Nicotine Vaping Product Analysis: Evidence from the University of Wollongong

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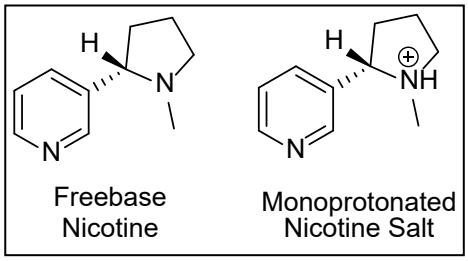
DISCLAIMER: The information presented in this document is informed by research performed at the University of Wollongong examining: the analytical content of nicotine vaping products (NVPs); website analysis to determine products available for importation to Australia; and conversations with existing NVP users. It is not based on clinical evidence of vaping as a tool for smoking cessation. This document aims to assist with guidance for the prescription of nicotine for use in electronic cigarette devices, providing a starting point for conversations with patients, dosage will vary between individuals. It is important to consider that there are two types of patients: new NVP users who wish to trial vaping as a method of smoking cessation; and existing NVP users who likely have established consumption methods and dosages. The approach will vary between these two groups. Vapers will need to be regularly assessed to evaluate if the prescribed dose is suitable and titration to higher or lower concentrations can be achieved.

Nicotine Toxicity

The lethal oral exposure dose of nicotine is controversial with older estimates of 30 - 60 mg in adults recently being replaced by a more generous 500 – 1000 mg.[1] Using 500 mg, the fatal dose for exposure to a 100 mg/ml nicotine solution is as low as 5 ml for an adult, and only 0.8 ml for an average 2-year-old child (12.7 kg).[2,3] These doses are an indicative average with significantly lower doses capable of causing poisoning and morbidity.

Freebase Nicotine vs Nicotine Salts

Freebase nicotine is the bioactive form, however, inhalation of high concentrations of freebase nicotine causes a harsh 'burning' sensation in the throat. Recent years have seen an increase in the availability of nicotine salts, where one of nicotine's basic nitrogens is protonated by the addition of acid.[4] The nicotine salt, which is the form present in tobacco, is less harsh on the throat allowing for higher concentrations of nicotine to be achieved. Most nicotine salt products do not specify the acid used.

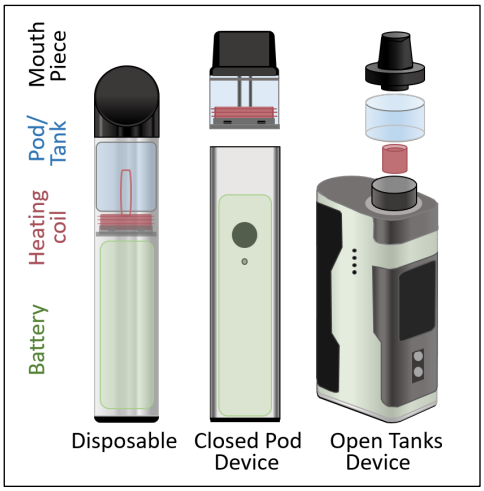


One potential advantage of using higher concentration nicotine salts (available concentration range 20 – 60 mg/ml) is the consumption of lower volumes of vaping fluid, with pharmacokinetics which more closely replicate nicotine from smoking.[5,6] Higher concentration nicotine salts have been shown to produce plasma nicotine concentrations which more closely replicate smoking than freebase nicotine products.[5,7] Low concentrations of toxic compounds (including volatile aldehydes such as formaldehyde) are produced as pyrolysis products when the carrier fluids, propylene glycol (PG) and vegetable glycerine (VG) are heated.[8] Reducing the volume of e-liquid vaporised can reduce exposure to these compounds and other flavouring molecules with unknown toxicity.[8] The pharmacokinetic profile of nicotine following inhalation from electronic cigarettes is affected not only by the type and concentration of nicotine present but also by the inhalation pattern used, vaping experience of the user and the electronic cigarette device efficiency.

Open vs Closed E-Cigarette Devices

Open system devices include all electronic cigarettes which need to be manually filled with e-liquid before use (e-liquid refills below). Closed system devices include pods and disposables where the e-liquid is enclosed in a sealed container. Closed system devices are generally considered safer due to decreased risk of contact with liquid nicotine through accidental oral or dermal exposure.

- Open system devices require users to refill the e-cigarette with e-liquid and replace the heating coils.
- Pod-style devices require users to exchange the pod (which includes a coil) once the e-liquid has run out. Pods come in a range of shapes and are only compatible with specific devices.
- Disposable devices are thrown away once out of e-liquid or when the battery runs flat (cannot be refilled or recharged).



Flavours

Most of the variability among the thousands of e-liquid products available arises from the variation in flavours. There are currently more than 20,000 unique products available and even flavours with similar names can have significant variation in the actual flavouring molecules present. There is a specific list of banned flavour molecules available in the TGO110. The most common flavours available for sale (2017 study) are fruit-based (34%), tobacco (16%) and dessert flavoured (10%).[9] GPs are able to specify flavour on a prescription if they wish but this is not required. If the flavour is not explicitly provided on a prescription, new or existing NVP users should be notified that depending on how they choose to fill their prescriptions, local pharmacies vs online pharmacies or online shops, they may only have access to a selected range of available flavours. Existing NVP users will likely already have a preferred flavour and may wish to continue to import this product through use of the personal importation scheme.

Domestic Purchase vs Personal Importation Scheme

Pharmacies (in store purchase) will most likely have a narrower range of products available (nicotine concentrations (salt and freebase), types of pods, and flavours) than their online counterparts – it is important to confirm the availability and concentrations of these products before prescribing. A wider range of products are available via online pharmacies or for import through the personal importation scheme, this may be particularly relevant for existing NVP users who have preferred devices, concentrations and flavours which may not be available domestically. If pod-based devices are recommended, users should be warned before purchasing their device to ensure it is compatible with available pods.

Types of Available NVPs

Disposable Devices

- Advantages: limits accidental oral and dermal exposure to nicotine; no handling of nicotine e-liquid solution; no requirement to replace coils.
- Disadvantages: these devices contain a liquid soaked material wick, rather than a coil directly exposed to e-liquid, this can cause scorching of the wick potentially releasing additional harmful chemicals; batteries are not rechargeable which produces significant waste.
- Only available as nicotine salts.
- Volumes range from 1 – 5 ml (dependent on brand and 'number of puffs').
- Common nicotine salt concentrations: 50 and 60 mg/ml (dependent on brand).

SUGGESTED STARTING POINT FOR NEW NVP USERS: Not recommended as an initial vaping method due to high nicotine concentrations, non-rechargeable batteries and potential added exposure to toxic molecules.

Nicotine Pods

- Advantages: limits accidental oral and dermal exposure to nicotine; simple to use as only replace cartridge; no handling of nicotine e-liquid solution; no requirement to replace coils.
- Disadvantages: most brands only have a limited number of concentrations available (often lowest is 30 mg/ml) making titrating down nicotine with these products more difficult.
- Volumes range from 0.7 – 4 ml (dependent on brand and device), sold in packs of 3/4/5 pods.
- Almost all pods currently available for sale are nicotine salts.
- Common nicotine salt concentrations: 20, 30, 35, 40, 50 and 60 mg/ml (dependent on brand).

SUGGESTED STARTING POINT FOR NEW NVP USERS: Start at 20 mg/ml for light smokers (<20 cigarettes per day) and 35 mg/ml nicotine salt pods for heavy smokers (>20 cigarettes per day). These concentrations are commonly available in pod form with a step up to higher concentrations available for most brands if required. Follow up discussion regarding titrating up concentration if usage exceeds 1 pod (~2 ml) per day. Three-month supply estimate: 100 pods (~200 ml).

e-Liquid Refills

Ready-made solutions

- Advantages: wide range of concentrations available (both freebase and salt).
- Disadvantages: risk of accidental exposure to nicotine whilst filling device (risk further increased at higher concentration).
- Common volumes: 10, 30, 60, 100 and 120 ml.
- Common concentrations for freebase nicotine: 3, 6, 12 and 18 mg/ml (range 3 – 24 mg/ml).
- Common concentrations for nicotine salts: 24, 35, 48, 50, 60 mg/ml (range 18 – 70 mg/ml).

SUGGESTED STARTING POINT FOR NEW NVP USERS: Start at 6 mg/ml freebase nicotine (allows titration up or down as required). Estimate volume usage for 6 mg/ml freebase nicotine is 4-6 ml per day.[10] Three-month supply estimate: 600 ml. For heavy smokers, nicotine salts may be preferable. It is suggested that nicotine salts are started using a closed-pod system to decrease risk of accidental exposure to nicotine.

Dilute your own

- Method involves importation/pharmacy purchase of high concentration nicotine which can be mixed with nicotine free solutions by the end-user.
- Advantages: allows flexibility in nicotine concentration; more cost effective; larger choice of flavours.
- Disadvantages: this method has the highest risk of accidental exposure to high concentrations of nicotine; containers have open-necks to allow for liquid to be syringe transferred which results in increased risk of accidental dermal and oral exposure during the dilution process.
- Volumes range from 100 ml - 1 L.
- Concentration: 100 mg/ml freebase or nicotine salts, higher concentrations banned (TGO110).

SUGGESTED STARTING POINT FOR NEW NVP USERS: This pathway is not recommended as an initial vaping method due to high nicotine concentrations. For existing NVP users currently using this method conversations should include training on best practice for syringe transfer, ensuring children are not present whilst the product is open, and use of appropriate PPE (especially gloves).

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Declaration of Interest

Authors report no conflict of interest.

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