The Lancet.* 2015;386(10000):1237-1238.
30. Stephens WE. Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. *Tob Control.* 2018;27(1):10-17.
31. McNeill A, Munafò MR. Reducing harm from tobacco use. *J Psychopharmacol.* 2013;27(1):13-18.
32. Shahab L, Goniewicz ML, Blount BC, et al. Nicotine, carcinogen, and toxin exposure in long-term e-cigarette and nicotine replacement therapy users: a cross-sectional study. *Ann Intern Med.* 2017;166(6):390-400.

33. George J, Hussain M, Vadiveloo T, et al. Cardiovascular effects of switching from tobacco cigarettes to electronic cigarettes. *J Am Coll Cardiol*. 2019;74(25):3112-3120.
34. Gotts JE, Jordt S-E, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? *BMJ*. 2019;366:l5275.
35. Alison Branley. Health experts alarmed after rise in accidental poisoning from e-cigarettes. 2014; <https://www.abc.net.au/news/2014-08-27/accidental-poisoning-from-e-cigarettes-on-the-rise/5699592>. Accessed January 29, 2020.
36. Centers for Disease Control and Prevention (CDC). Outbreak of Lung Injury Associated with the Use of E-Cigarette, or Vaping, Products. 2019; https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html. Accessed February 1, 2020.
37. Food and Drug Administration (FDA). Statement on consumer warning to stop using THC vaping products amid ongoing investigation into lung illnesses. 2019; <https://www.fda.gov/news-events/press-announcements/statement-consumer-warning-stop-using-thc-vaping-products-amid-ongoing-investigation-lung-illnesses>. Accessed February 1, 2020.
38. Nyakutsikwa B, Britton J, Bogdanovica I, Langley T. Vitamin E acetate is not present in licit e-cigarette products available on the UK market. *Addiction*. 2019;In-press.
39. Kalkhoran S, Glantz SA. Modeling the health effects of expanding e-cigarette sales in the United States and United Kingdom: a Monte Carlo analysis. *JAMA Intern Med*. 2015;175(10):1671-1680.
40. Levy DT, Borland R, Villanti AC, et al. The application of a decision-theoretic model to estimate the public health impact of vaporized nicotine product initiation in the United States. *Nicotine Tob Res*. 2017;19(2):149-159.
41. Addiction EMCfDaD. *Harm reduction: evidence, impacts and challenges*. Luxembourg: Publications Office of the European Union 2010.
42. Green LW, Fielding JE, Brownson RC. The debate about electronic cigarettes: harm minimization or the precautionary principle. *Annu Rev Public Health*. 2018;39:189-191.
43. Pollay RW, Dewhirst T. The dark side of marketing seemingly “Light” cigarettes: successful images and failed fact. *Tob Control*. 2002;11(suppl 1):i18-i31.
44. Ramström L, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tob Control*. 2006;15(3):210-214.
45. Gartner CE, Hall WD, Vos T, Bertram MY, Wallace AL, Lim SS. Assessment of Swedish snus for tobacco harm reduction: an epidemiological modelling study. *The Lancet*. 2007;369(9578):2010-2014.
46. Foulds J, Ramstrom L, Burke M, Fagerström K. Effect of smokeless tobacco (snus) on smoking and public health in Sweden. *Tob Control*. 2003;12(4):349-359.
47. Public Health Agency of Sweden. Tobacco. 2018; <https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/living-conditions-and-lifestyle/alcohol-narcotics-doping-tobacco-and-gambling/tobacco/>. Accessed January 22, 2020.
48. Ramström L, Wikmans T. Mortality attributable to tobacco among men in Sweden and other European countries: an analysis of data in a WHO report. *Tob Induc Dis*. 2014;12(1):14.
49. National Institute for Health and Care Excellence. Stop smoking interventions and services: NICE guideline. 2018; <https://www.nice.org.uk/guidance/NG92>. Accessed February 1, 2020.
50. McEwen Andy, McRobbie Hayden. Electronic cigarettes: A briefing for stop smoking services. 2016; http://www.ncsct.co.uk/publication_electronic_cigarette_briefing.php. Accessed February 1, 2020.
51. National Centre for Smoking Cessation and Training. E-cigarettes: a guide for healthcare professionals. 2018; http://elearning.ncsct.co.uk/e-cigarettes-stage_1. Accessed February 1, 2020.

52. New Zealand Ministry of Health. Ministry of Health position statement – Vaping products. 2018; <https://www.health.govt.nz/our-work/preventative-health-wellness/tobacco-control/vaping-and-smokeless-tobacco>. Accessed February 1, 2020.
53. Etter JF. Gateway effects and electronic cigarettes. *Addiction*. 2017;113(10):1776-1783.
54. Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr*. 2017;171(8):788-797.
55. Zhong J, Cao S, Gong W, Fei F, Wang M. Electronic cigarettes use and intention to cigarette smoking among never-smoking adolescents and young adults: a meta-analysis. *Int J Environ Res Public Health*. 2016;13(5):465.
56. Vanyukov MM, Tarter RE, Kirillova GP, et al. Common liability to addiction and “gateway hypothesis”: theoretical, empirical and evolutionary perspective. *Drug Alcohol Depend*. 2012;123:S3-S17.
57. Centers for Disease Control and Prevention (CDC). Trends in the Prevalence of Tobacco Use National YRBS: 1991—2017. 2018; <https://www.cdc.gov/healthyyouth/data/yrbs/results.htm>. Accessed February 1, 2020.
58. Murthy VH. E-cigarette use among youth and young adults: A major public health concern. *JAMA Pediatr*. 2017;171(3):209-210.
59. U.S. Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General*. Atlanta, GA: : U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health;2016.
60. Food and Drug Administration (FDA). Statement from FDA Commissioner Scott Gottlieb, M.D., on new steps to address epidemic of youth e-cigarette use. 2018; <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620185.htm>. Accessed February 2, 2020.
61. Bauld L, MacKintosh A, Eastwood B, et al. Young people’s use of e-cigarettes across the United Kingdom: findings from five surveys 2015–2017. *Int J Environ Res Public Health*. 2017;14(9):973.
62. Wang M, Wang J-W, Cao S-S, Wang H-Q, Hu R-Y. Cigarette smoking and electronic cigarettes use: a meta-analysis. *Int J Environ Res Public Health*. 2016;13(1):120.
63. Zhuang Y-L, Cummins SE, Sun JY, Zhu S-H. Long-term e-cigarette use and smoking cessation: a longitudinal study with US population. *Tob Control*. 2016;25(Suppl 1):i90-i95.
64. Biener L, Hargraves JL. A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: association with smoking cessation and motivation to quit. *Nicotine Tob Res*. 2014;17(2):127-133.
65. Giovenco DP, Delnevo CD. Prevalence of population smoking cessation by electronic cigarette use status in a national sample of recent smokers. *Addict Behav*. 2018;76:129-134.
66. Gartner CE, Bromberg M. One does not simply sell e-cigarettes in Australia: An overview of Australian e-cigarette regulations. In: Gruszczynski L, ed. *The Regulation of E-cigarettes: International, European and National Challenges*. : Edward Elgar Publishing; 2018.
67. Therapeutic Goods Administration. Poisons Standard. . 2018; <https://www.legislation.gov.au/Details/F2018L00168>. Accessed January 22, 2020.
68. Therapeutic Goods Administration. Liquid nicotine and personal importation for use in electronic cigarettes. . 2014; <https://www.tga.gov.au/behind-news/liquid-nicotine-and-personal-importation-use-electronic-cigarettes#.U7o-O8hiuDQ>. Accessed February 1, 2020.
69. Department of Health. Policy and regulatory approach to electronic cigarettes (e-cigarettes) in Australia. 2018; <https://www.health.gov.au/resources/publications/principles-that-underpin->

- [the-current-policy-and-regulatory-approach-to-e-cigarettes-in-australia](#). Accessed February 1, 2020.
70. Pharmacy Board of Australia. Guidelines on practice-specific issues. 2015; <http://www.pharmacyboard.gov.au/Codes-Guidelines.aspx>. Accessed February 2, 2020.
71. Pharmacy guild of Australia. Excellence. 2015; https://www.guild.org.au/_data/assets/pdf_file/0018/5274/excellence_winter2015_web.pdf. Accessed February 3, 2020.