Australian Government
Department of Health
Therapeutic Goods Administration

Nicotine vaping products, the NZ smoking cessation experience

Practical tips for Australian prescribers

Chair

Adj Professor John Skerritt, Therapeutic Goods Administration, Department of Health

Panel

Dr Natalie Walker, Associate Professor in Population Health at the National Institute for Health Innovation, University of Auckland, NZ

Dr George Laking, medical oncologist at Auckland and Northland District Health Boards, NZ

Dr Hayden McRobbie, Professor at National Drug and Alcohol Research Centre, UNSW, Consultant in Lifestyle Medicine, Rotorua, NZ

TGA Health Safety Regulation

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Welcome and introduction

Adjunct Prof John Skerritt

Deputy Secretary

Australian Department of Health's, Therapeutic Goods Administration (TGA)

TGA Health Safety Regulation

Meet the panel

Dr Natalie Walker is Associate Professor in Population Health at the National Institute for Health Innovation, University of Auckland, New Zealand, and Director of the Centre for Addiction Research, Faculty of Medical and Health Sciences. Her primary area of interest is the conduct of phase III pragmatic community-based clinical trials, particularly in the field of smoking cessation. She has published on e-cigarettes, cytisine, varenicline, nicotine reduction, exercise, hypnotherapy, and incentives for smoking cessation.

Dr George Laking is a medical oncologist at Auckland and Northland District Health Boards. He has spent many years in treatment of lung cancer, and this led to his interest in tobacco control. George is the Chair of End Smoking New Zealand, and is involved in Māori Health as a past Chair of Te ORA (the Māori Medical Practitioners' Association), as a member of the Māori Health Committee of the RACP, and a board member of Hei Ahuru Mowai Maori Cancer Leadership Aotearoa.

Professor Hayden McRobbie, MB ChB (Otago), PhD (London), FASLM

Hayden has worked in the field of behavioural medicine for more than 20 years and is a senior clinician with a specialist interest in lifestyle medicine. He holds a medical degree from the University of Otago, a doctorate from the University of London, and is Professor in Public Health Interventions at the National Drug and Alcohol Research Centre, UNSW, and a Fellow of the Australasian Society for Lifestyle Medicine. Hayden has played a key role in Tobacco Control in New Zealand, and his current work includes prevention and management of long-term conditions, with a particular focus on improving health outcomes for Māori in New Zealand.

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Clinical trials using nicotine vaping products and the typical quitting journey of a smoker

Associate Professor Natalie Walker

Associate Professor in Population Health,

NIHI Programme Leader – Tobacco and Addictions,

Director, Centre for Addiction Research, Faculty of Medical and Health Sciences

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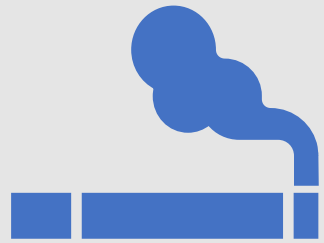
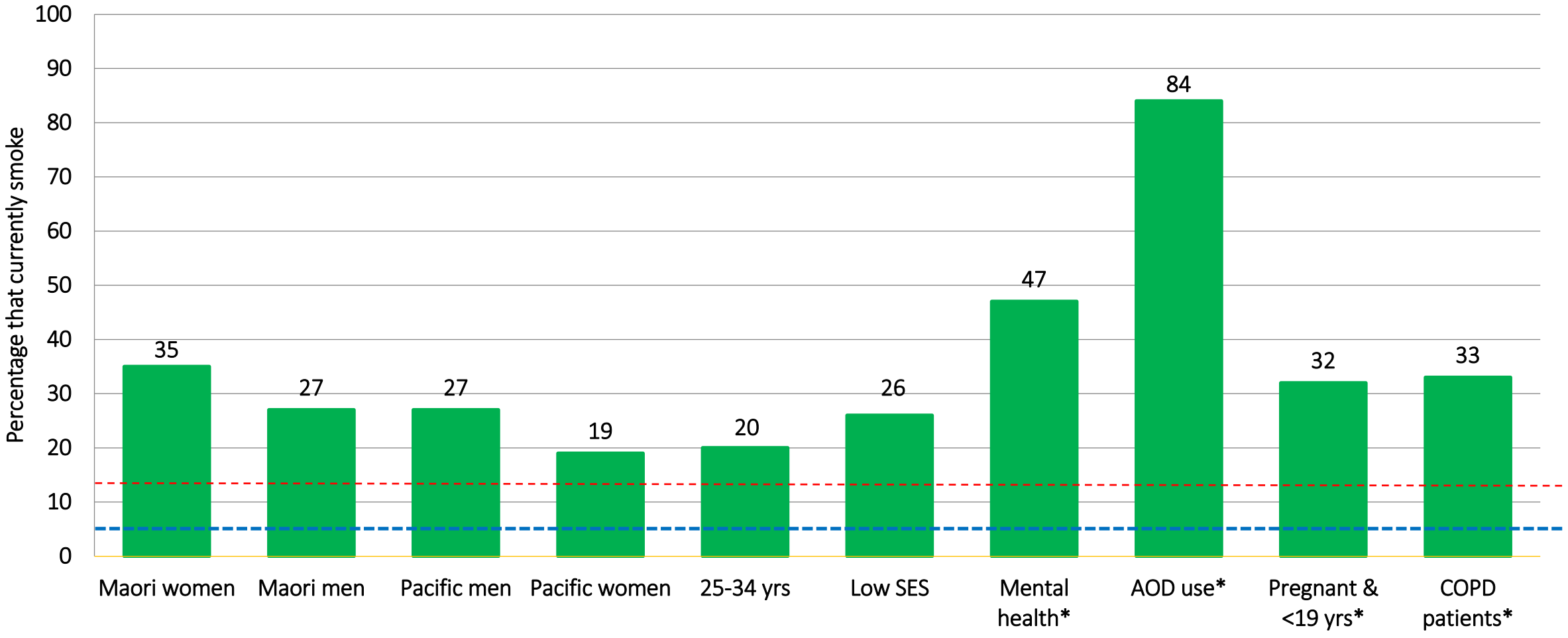
Nicotine vaping products: the New Zealand smoking cessation experience

Clinical trials using nicotine vaping products and the typical quitting journey of a smoker



Associate Professor Natalie Walker, University of Auckland

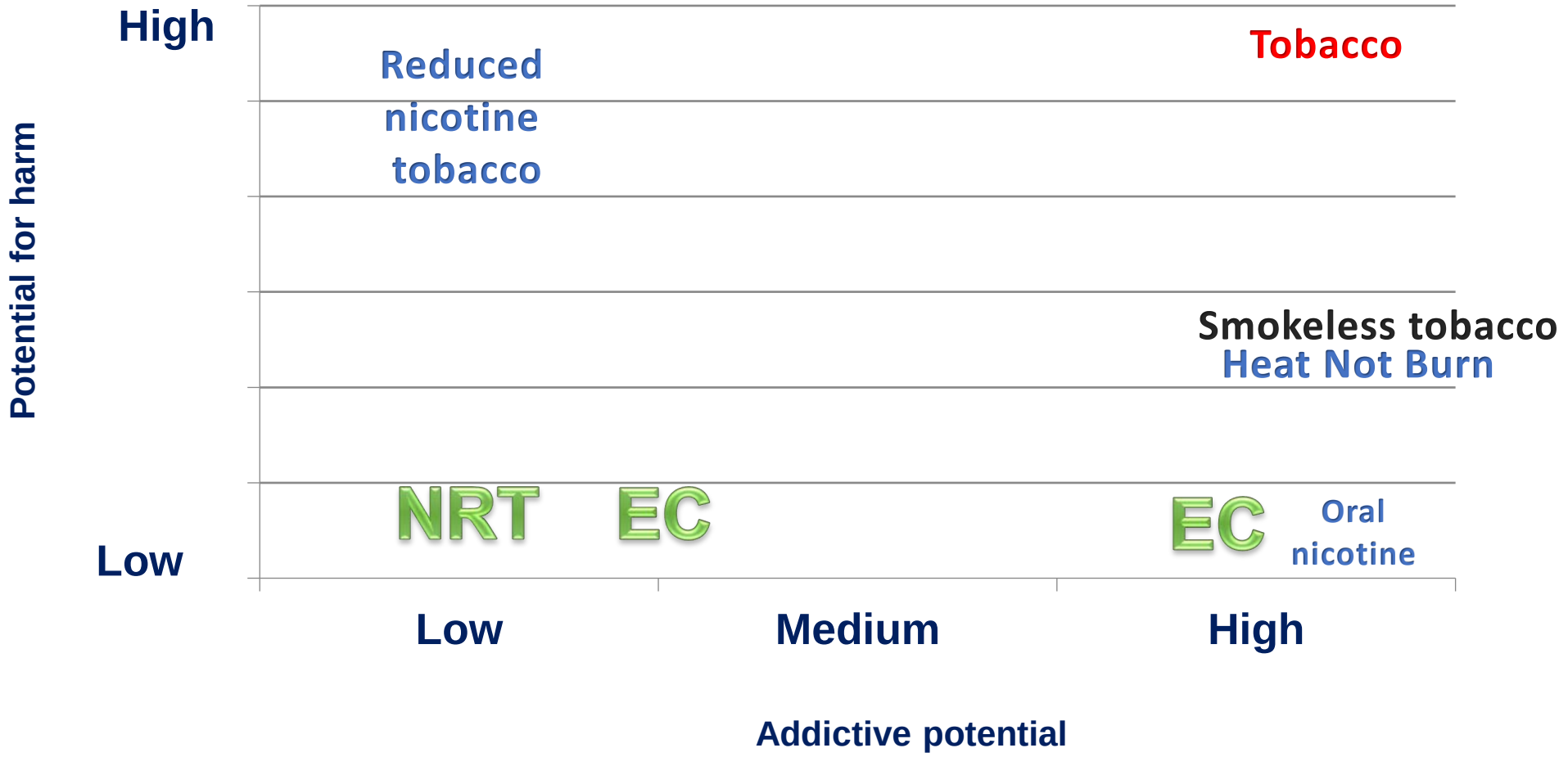
Prevalence of current smoking in New Zealand



~535,000 NZ adults (13%) were current smokers (smoked more than 100 cigarettes in lifetime and currently smoke at least once a month)

*Source: NZ Health Survey 2019/20: 15 yrs and older. *Data from other sources*

The Future: Reduced Harm Products

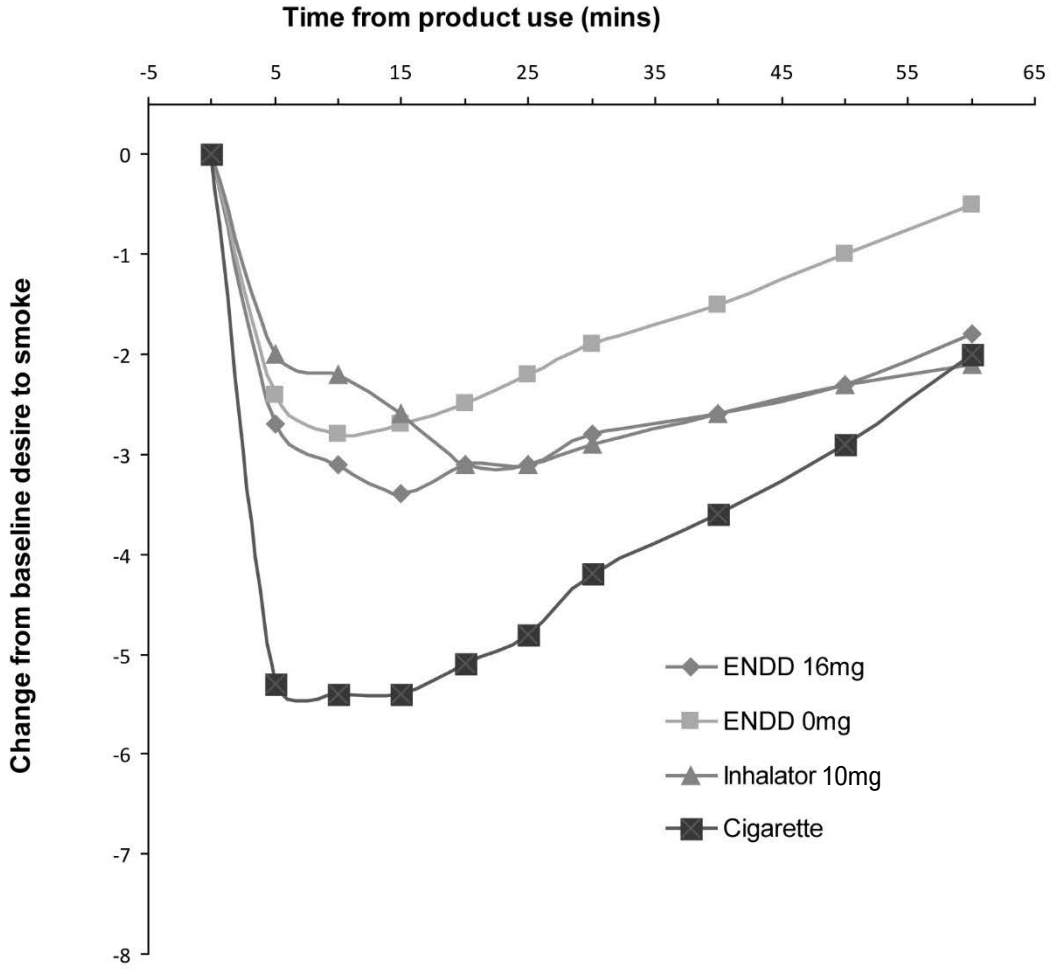


E-Cigarettes

WIRED → ASCEND → ASCEND2 → CESS@TION

Q1: What's in them, do they help with craving, and do people like them?

Change in desire to smoke from baseline over the first hour after each product use.



At this time in NZ nicotine containing e-cigarettes were considered a medicine: so were not permitted to be sold or advertised, or to make a cessation claim.

Bullen C, McRobbie H, et al. *Tobacco Control* 2010: 19; 98-103.

Q2: Do they help people quit smoking?
Q3: Are there any side-effects?
Q4: Does nicotine need to be in the device?

- Under ‘real world’ conditions
- Heterogeneous population

- Under ‘ideal’ conditions
- Homogeneous population

Pragmatic trial (Effectiveness)

Explanatory trial (Efficacy)

General population pragmatic trials

	ASCEND	ASCEND 2
Recruitment	2011-13	2016-18
Research questions	Are nicotine e-cigarettes more effective than nicotine patches? Are nicotine e-cigarettes more effective than nicotine-free e-cigarettes?	Is combining a nicotine patch with a nicotine e-cigarettes more effective than combining a nicotine patch with a nicotine-free e-cigarettes? Is combining a nicotine patch with a nicotine e-cigarettes more effective than a nicotine patch?
Sample size	657	1124
Māori	213 (32%)	451 (40%)
	Bullen et al. Lancet 2013	*Walker et al. Lancet Respir Med 2019*

Total N=1,781

First e-cigarette trials

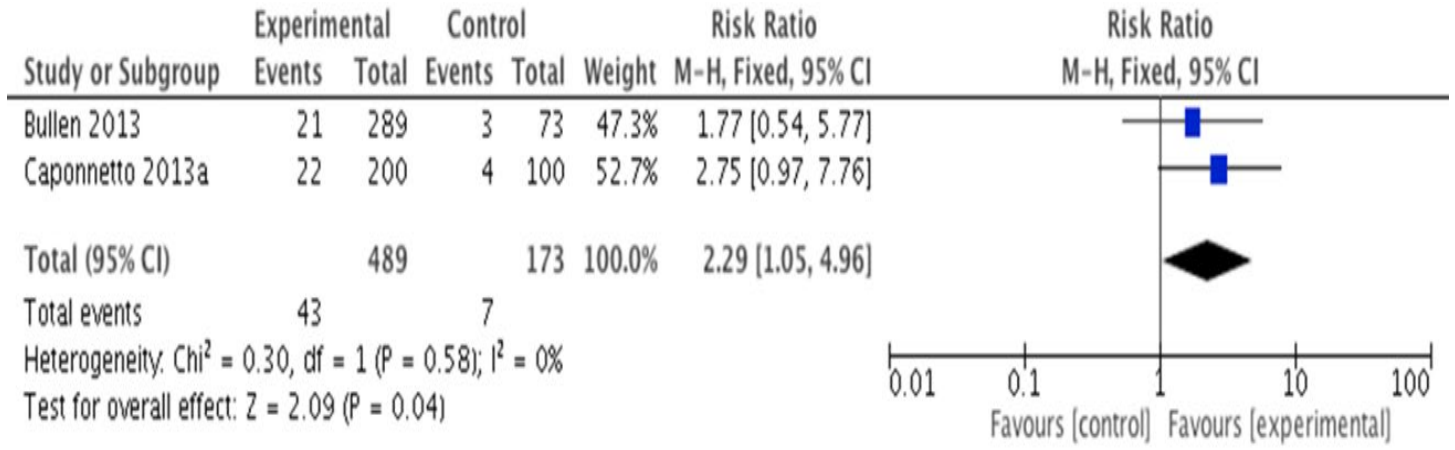
	ECLAT - Caponnetto (2013)	ASCEND - Bullen (2013)
Population	Unmotivated to quit	Motivated to quit
Inclusion criteria	≥10cpd for at least 5 years, 18-70 years	≥10cpd for last year, ≥18 years
Brand	Categoria	Elusion
Location	Clinic-based	National
Sample size	300 (1:1)	657 (4:4:1)
Intervention	7.2 mg E-cig 7.2-5.4 mg E-cig 0 mg E-cig No behavioural support	16mg E-cig 21mg NRT patch 0mg E-cig Minimal behavioural support
Intervention period	12 weeks	13 weeks (includes one week pre-quit)
Power	75%	80%
Primary outcome	Verified continuous abstinence at 6 months	Verified continuous abstinence at 6 month

Findings

	ECLAT - Caponnetto (2013)	ASCEND - Bullen (2013)
Continuous abstinence at 6 months	7.2 mg E-cig: 12% 7.2-5.4 mg E-cig: 10% 0 mg E-cig: 5% (NS)	16mg E-cig: 7% 21mg NRT patch: 6% 0mg E-cig: 4% (NS)
Cigarettes per day	Significantly reduced	Significantly reduced
Time to relapse (median)*	-	16mg E-cig: 35 days* 21mg NRT patch: 14 days 0mg E-cig: 12 days*
Adverse events	No difference in frequency between groups	No difference in frequency between groups

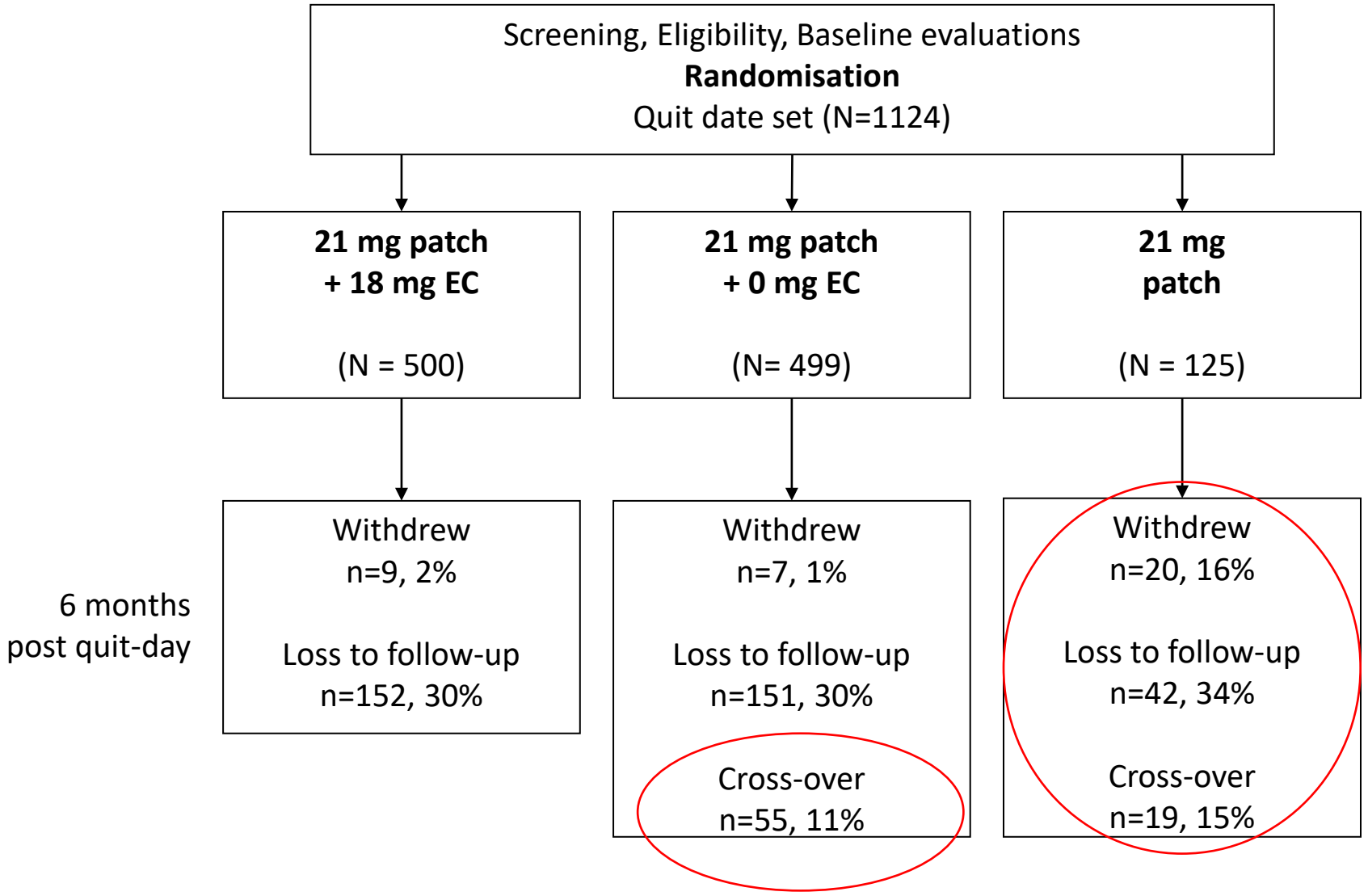
Quitlines and telephone counselling: 10%: SMS text interventions: 9%

Cochrane review

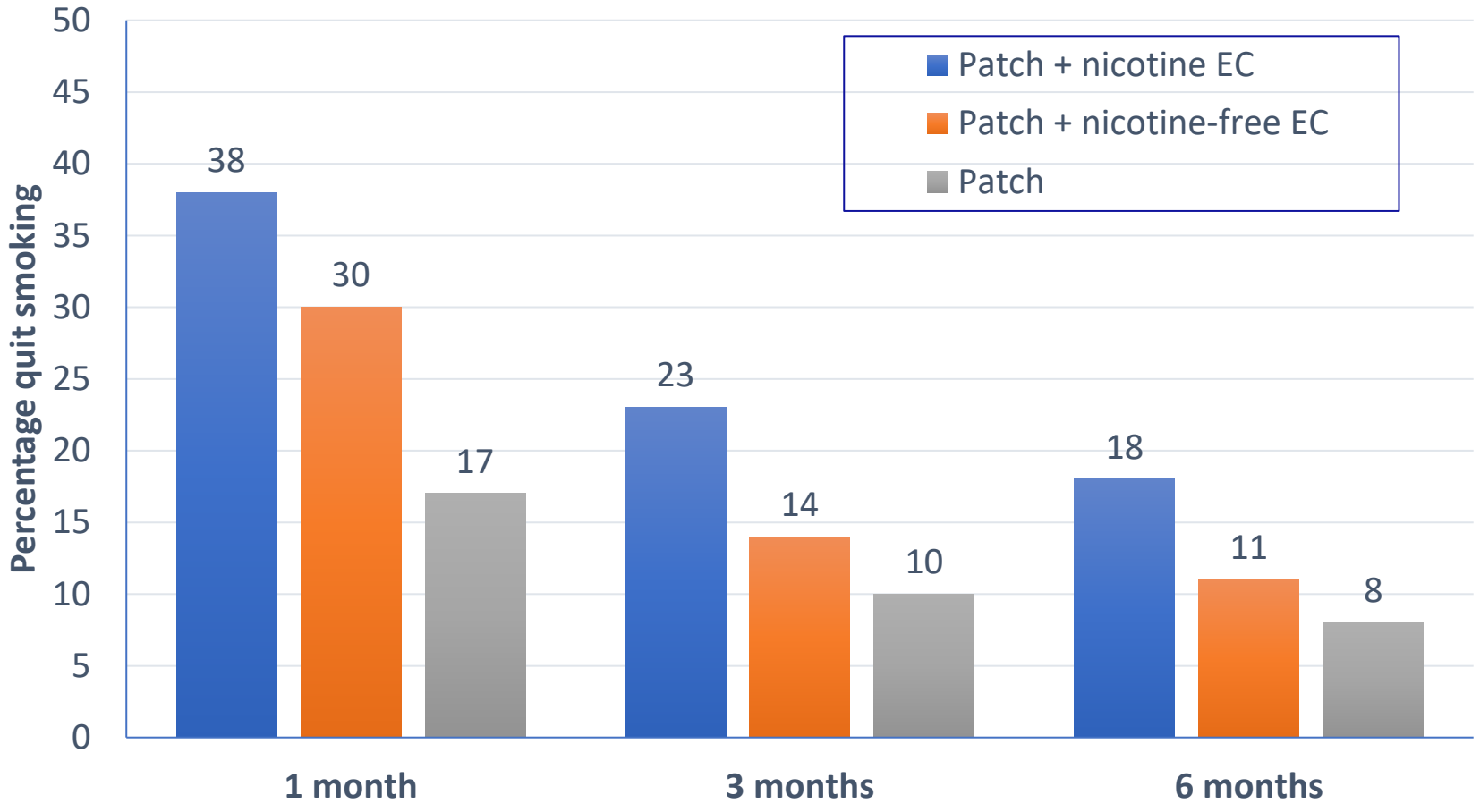


Six month continuous abstinence from smoking when using e-cigarettes with nicotine compared to e-cigarettes with no nicotine

ASCEND 2 trial



Self-Reported Continuous Abstinence*



*Since quit day, allowing ≤5 cigarettes in total

Summary

Self-reported smoking abstinence: in favour of patches plus nicotine e-cigarettes for both comparisons at all time points.

6 month self reported quit rates	N	Nicotine EC	0mg EC	NRT
ASCEND-II	1124	18%	11%	8%
Hajek, 2019 (UK)	886	35%		25%

Safety findings are consistent with previous e-cigarette trials and cohort study findings.(Hajek 2019, Hartmann-Boyce 2021)

Dual use: Use of smoked tobacco together with other nicotine products

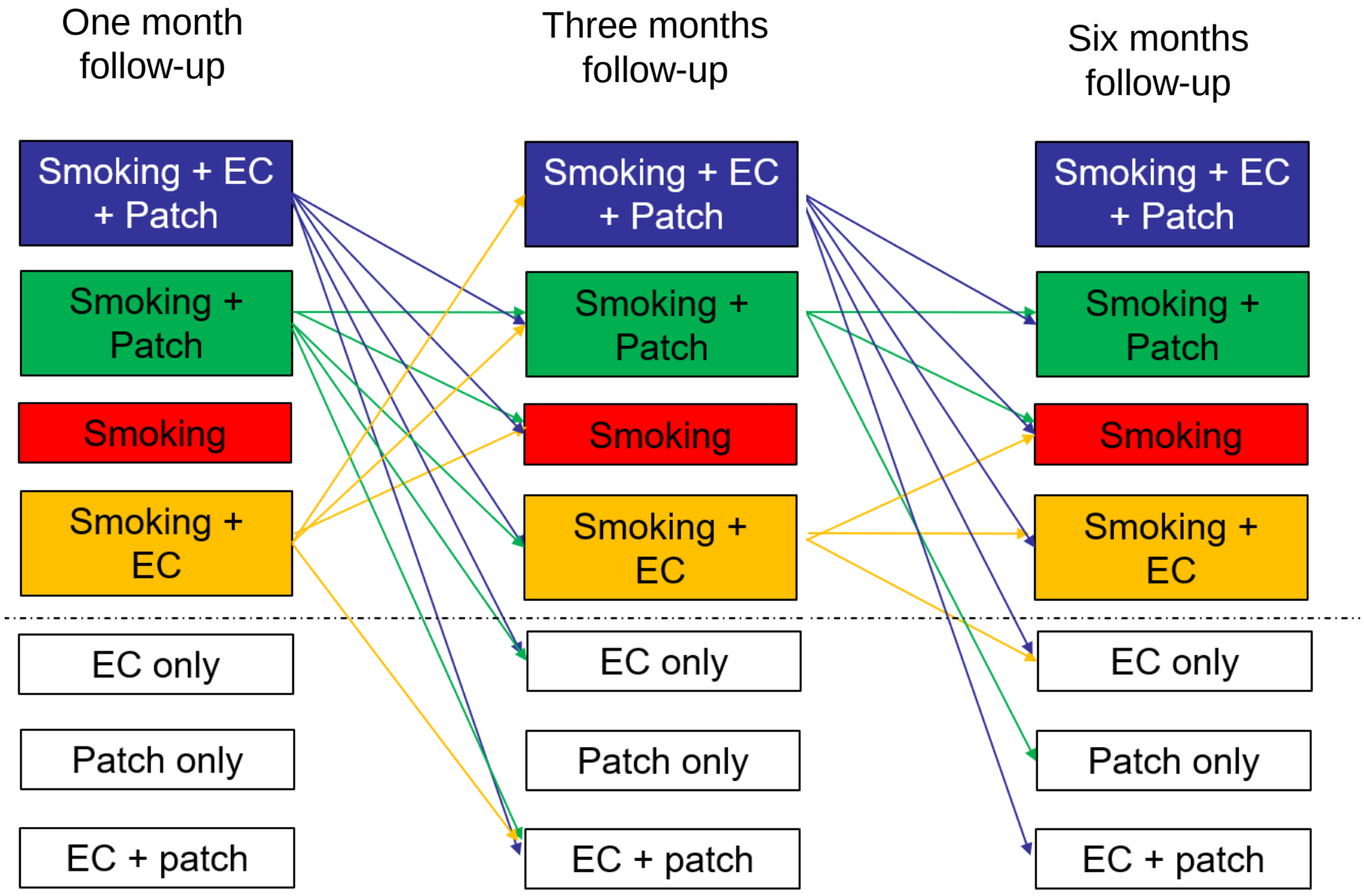
Dual use with NRT was more common, than dual use with e-cigarettes: consistent with data from England.

Very few people were sustained dual users (4% at six months)

Dual users were more cigarette dependent, so behavior likely due to insufficient nicotine replacement

Dual use is a transient state: people shift in and out of the state over time, and within different use states

Patch plus nicotine e-cigarette group



61 studies in 16,759 adults who smoked.

“More people probably stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement therapy (4 studies, 1924 people), or nicotine-free e-cigarettes (5 studies, 1447 people).”

“Nicotine e-cigarettes may help more people to stop smoking than no support or behavioural support only (6 studies, 2886 people).”

Side effects with nicotine e-cigarettes

- Throat/mouth irritation
- Dry cough
- Headache*
- Nausea

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Vaping in context

George Laking MD PhD FRACP,
Medical Oncologist
Chair, End Smoking New Zealand

TGA Health Safety Regulation

14 October 2021

Vaping in Context

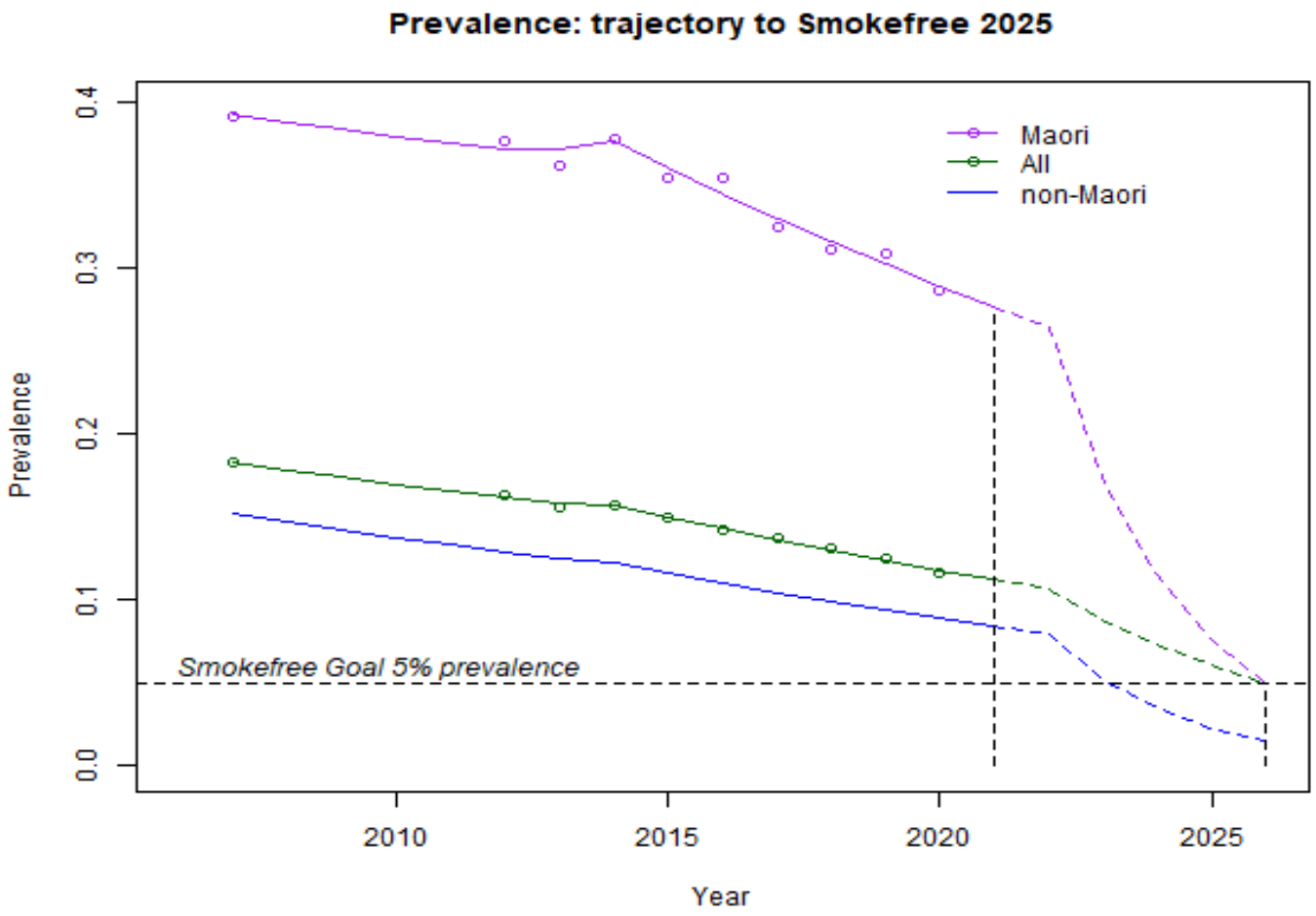
George Laking MD PhD FRACP, Medical Oncologist
Chair, End Smoking New Zealand

These are personal opinions

I previously accepted an honorarium from GSK to present this material

October 2021

Smokefree Aotearoa 2025

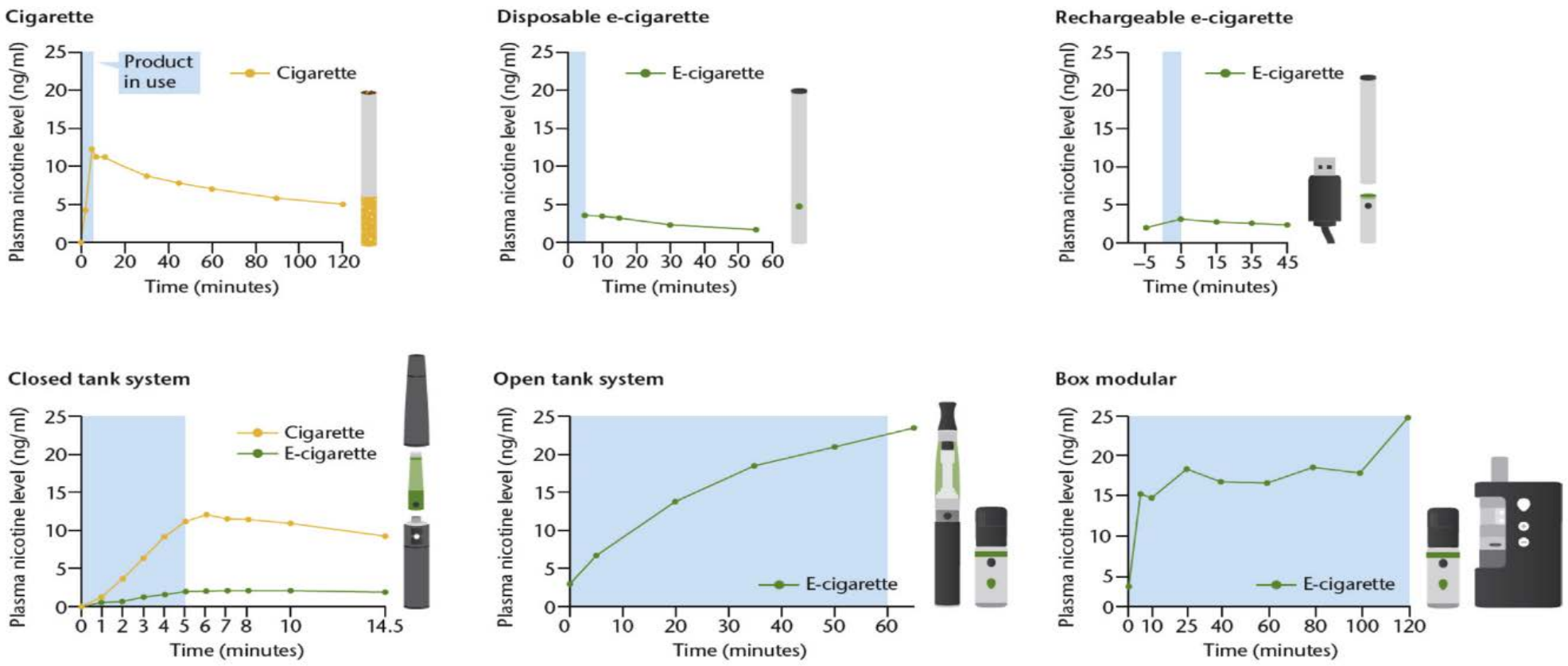


Goal is 5% Prevalence

Across 2011 to 2021, prevalence of daily smoking fell from 0.17 to 0.12 of all adults, a 29 percent change. The goal requires a further 58 percent fall in half the time (blue curve).
The challenge is greater for Māori, who had a 23 percent fall in prevalence, but who now need a further 83 percent fall (purple curve).

Vaping as a Health Technology

Acceptability: rapid onset nicotine pharmacokinetics



Fearon, I. M. et al. Nicotine pharmacokinetics of electronic cigarettes: A review of the literature. Regulatory Toxicology and Pharmacology 100, 25–34 (2018).

Vaping as a Health Technology

- Effectiveness
  - Moderate strength of evidence, small absolute effect size
  - Potential to improve in a favourable regulatory environment
  - Potential product improvement
- Efficiency
  - Cost-effective for smoking cessation, since people self-fund
- Equity
  - Smoking is highly inequitable, vaping may mitigate this
- Timeliness
  - Available on demand here and now

How safe are electronic cigarettes?

- Polarised opinion
- The e-cigarette is not a medicine, it is a presentation
  - Depending on what is internalised, vaping could be harmless or lethal
  - In itself the electronic cigarette is neutral
- There are no long term safety studies
- Toxicology suggests it would be a great surprise if e-cigarettes turned out to be as hazardous as combustibles in the long term

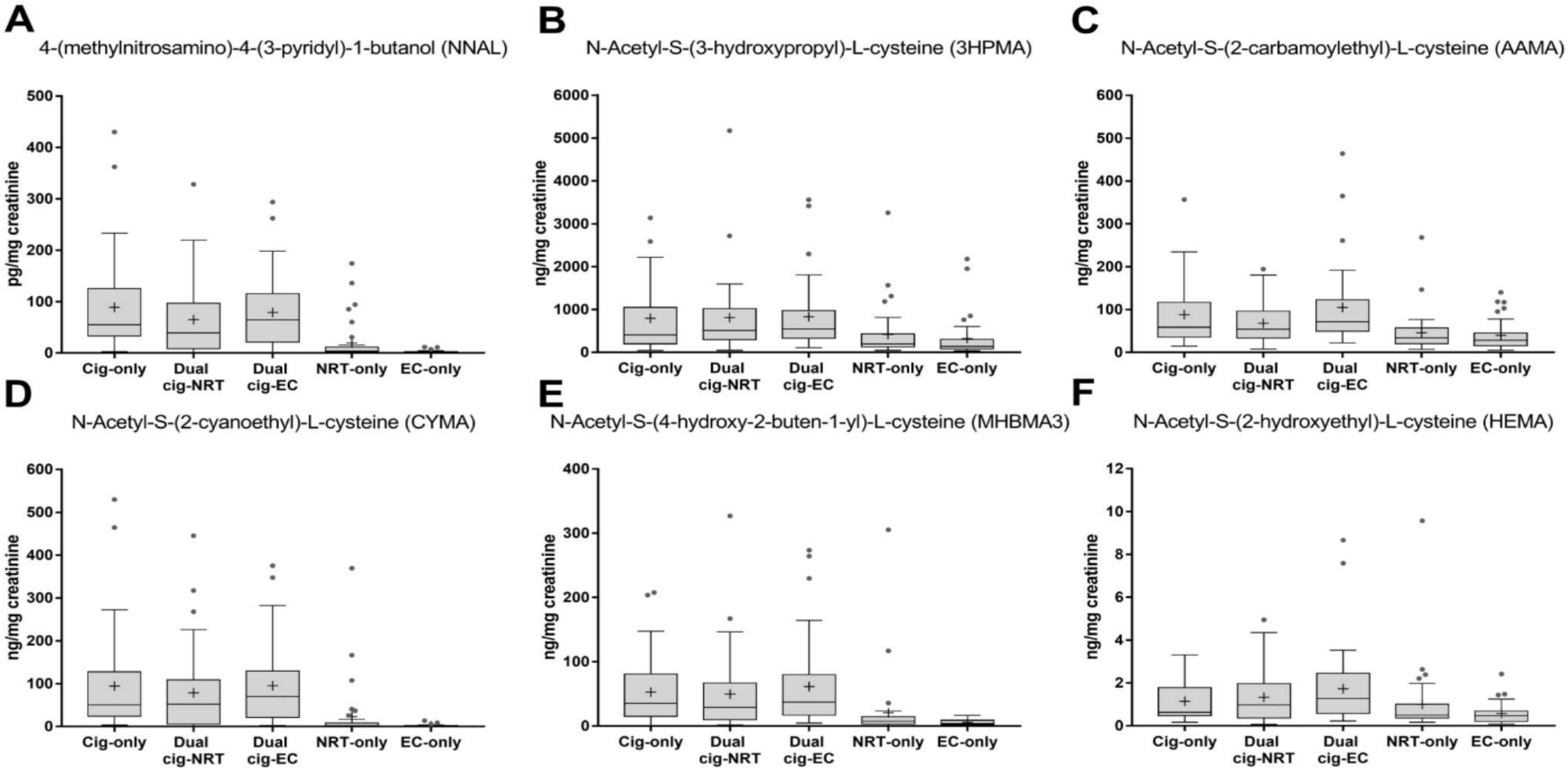
EVALI

- Adulteration of cannabis-containing liquids with vitamin E acetate
- Vitamin E acetate in 94% of bronchoalveolar lavage samples of EVALI patients, and 0% of healthy controls
- Vitamin E was used to thicken cannabis oil
- No such thickener is used for nicotine-containing e-liquids
  - Blount, BC., et al. "Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI." New England Journal of Medicine 382.8 (2020): 697-705.

Can we make the uncertainty tolerable?

- Context is the known danger of smoking
- Tobacco smoke
  - >7000 chemicals, >69 carcinogens
  - Generated by pyrolysis and oxidation of a complex substrate at ~900°C
- E-cigarette coil
  - 200—250°C Celsius: a different realm of chemistry
  - E-cigarette aerosols have been shown to contain carcinogens and toxicants acetaldehyde, acrolein, diacetyl, and formaldehyde
  - Levels in cigarette smoke are much higher than in vaping under realistic conditions
    - Farsalinos, K. E. & Gillman, G. Carbonyl emissions in e-cigarette aerosol: A systematic review and methodological considerations. Frontiers in Physiology vol. 8 (2018).

Biomarkers



Shahab, L. et al. Nicotine, carcinogen and toxicant exposure in long-term e-cigarette and nicotine replacement therapy users: a cross-sectional study Europe PMC Funders Group. Ann Intern Med 166, 390–400 (2017).

Regulatory environment

- Regulation determines direction of travel through a Gateway
- Movement must always be towards the less harmful
- Because vaping is a new technology, regulation can be imposed and evolve free of the dead weight of historical expectation
- Vaping has a product improvement pathway
- We must also think about people who do not smoke and are not addicted to nicotine, especially children and adolescents
- New Zealand policy has kept a balance
  - Smokefree Environments and Regulated Products Act 1990

VAPING TO QUIT SMOKING.

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Nicotine Vaping products

Some practical considerations

Hayden McRobbie
Professor, NDARC, UNSW, Sydney Australia
Consultant in Lifestyle Medicine, Lakes District Health Board, Rotorua, New Zealand

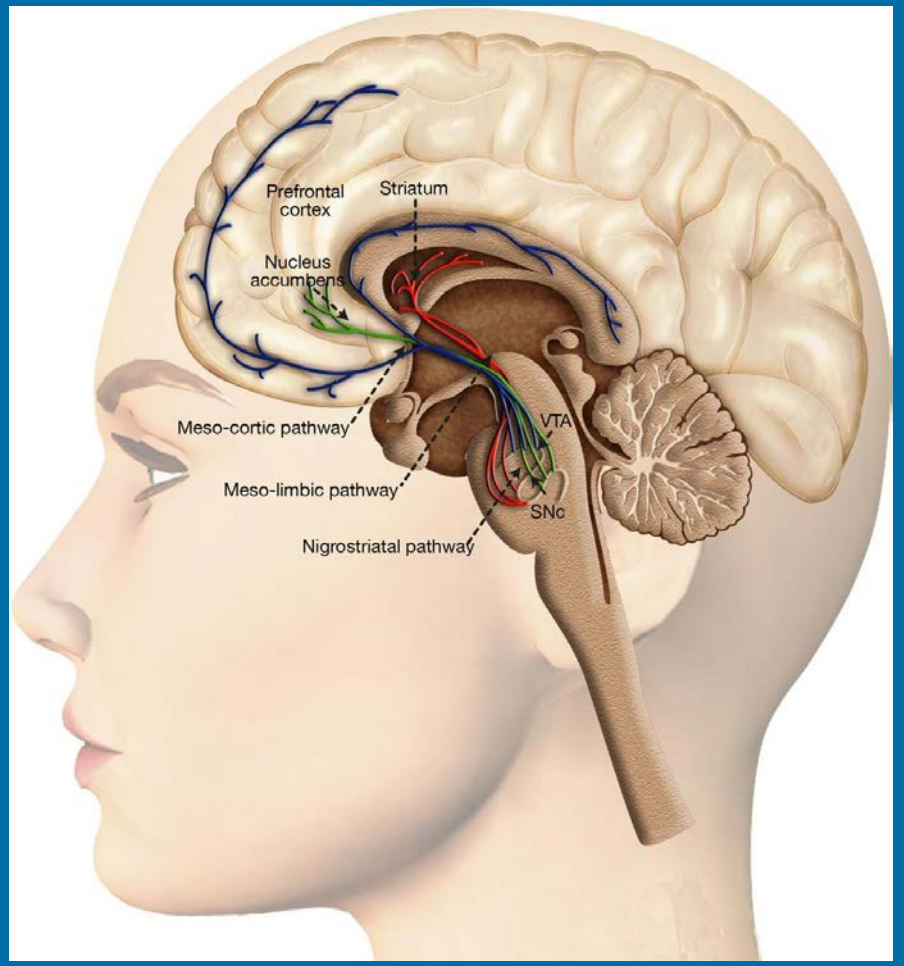
TGA Health Safety Regulation

14 October 2021

Disclosures

- In the past 3 years, I have received:
  - Honoraria for speaking at smoking cessation meetings and attending advisory board meetings that have been organised by Pfizer
  - Grants from the National Institute of Health Research (UK), National Health and Medical Research Council (Australia), and the Health Research Council (New Zealand)
  - I have no links with the manufacturers of tobacco or vaping products.

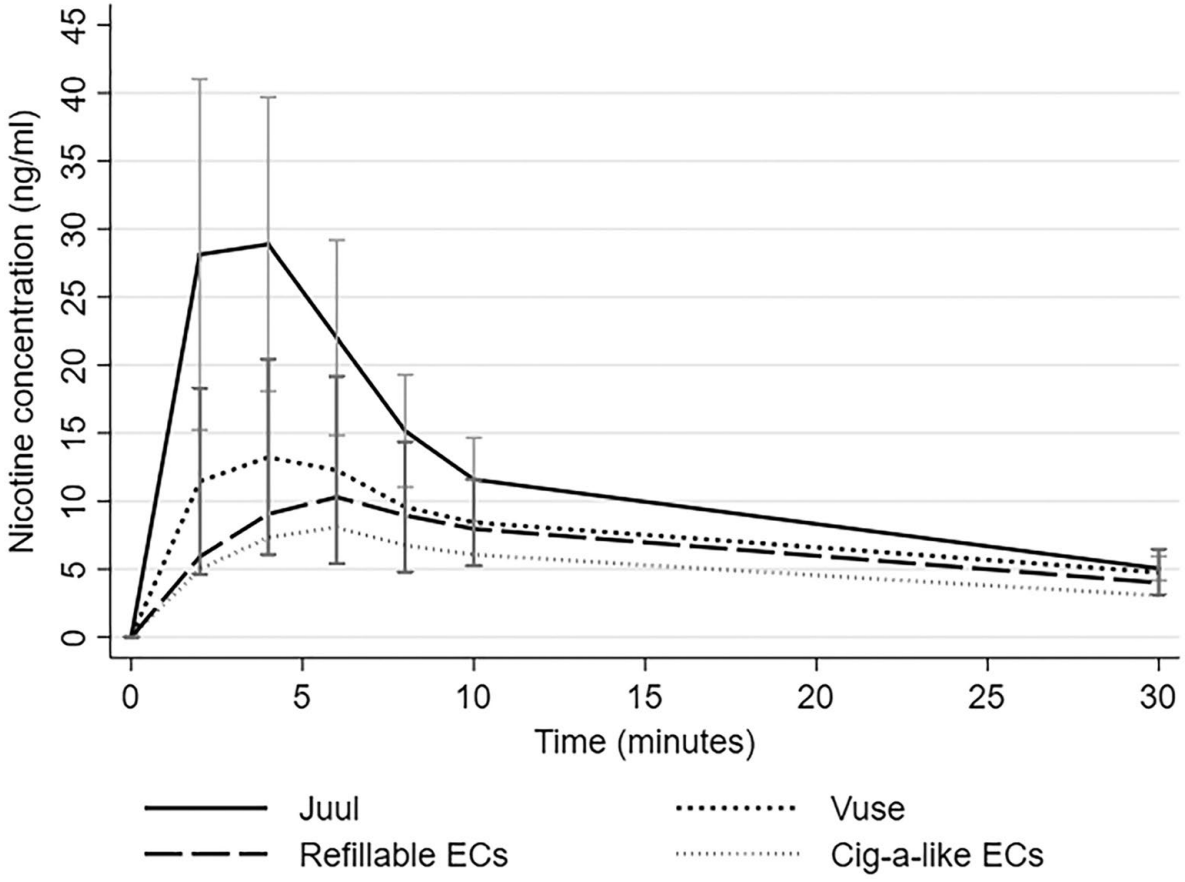
Nicotine

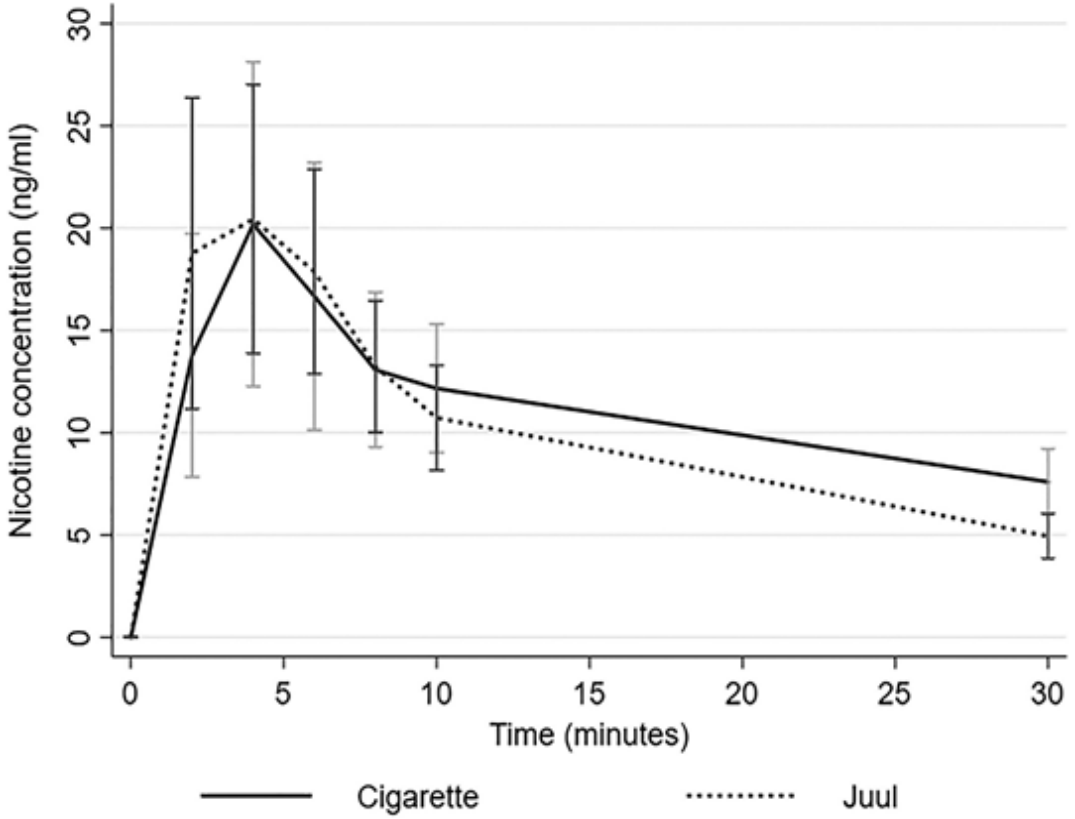


- Contained in the tobacco leaf in as a nicotine salt
- Increasing alkalinity converts it to a freebase form (more readily absorbed)
- Acts on the mesolimbic dopaminergic pathway (‘rewards’ behaviour)

People smoke for the nicotine but die from the tar

Nicotine delivery from vaping products





•Hajek, P., Pittaccio, K., Pesola, F., Myers Smith, K., Phillips-Waller, A., and Przulj, D. (2020) Nicotine delivery and users' reactions to Juul compared with cigarettes and other e-cigarette products. Addiction, 115: 1141– 1148. https://doi.org/10.1111/add.14936.

Nicotine delivery

- The amount of nicotine delivered to the user depends on various factors
  - the **concentration of nicotine** in the e-liquid
  - **other constituents of the e-liquid (such as the ratio of propylene glycol to vegetable glycerine)**
  - **heating of the e-liquid**
  - **technique of the user**

Nicotine: Freebase vs. salts

- Freebase
  - Bioactive form
  - Often experience as harsh or burning
  - Often used in tank-type vaping products
- Nicotine salts
  - The form that is present in tobacco
  - Less harsh
  - Allows for higher concentrations to be used
    - …and subsequently lower volumes
      - …and subsequently potentially less exposure to toxicants

Practice is important

Nicotine delivery after trying an e-cigarette for the first time

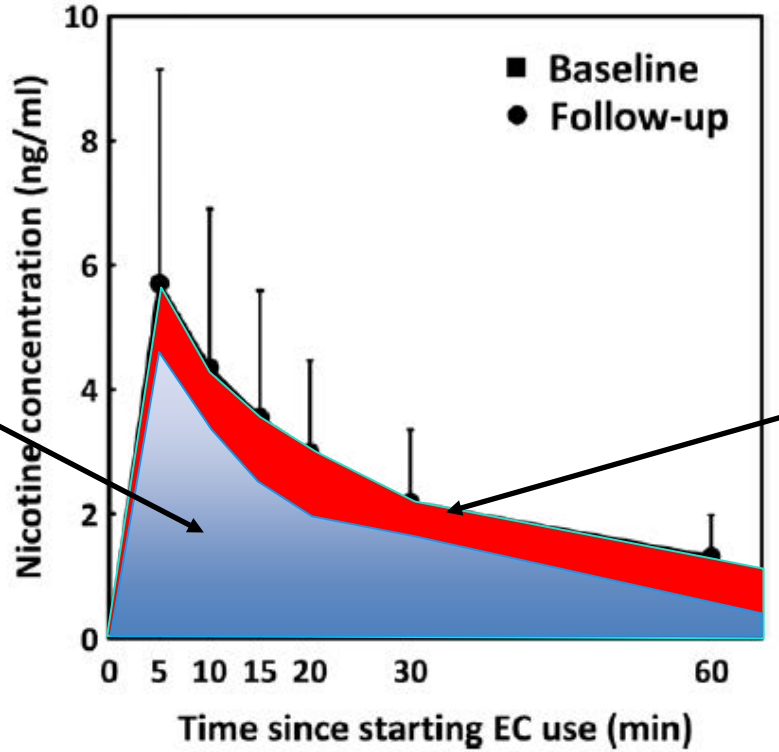


Figure 1. Plasma nicotine concentrations after 5 min of ad lib electronic cigarette use at baseline and at 4-week follow-up.

Nicotine delivery after 4-weeks of practice

Hajek et al Nicotine Tob Res 2015;17:175–9.

Prescribing nicotine

- Need to consider what nicotine concentration and type of product being used
  - Cartridges/pods
  - Pre-mixed or concentrated nicotine
- Consumers will only be able to access a product with a concentration matching that specified in their prescription.
- Individuals may import up to a three month supply of medicines per import (based on the maximum daily dose recommended by the manufacturer), but not exceed 15 months supply in a 12-month period.
- They must arrange for a copy (scan or photocopy) of their prescription to be enclosed with the package the product is sent in.

Suggested dosing

Vaping devices		Cigarette smoking equivalent		Freebase nicotine	Nicotine salts
High Vapour Production Open tank devices	**Medium Vapour Production** All devices	No longer smoking		Nicotine free solution - 0 mg/mL	
		1-6 cigarettes/day	**Light**	3 mg/mL	≤ 10 mg/mL**
		6-12 cigarettes/day	Smoker type	6 mg/mL	20 mg/ml
		12-20 cigarettes/day		9 mg/mL	25 mg/mL
Low Vapour Production Pod devices		20-25 cigarettes/day		12 mg/mL	30 mg/mL
		25+ cigarettes/day		18 mg/mL	35 mg/mL
		2+ packs/day	**Heavy**	24-36 mg/mL*	50-60 mg/mL

* Harsh throat hit for concentrations above 20 mg/ml, throat hit of 6 mg/ml free base similar to 20-25 mg/mL nicotine salts
** Uncommon salt concentrations.
Suggested starting concentrations highlighted

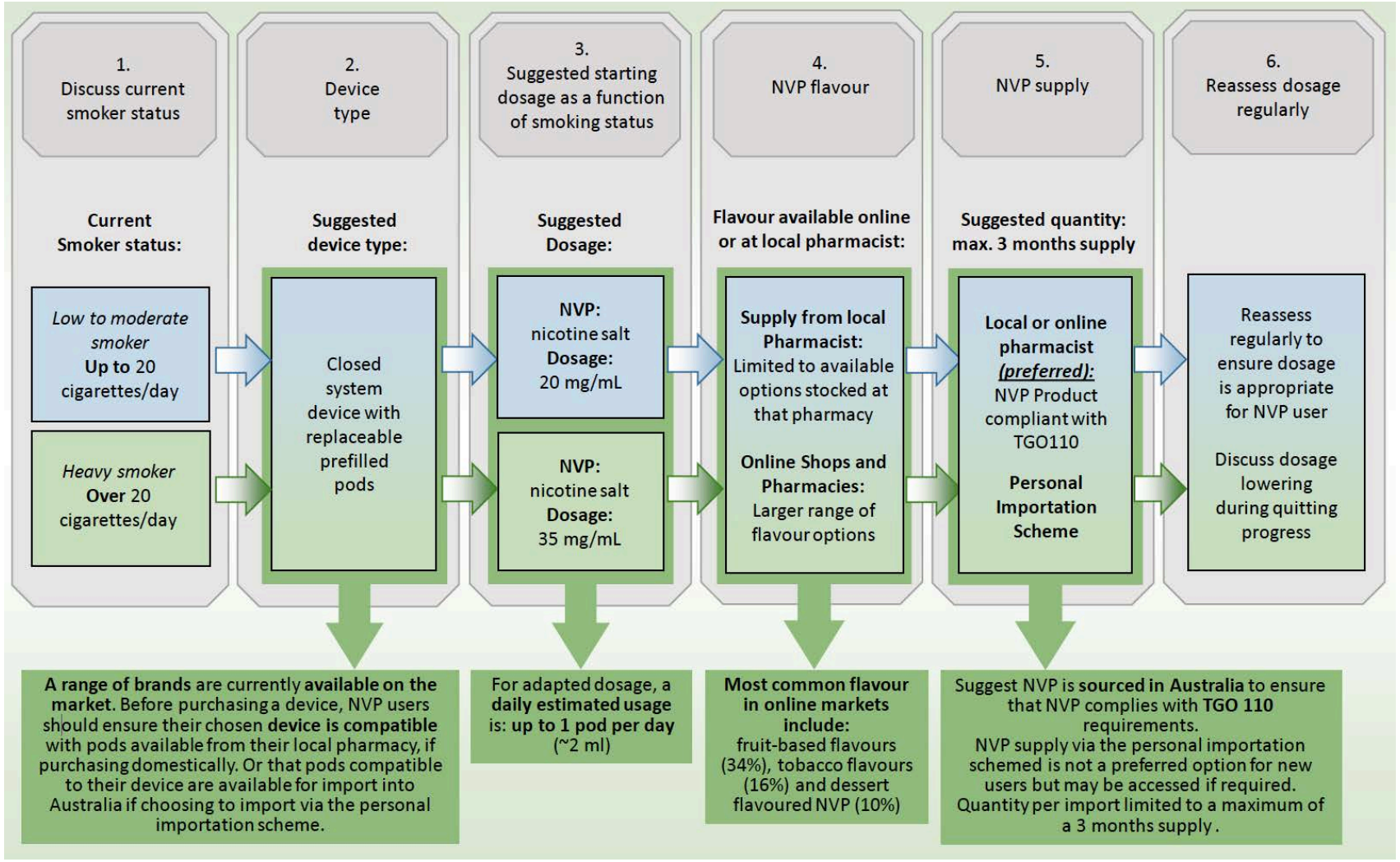
Suggested supply

	Estimated volume usage	
	Daily	**3 months**
Open tank devices 3-6 mg/ml (free base)	4-6 ml	600 ml
Pod devices 30 mg/ml (salt)	1 pod (2 ml)	100 pods (200 mL)
High concentration solutions (100 mg/ml) for "mix your own" preparations*		
Free base nicotine	Up to 2mL	Up to 120 mL
Nicotine salts	Up to 3mL	Up to 300 mL

* Based on the use of 100 mg/ml solution to prepare 600 mL of 3-20 mg/ml free base nicotine solutions, and 200 mL of 30-50 mg/ml nicotine salt solutions for use in open tank devices.

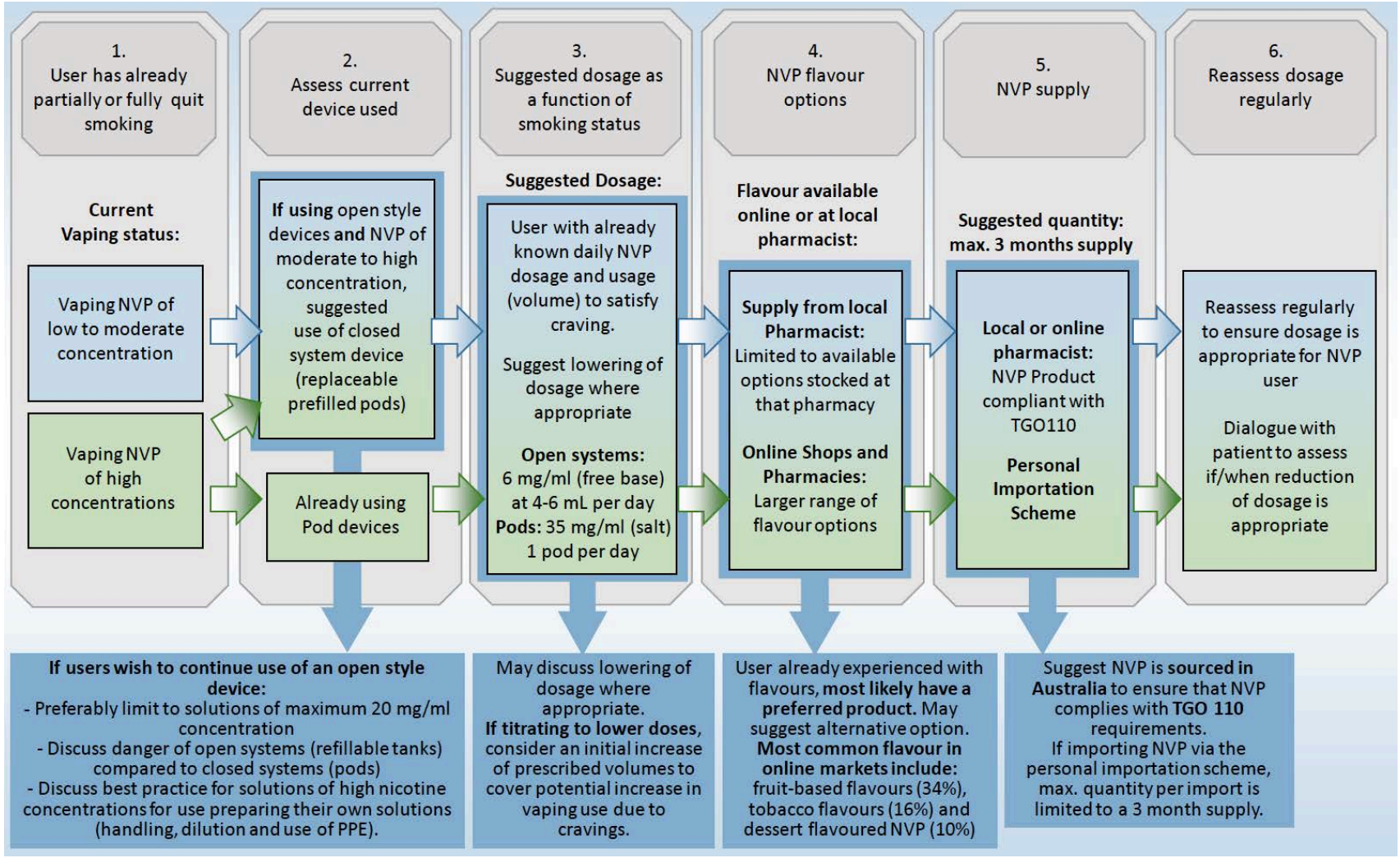
Guidance for new users

Nicotine Vaping Product Analysis: Evidence from the University of Wollongong - Accompanying document



Guidance for existing users

Nicotine Vaping Product Analysis: Evidence from the University of Wollongong - Accompanying document



Using lower nicotine concentration may not be better

Compound	6 mg/ml nicotine 5.04 sec puff Mean ± SD	24 mg/ml nicotine 3.76 sec puff Mean ± SD	Statistical significance of the difference (t-test)
Formaldehyde	46.1 ± 12.8 (↑45%)	31.7 ± 6.4	p=0.03
Acetaldehyde	29.3 ± 4.9 (↑33%)	22.1 ± 2.7	p=0.01
Acetone	9.9 ± 2.7 (↑65%)	6.0 ± 3.1	p=0.04
Acrolein	ND	ND	

Kosmider et al *Nicotine & Tobacco Research*, 2018, Vol. 20, No. 8

Adverse effects associated with vaping

- There were low numbers of adverse effects in all study groups
- Low certainty evidence that there is no difference in the adverse event rate between groups

- Most common side effects associated with ENDS use include:
  - Throat or mouth irritation
  - Headache
  - Cough
  - Nausea
- No significant difference in serious adverse events

Hartmann-Boyce et al. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews 2021

Writing a prescription

- Non-PBS
- Must include the following
  - Nicotine concentration
  - Volume of liquid or number of pods for a 3 month supply
  - Number of repeats (up to 3)

Pods

```
Nicotine pods for vaping (Up to 2mls)
50mg/ml nicotine liquid
90 pods Repeat x3
```

Pre-mix

```
Nicotine liquid for vaping
12mg/ml
450ml Repeat x3
```

Concen-trate

```
Nicotine liquid for vaping
100mg/ml
120ml Repeat x3
```

For someone who uses 120mls per 3 months
Or you will need to work it out based on what they are using
5ml x 12mg/ml per day = 60mg per day
= 5,400 mg per 3 months
= 54 ml of 100mg/ml

Acknowledgement: Dr Colin Mendelsohn

Flavours

- Prescribers can specify flavour on a prescription, but this is not a requirement
- In general you can advise:
  - There is a vast range of different flavours
  - May need to try several before finding one they like
- Online stores will have a wider selection than pharmacies

How can you help people who smoke?

- Explain what you can offer
  - E.g. combination of stop smoking medicine and behavioural support
- For those who wish to use an e-cigarette, ask permission to tell them what you know
  - Vaping can help people quit smoking, but they are no magic cure
  - Vaping pose lower health risks than smoked tobacco, **but** we do not know the health risks associated with long-term use of e-cigarettes, only that they are likely to be many times less than with smoking
  - Vaping of any kind should not be used by people who do not smoke

What can you say about vaping?

- Daily vaping use is generally more effective for quitting smoking than intermittent use.
- More advanced vaping models that deliver nicotine more efficiently seem to work best for those trying to quit smoking tobacco cigarettes.
- Carefully read and understand the manufacturer's recommendations for use and care of the device.
- It may take practice to learn to use the device to deliver the proper amount of nicotine to relieve the urge to smoke.
- Stop use of combustible tobacco cigarettes as soon as possible and discontinue vaping when you are comfortable that you have quit cigarette smoking for good

Cummings et al. J Am Heart Assoc. 2018 Jul 14;7(14)

Safety Tips

- Only purchase e-liquid containing nicotine with a valid prescription
- Investigate the safety and quality of products before purchasing
- Only use the charger supplied by the manufacturer to charge your device
- Do not modify your vaporiser device and use only approved parts
- Never charge your vaporiser unattended for long periods, especially overnight or while you are out of the house
- Never keep loose vape batteries in your pocket, particularly next to keys or coins
- Protect your vape from extreme temperatures and direct sunlight
- Never vape near medical oxygen
- Keep out of the reach of children and pets
- If you spill any e-liquid and it makes contact with your skin – wash your hands immediately – remember nicotine contained in both tobacco and nicotine replacement products is a poison
- Do not dry burn your coils
- Heed any warnings supplied with the product

Screening for vaping and documentation

- **Vaping is not smoking**, so a person who
  - has switched completely from cigarettes to vaping should be categorized as an **ex-smoker**
  - is vaping and is still smoking cigarettes, even as little as one cigarette per day, should be documented as a **current smoker**
  - is vaping, but has never smoked, code them as a **non-smoker**
- Vaping should be recorded in the clinical record

Conclusions

- E-cigarettes can help people stop smoking, but not a ‘silver bullet’
- There are likely to be some adverse health effects associated with long-term vaping, so concern is warranted, however…
  - this concern needs to be balanced with the concerns for the health and wellbeing of people who continue to smoke
- For smokers, switching to vaping (and stopping smoking completely) is likely to be associated with a reduction in health risks
  - This is supported by the current literature
  - To mitigate concern over unknown health risks associated with long-term vaping, ex-smokers can be advised to stop vaping as soon as they feel able not to relapse to smoking

Website and link references | Nicotine Vaping Products (NVP)

Nicotine vaping products	https://www.tga.gov.au/nicotine-vaping-products
Information for prescribers	https://www.tga.gov.au/nicotine-vaping-products-information-prescribers
Frequently Asked Questions	https://www.tga.gov.au/nicotine-vaping-products-frequently-asked-questions
Guidance for the use of nicotine vaping products for smoking cessation	https://www.tga.gov.au/guidance-use-nicotine-vaping-products-smoking-cessation
New NVP users	https://www.tga.gov.au/sites/default/files/nicotine-vaping-products-flow-chart-university-wollongong.pdf

More information – Social media

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	Instagram	https://www.instagram.com/tgagovau/?hl=en

How did we go?

LIVE POLL

We are currently reading over your submitted questions.

We'll be back shortly for Q&A

Questions?

Natalie Walker

George Laking

Hayden McRobbie

Australian Government

Department of Health

Therapeutic Goods Administration