ANSWERS TO QUESTIONS TAKEN ON NOTICE DURING THE WEBINAR

Q: What are practicalities of prescribing?

A: (RACGP) Practicalities of prescribing including what to write on a prescription, dosing considerations and advice considerations will be covered in the RACGP clinical guidelines.

Q: Is there a recommended daily maximum nicotine to prescribe?

A: (RACGP) It is not possible to provide definitive advice on dosing as there is no clear evidence and no guidelines on dosing at this time. In addition the dose received by the patient can vary according to the type of vaping device, concentration of nicotine and inhalation technique. The RACGP clinical guidelines will provide suggestions to assist in making prescribing decisions with respect to dosing (acknowledging the lack of evidence). As with an intervention for smoking cessation, follow-up is important to discuss progress and provide support. Dose titration may be needed with ongoing follow-up.

Q: What will big tobacco in Australia look like? And how long would a personal import scheme take?

A: (TGA) It is not clear what the first question means.

(Quit) The delivery time is likely to be quite variable for a product prescribed through the Personal Importation Scheme, as it will depend on stock availability / preparation for shipping etc by the supplier, transport time (depending on courier or post) and how long it takes to clear Customs.

Q: What is being done to train GPs in vaping and how to write a nicotine prescription? Most GPs know very little about it and patients are reporting that doctors are refusing to prescribe.

A: (Quit) Considerations for prescribing (including what needs to be included on a prescription) will be covered in the RACGP clinical guidelines. A further webinar is planned once the guidelines have been finalised. Online training is also under development.

Q: There are few RCTs for effectiveness. However, the results are supported by observational and population studies and changes in national smoking rates in countries where vaping is available. Have you taken this into account in determining effectiveness? Also as vaping is far more popular than other treatments, it is likely to lead to a greater population effect.

A: (RACGP) An updated evidence review was conducted by the Australian National University (ANU) and compared nicotine e-cigarettes versus NRT. The review identified RCTs that met the inclusion criteria. The GRADE (Grading of Recommendations, Assessment, Development and Evaluation (GRADE)) process was used. The evidence review resulted in a GRADE Summary of Findings table which was then incorporated into the Evidence to decision framework. The Expert Advisory Group moved the evidence to making practice recommendations.

Q: What is the doctor's legal responsibility if a patient imports a low quality product that causes harmful effects?

A: (RACGP) It's not possible to provide a definitive response. Suggest ask Medical Defence Organisation for their view.

Q: Why is flavour part of the equation for prescribing nicotine vaping products for the purposes of nicotine cessation?

A: (TGA) Although the standard does not restrict the flavours of nicotine vaping products (other than those containing prohibited ingredients) or container sizes, it is important to remember that these factors, and others, are restricted by the person's prescription. This allows the prescribing health professional and patient to work together to make sure that the right product is supplied to support

A: (Quit) It's an interesting question as to whether flavour has a therapeutic purpose. Flavourings can reduce the harshness of nicotine, which can assist complete switching to NVPs from cigarettes and can increase compliance. However, flavourings can also increase the appeal and reduce the appeal of NVPs. It is important to note that flavourings are considered for ingestion, but this does not mean they are safe to inhale. The RACGP guidelines will provide advice to prescribers on flavours.

Q: What would you advise a patient who is unable to stop vaping and is at risk of relapse to smoking?

A: (RACGP) Cessation of both tobacco smoking and use of other forms of nicotine is always the preferred option. However, there may be instances in selected patients where the doctor and patient agree that a longer term use of NVP is needed to avoid a relapse to tobacco use. Dual use should be avoided. If considering ongoing use of NVPs, the patient should be counselled on the risks and benefits versus re-trying other approved smoking cessation pharmacotherapies. This discussion should include that the long-term safety of NVPs is unknown and that people who use NVPs have an approximately double the risk of relapse to smoking compared with non-NVP users. Regular follow-up, monitoring and consideration of re-trialling other first-line interventions over time is recommended.

Q: Will the liquid nicotine be subsidised on PBS?

A: (TGA) There are currently no TGA approved nicotine vaping products registered in the Australian Register of Therapeutic Goods. Before a medicine can be listed on the PBS, it must first be registered by the Therapeutic Goods Administration.

Q: The National Drug Strategy Household Survey 2019 estimates that there are 520,000 liquid nicotine users, just as there are plenty of anecdotal cases of former smokers transitioning to e-cigarettes without an authorised prescription. In the instance that these people are considered ineligible to access a prescription from October 1, what other avenues will these people have to prevent them from sourcing liquid nicotine from black markets?

A: (TGA) Please note that premise of this question is incorrect; the NDSHS estimated there are 222,000 Australians 14+ who vape daily (daily) and 120,447 who vape weekly but not daily. Vaping

less than daily indicates a person is unlikely to be addicted to nicotine. The 500K+ figure is based on any lifetime use, including experimentation.

The decision that nicotine is a prescription only medicine facilitates a medical practitioner's full assessment of a patient's cessation needs and treatment options and is anticipated to include the risk to which the question refers. Ultimately, whether or not a nicotine vaping product is suitable for any particular individual will be a decision for the health practitioner in consultation with their patient, taking into account their patient's unique needs. The work that the TGA and the ABF is doing (in consultation with the states and territories) is also taking a risk based proportionate approach to address the risk to which the question refers.

Q: Can you give an example of how to write a script, ie specifically what do you need to include?

A: (RACGP) Considerations for prescribing (including what needs to be included on a prescription) will be covered in the RACGP clinical guidelines.

Q: Prof Zwar, one of my concerns with nicotine ECs vs NRT meta-analyses containing Hajek 2019 is that is heavily weighted, and a vast majority (~80% from memory) of participants in the nicotine EC arm of that trial were continuing to use the device at 12 months. What are your (and the EAGs) thoughts on the challenges using that trial as evidence when the RACGP EAG can not yet recommend long term use?

A: (RACGP) The trial is the largest and best quality one available and needs to be included in any review of the evidence. The concern about longer term use is discussed in the guidelines.

Q: Does a nicotine vaping product need to go through a phase III clinical trial to potentially receive TGA approval?

A: (TGA) Yes.

Q: How will the ABF monitor authentic prescriptions? if an AP doctor is known people could copy these and try cheat the ABF

A: (TGA) The TGA is working with the ABF on appropriate compliance and enforcement activities at the border and this will include consideration of the risk of forged prescriptions. This is something which the two agencies already consider as a part of their compliance and enforcement activities at the border.

Q: Can we use an authenticator - there are some technology addons to help couriers recognise legitimate prescriptions?

A: (TGA) The TGA is aware of the technology and it will be considered as part of the compliance and enforcement activities of the two agencies.

Q: Is there any data on safety of NVP vs cigarette smoking? Rather than against NRT?

A: (RACGP) NVPs are likely to be safer than smoking in that the exposure to toxins is far less, but it is not possible to quantify how much safer.

Q: I'm still not sure what practically is typed/written on the prescription come Oct 1st, with no TGA items yet approved. I would think that our medical software's medication list won't have anything listed for us to select. RTPM are usually solely focused on preventing overdose deaths
A: Considerations for prescribing (including what needs to be included on a prescription) will be covered in the RACGP clinical guidelines.

Q: I run a smoking cessation clinic in an adult mental health service with lots of long term and heavy smokers. What is your attitude to switching these patients to vaping for harm reduction whilst trying to work on their motivation to quit when reducing prescriptions? Does the RANZCP have a position on this kind of thing?

A: (QUIT) RANZCP are developing guidelines for NVP use by people living with a mental illness, which might better answer this question.

Q: Does vaping mist cause a large droplets sprayed? With present social distancing, does this need further distancing?

A: (Quit) The emission from an NVP is an aerosol and does contain droplets. It is theoretically possible that aerosols from NVPs could transmit COVID-19 either in the air or as the particulate matter/droplets settle on surfaces. Research is needed to examine whether this happens in real life use.

Q: Will there be guidelines for prescribing nicotine like there is for prescribing opioid agonist therapy?

A: (RACGP) Clinical guidelines on NVPs are being finalised and will be made available prior to October 1.

Q: You mentioned some specific groups of interest to working with - is there work being done for cessation treatments within Dept. Corrections (ie cessation while incarcerated)?

A: (Quit) Different jurisdictions in Australia are using different approaches to support people who are incarcerated to quit smoking. It is extremely unlikely, for a variety of issues related to intentional misuse, that vaping devices would be permitted in prisons.

Q: If a patient presents who is regularly vaping, is advice for a prescriber to have patient use first line therapies first?

A: (RACGP) If considering ongoing use of NVPs, counsel the patient on the risks and benefits versus re-trying other approved smoking cessation pharmacotherapies. This discussion should include that

the long-term safety of NVPs is unknown and that people who use NVPs have an approximately double the risk of relapse to combustible tobacco smoking compared with non-NVP users. Regular follow-up, monitoring and consideration of re-trialling other first-line interventions over time is recommended.

Q: Are there time limits on how long doctors should be prescribing e-cigarettes for a patient? i.e. 6 weeks, 12 weeks etc

A: (RACGP) If considering ongoing use of NVPs, counsel the patient on the risks and benefits versus re-trying other approved smoking cessation pharmacotherapies. This discussion should includes that the long-term safety of NVPs is unknown and that people who use NVPs have an approximately double the risk of relapse to combustible tobacco smoking compared with non-NVP users. Regular follow-up, monitoring and consideration of re-trialling other first-line interventions over time is recommended.

Q: Script writing - 1 month supply, 3 months supply- what is appropriate?
A: (RACGP) Recommend limiting the quantity of NVPs per prescription to a maximum of 3 months' supply. Also, consider aligning the duration of supply with the timing of follow-up.

Q: What will happen for doctors wishing to become an authorized prescriber in the hospital setting?

A: (TGA) If prescription medicines are extemporaneously compounded in a hospital pharmacy they would not be required to be registered on the Australian Register of Therapeutic Goods making it unnecessary for the prescriber to have TGA authorisation to be an Authorised Prescriber.
(Quit) Note that TGO 110 *does* apply to extemporaneously compounded NVPs.

Q: How does the "hit" of nicotine in NVPs compare with the "hit" dispensed by nicotine spray products?

A: (RACGP) The pharmacokinetics of nicotine delivery, which includes rapidity of onset and peak nicotine levels, is variable and is a function of the form of the nicotine, NVP concentration, the vaping device, and inhalation technique.

Q: What is the research on nicotine dependence (does it increase, stay the same with NVPs)?

A: (Quit) There is evidence to suggest that nicotine salts have greater absorption in the blood and may be more addictive and have nuanced effects on the inherent harms of e-cigarette exposure. There is also a risk that people might increase their addiction by increasing their scope of use (i.e. use an NVP more frequently and for longer) than they would use a cigarette, which has a natural end (smoked to the butt).

[Reference: Gholap, Pearcy and Halquist. Potential factors affecting free base nicotine yield in electronic cigarette aerosols. Expert Opinion on Drug Delivery. 2021 Mar 2:1-11). Leventhal et al., Effect of Exposure to e-Cigarettes With Salt vs Free-Base Nicotine on the Appeal and Sensory Experience of Vaping: A Randomized Clinical Trial. Journal of the American Medical Association Network Open, 2021. 4(1): p. e2032757).]

Q: What is the risk of relapse to cigarettes/dual use when there is continued use of NVPs?

A: (Quit) Based on available longitudinal studies, people who use NVPs have an approximate doubled rate of relapse to tobacco use compared with those who don't use NVPs.

[Baenziger O, Ford L, Yazidjoglou A, Joshy G, Banks E. E-cigarette use and combustible tobacco cigarette smoking uptake among non-smokers, including relapse in former smokers: umbrella review, systematic review and meta-analysis. BMJ Open 2021;11:e045603. doi: 10.1136/bmjopen-2020-045603]

Q: Does dual use have additive health effects?

A: (Quit) Dual use is associated with greater odds of developing respiratory symptoms and higher risk of cardiovascular disease. Dual use is associated with high exposure to toxicants, and at levels that can be higher than smoking alone. Dual use may also lead to greater nicotine dependence which can prolong smoking and impede cessation.

[References: Osei, A. D. et al. Association Between E-Cigarette Use and Cardiovascular Disease Among Never and Current Combustible-Cigarette Smokers. Am J Med 132, 949–954 (2019). Bhatta, D. N. & Glantz, S. A. Electronic Cigarette Use and Myocardial Infarction Among Adults in the US Population Assessment of Tobacco and Health. J Am Heart Assoc 8, e012317, https://doi.org/10.1161/JAHA.119.012317 (2019). Bhatnagar, A., Payne, T. J. & Robertson, R. M. Is There A Role for Electronic Cigarettes in Tobacco Cessation? J Am Heart Assoc 8, e012742, https://doi.org/10.1161/JAHA.119.012742. Reddy KP, Schwamm E, Kalkhoran S, Noubary F, Walensky RP, Rigotti NA. Respiratory Symptom Incidence among People Using Electronic Cigarettes, Combustible Tobacco, or Both. Am J Respir Crit Care Med. 2021 Jul 15;204(2):231-234. doi: 10.1164/rccm.202012-4441LE. PMID: 33857396. (2019). Goniewicz ML Smith DM Edwards KC et al. Comparison of nicotine and toxicant exposure in users of electronic cigarettes and combustible cigarettes. JAMA Netw Open. 2018; 1e185937. US Department of Health and Human Services Smoking cessation: a report of the Surgeon General.US 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, Atlanta, GA2020. Martínez Ú Martínez-Loredo V Simmons VN et al. How does smoking and nicotine dependence change after onset of vaping? A retrospective analysis of dual users. Nicotine Tob Res. 2020; 22: 764-770]

Q: What will happen to the current vapers who do not wish to quit - will doctors be supported to say no to prescribing nicotine liquids?

A: (RACGP) The guidelines will provide suggestions on how to negotiate this difficult situation

Q: What are the medicolegal issues with prescribing?

A: (RACGP) There are a range of considerations which will be briefly discussed at the next webinar.

Q: What products should I choose/prescribe and what is available?

A: (RACGP) Considerations for prescribing NVPs will be covered in the RACGP clinical guidelines. At the time of writing, the specific products that will be available in Australian pharmacies is not known.

Q: How do I determine the dose for the patient?

A: (RACGP) It is recommended to choose a starting dose based on the patient's level of nicotine dependence. Some suggested starting doses will be outlined in the RACGP clinical guidelines.

Q: How do I manage a patient that only wants to use a NVP for smoking cessation?

A: (RACGP) Explore reservations about the use of first-line with the patient, and explain the risks of using an unapproved NVP.

Q: What is the advice on devices?

A: (RACGP) This will be discussed briefly at the next webinar.

Q: Why are we actually allowing this, when the evidence is poor & the risks seem quite high?
A: (TGA) On 21 December 2020, the Therapeutic Goods Administration (TGA) announced a decision that from 1 October 2021, consumers will need a valid prescription to import nicotine vaping products, such as nicotine e-cigarettes, nicotine pods and liquid nicotine. This means that when a consumer purchases the products online from an overseas supplier, they will legally require a prescription from an Australian registered medical practitioner.

There has been a significant increase in the use of nicotine e-cigarettes and other nicotine vaping products by young people in Australia and in many other countries. There is evidence that nicotine vaping products act as a 'gateway' to smoking in youth and exposure to nicotine in adolescents may have long-term consequences for brain development.

This decision balances the need to prevent adolescents and young adults from taking-up nicotine vaping products while allowing current smokers to access these products for smoking cessation with appropriate medical advice.

Q: There is evidence that tobacco companies are providing incentives to retailers for the sale of tobacco from retail stores. With these tobacco company tactics in mind, will the nicotine be supplied by the tobacco industry or by a pharmaceutical company?

A: (TGA) Import and supply of nicotine vaping products is only lawfully carried out by a sponsor (a pharmaceutical company) or a community pharmacy.

Q: Motivational interviewing techniques

A: (Quit) The question is unclear. Motivational interviewing to encourage a patient to quit vaping is unlikely to be different to that used to encourage a patient to quit smoking. If the question refers to behavioural intervention (a mix of motivational interviewing, cognitive behavioural therapy, acceptance and commitment therapy and psychoeducation), then available evidence suggests that it

is likely to be the same whether supporting someone to quit smoking or to quit vaping. Clinical trials showing efficacy of NVPs have both used behavioural intervention alongside NVPs.

The Quitline has developed modified counselling protocols to support clients to quit vaping and also to support clients making a smoking cessation attempt using NVPs.

Q: Can you explain when doctors write years smoked?

A: (RACGP) The term 'pack years' is sometimes used as a note on heaviness of smoking over time. One (1) pack year is usually 20 to 25 per day for a year.

(Quit) Pack years can be an indicator of changes in smoking behaviour over time and not an indicator of level of nicotine dependence. Heaviness of smoking (HSI) is the validated tool for assessing nicotine dependence.

Q: The TGA says prescribing enables smokers to access these products for cessation with appropriate medical advice yet none of the products are approved while the current NHMRC statement does not endorse their use. How can clinician reconcile mixed messages?

A: (TGA) Clinicians can be guided by the revised nicotine vaping products component of the RACGP smoking cessation guidelines.

Q: What advice would you give to patients who are used to nicotine gum on long-term basis?

A: (RACGP) Not an ideal situation, but there is no evidence of significant long term harms.

(Quit) Clinician could consider referring the patient to multi-session behavioural intervention provided by Quitline to break triggers and habits associated with the rare cases of ongoing use of TGA-approved NRT products.

Q: How can I determine if a nicotine e cigarette device is safe or not?

A: (TGA) The TGA has published guidance on the application of TGO 110 to unapproved nicotine vaping products. From 1 October The TGA will be carrying out a testing programme for which the results will be published, likely later this year and early 2022.

The TGA does not assess the safety, quality and efficacy of 'unapproved' nicotine vaping products nor of Export Only products listed on the ARTG (together, unregistered nicotine vaping products). The long-term health risks of nicotine vaping products are still unclear and evidence of their potential efficacy for smoking cessation is currently mixed, with more reliable, large-scale studies required (References: Hartmann-Boyce et al. 2021, Patnode et al. 2021, Pound et al. 2021, SCHEER 2021, Wang et al. 2021, Zhang et al. 2021).

Q: Can vaping products be sold by a tobacconist?

A: (TGA) It is not lawful for a tobacconist to supply any prescription only medicine including nicotine vaping products. Tobacconists can supply vaping products which do not include nicotine.
(Quit) Note that it is illegal in all states and territories to supply vaping products to minors, whether they contain nicotine or not.

Q: Are vapes currently illegal?

A: (TGA) It is presently unlawful in every state and territory to supply nicotine vaping products; supply of vaping products which do not include nicotine is lawful.
(Quit) Note that it is illegal in all states and territories to supply vaping products that do not include nicotine to minors.

Is there a way to modify the HSI score for vaping?

A: (RACGP) There is no evidence, as yet, to how the Heaviness of Smoking Indicator (HSI) can be modified for vaping.

What should GPs look for when selecting a NVP or vaping device to recommend?

A: (TGA) The RACGP Guidelines are currently being updated to include information about unapproved nicotine vaping products, including:

- evidence on the place of nicotine vaping products in supporting smoking cessation
- information on what is known about the safety of nicotine vaping products
- practical advice on prescribing unapproved nicotine vaping products.

Prescribers need to consider what nicotine concentration and type of product is appropriate for a particular person's smoking cessation needs. Consumers will only be able to access a product with a concentration matching that specified in their prescription.

TGO 110 sets a maximum nicotine concentration limit for unapproved nicotine vaping products of 100 mg/mL (base form or equivalent base form concentration). Even with a prescription, consumers will not be able to access products with a concentration above this limit. This does not mean that products with a concentration of 100 mg/mL are safe or necessarily appropriate for use. The 'Limits on nicotine concentration' section of our Guidance on TGO 110 includes information on the risks of higher concentration products that require 'at-home mixing' (i.e. dilution by consumers) prior to use.

Practical information for prescribers, including to raise awareness of how to prescribe nicotine vaping products in Australia, is also available in our Guidance for the use of nicotine vaping products for smoking cessation.
(Quit) Vaping devices are not regulated by the TGA. It's not possible to make a recommendation as there are currently no Australian quality or safety standards for devices.

Any discussion re Champix recall/nil availability in Australia?

A: (TGA) The TGA's investigation into unacceptable levels of *N*-nitrosovarenicline in Champix is ongoing. Pfizer paused global distribution of their varenicline products, including Champix, as a precautionary measure while this issue is under investigation. Pfizer has reported to the TGA that they are unable to confirm when this situation will be resolved. The current medicine shortage notification indicates Champix will be unavailable until 31 December 2021 (see: https://apps.tga.gov.au/prod/MSI/search)

If e-cigarettes are not approved by the TGA how can they be a prescribed product (this creates mixed messages as a cessation aid)?

A: (TGA) The Royal Australian College of General Practitioners (RACGP) *Supporting smoking cessation: A guide for health professionals* (published 2019) stipulate that nicotine vaping products are not first line treatment for smoking cessation. However, for people who have tried to achieve smoking cessation with approved pharmacotherapies but failed, and who are still motivated to stop smoking and have discussed nicotine vaping product use with their healthcare practitioner, nicotine vaping products may be a reasonable intervention to recommend.

There will be a complex mix of fed v state plus therapeutic vaping v retail vaping & smoking. TGA promised to Abetz at the last Senate Estimates to clarify all this but hasn't really done that yet or have they?

A: (TGA) The materials included in the TGA's nicotine vaping hub accurately reflect the state of play. The ACT, NT, SA, TAS require those selling / supplying a vaping device to hold a tobacco retailer's licence. We understand that each of those jurisdictions is giving policy consideration to whether to maintain that requirement for pharmacists. Anyone with concerns may wish to raise it with their state or territory.

Is it possible for a person to use the same prescription multiple times (as they need to provide only a scanned or photocopied script to accompany the import at the border)?

A: (TGA) From 1 October, the Australian Border Force and the TGA are focussed on working together (as well as with the states and territories) to stop importation by individuals without a prescription. Consumers are advised to arrange for their prescription to be enclosed with the package the product is sent in to prevent the package being held at the border. The ABF and the TGA have, since the beginning of the year, made this a planning priority in their broader 'border' work programme to provide for effective compliance and enforcement at the border. The issue you raise about multiple use of one prescription is part of this planning. Education is a key to this workplan and the TGA has written to known exporters (in other countries) and is, by its website notes for consumers, a short video to be published shortly to be promoted by social media channels as well as engagement with community groups, also making communication on access to nicotine vaping products a priority up to 1 October.