

26 January 2022

The Editor
Australian and New Zealand Journal of Public Health

Dear editor,

We are writing about a Commentary in the ANZJPH, *Time to rethink tobacco dependence treatment in Australia* (Buchanan T. ANZJPH 2021) and the rejection of a letter to the editor in response to this Commentary. (Mendelsohn CP Manuscript ID# ANZJPH-2021-318, *Vaping nicotine should be part of Australia's tobacco control policy*).

The Commentary argued rightly that tobacco dependence treatment services in Australia need to be improved to increase quitting but was dismissive of a role for vaping as part of the strategy.

Views on vaping nicotine are divided in the public health community. The Buchanan paper outlines one position, so the presentation of an alternative position, one supported by a significant proportion of people with expertise in the field, should be an obligation of a responsible scientific journal. As an example of this alternative view, we submit the attached paper co-authored by 15 past presidents of the Society for Research on Nicotine and Tobacco, the premier scientific society in the field. (Balfour et al.)

There are many examples of controversial issues in public health which become orthodox, mainstream practice with evolving evidence and experience. For example, the initial resistance to opiate substitution therapy use was followed by it becoming standard practice.

Regarding the rejection of the LTE by Mendelsohn, many of the reviewers' comments were not based on valid scientific evidence in our view. There were factual errors, unsubstantiated claims and selective use of data. The comments show a lack of understanding of tobacco harm reduction.

Some of the flawed claims include:

Claim	Response
EVALI was caused by nicotine vaping	False: EVALI was caused by illicit THC vaping oils adulterated with vitamin E acetate
'may replace one long-term habit with another for addicted smokers'	Misleading. Switching to a safer alternative is the basis of tobacco harm reduction and has substantial health benefits. We accept that a proportion of switchers (likely those who would never have quit cigarettes) will continue to vape.
Vaping nicotine has 'led to a number of deaths'	False: No confirmed deaths from inhaling nicotine vapour have been documented
Vaping has led to 'severe respiratory problems for young people'	False: Vaping has been associated with respiratory symptoms and increased asthma risk in young people but no causal link has been identified. No severe respiratory problems have been confirmed as vaping-caused.
Increased vaping would lead to	International evidence consistently shows that regular vaping by

widespread vaping by non-smokers	non-smokers is generally less than 0.5%.
E-cigarettes are not an effective stand-alone cessation tool	Probably false: The evidence from RCTs, meta-analyses of RCTs, population and observational studies suggests they are effective both when used with behavioural support and when used without any other help.
Vaping is a gateway to smoking for young people	Almost certainly false: The evidence is increasingly strong that vaping is diverting young people away from smoking. The association between vaping and subsequent smoking has been shown to be due of shared risk factors.
The involvement of the tobacco industry undermines vaping's value to public health	The public health priority is to prevent death and disease from smoking. Safer nicotine products reduce harm no matter who makes them.
The rapid decline in smoking prevalence in other countries where vaping is widely available is 'purely an association'	Almost certainly false: While causation cannot be proven, it is likely that vaping is playing a significant role. That smoking rates are declining more where there is vaping, and indeed dropping at all, is compelling evidence against any meaningful gateway, and plausibly due to vaping. No other plausible explanation has been proposed that is broadly consistent with the evidence.

Our response to their claims is outlined in more detail in the Appendix.

In order to advance the scientific debate on this important public health issue, we believe the letter from Mendelsohn should be accepted for publication or a Commentary commissioned to express alternative views to those of Buchanan et al. given these are widely held by credible experts in the field.

We look forward to hearing from you.

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Appendix

Response to reviewer comments

“the risks of vaping (still not completely understood, but as recent media reports show, can be catastrophic (i.e. occasionally fatal in the U.S, resulting in one young person in ICU in Australia)”

The reviewer is referring to EVALI (E-cigarette or Vaping-Associated Lung Injury) which was almost certainly not caused by nicotine vaping.

EVALI was a serious lung condition in 2019-2020 in North America attributed to the addition of Vitamin E acetate as a ‘cutting agent’ to illicit THC vaping oils. (Blount B. NEJM 2019) The outbreak cleared up after VEA was removed from the illicit cannabis supply chain in January 2020. ([CDC](#))

The CDC acknowledged in 2020 that ‘Vitamin E acetate is strongly linked to the EVALI outbreak’ although ‘Evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC or non-THC products, in some of the reported EVALI cases’.

A small number of EVALI sufferers denied using THC ([CDC MMWR 2020](#)) leading some commentators to question the role of nicotine vaping. Hall noted that cannabis was illegal in 38 US states and cannabis arrests can adversely affect underage users or the employment prospects of young people and this could discourage disclosure. (Hall W. Addiction 2020) Some of these patients were later found to have used VEA contaminated THC. ([CDC MMWR 2020](#))

VEA cannot be added to nicotine e-liquids as it is not soluble in the base liquids used for nicotine vaping. It has not been detected in nicotine e-liquids. (Kosarac I. Front Chem 2021)

Furthermore, if vaping nicotine was the cause of these lung injuries, many more cases should have been reported prior to and after this outbreak and in other countries where nicotine vaping was widespread, as there have been no significant changes to the composition of nicotine e-liquids since the outbreak. (Gartner C. DAR 2020)

According to Professor John Britton, Director of the UK Centre for Tobacco & Alcohol Studies in the UK:

“These studies provide further evidence that the outbreak of serious lung disease among vapers in the USA this year was caused by vaping THC, and may particularly be due to vaping THC solutions containing vitamin E acetate. The conclusions provide strong reassurance that people vaping nicotine as an alternative to tobacco smoking are unlikely to be affected, and should continue to vape instead of smoke.” [[Science Media Centre UK](#)]

The diagnosis of a case of Acute Respiratory Distress Syndrome in an Australian adolescent as a case of EVALI is questionable for several reasons. (Chan B. MJA 2021) Vitamin E acetate was not detected, other potential causes were possible and bronchoscopy was not performed (EVALI is a diagnosis of exclusion). A letter to the Medical Journal of Australia raising concerns about the diagnosis was rejected without peer-review. (Mendelsohn 2021 - unpublished)

“may replace one long-term habit with another for addicted smokers”

Switching to a safer nicotine alternative is a legitimate and accepted form of tobacco harm reduction. (RACGP 2020) The aim of tobacco harm reduction is to reduce harm in smokers who are not able to quit, not necessarily to eliminate nicotine use.

The potential harm from nicotine vaping is almost certainly minor compared to the alternative, continuing to smoke. The UK RCP has estimated that **long-term** vaping nicotine is likely to be no more than 5% of the harm of smoking. (RCP 2016)

Smokers who switch to vaping nicotine become less dependent than they were on cigarettes. (Shiffman S. Addiction 2020; Foulds J Nicot Tob Res 2014; Hughes J. Addict Behav 2018)

“completely ignores how the risks of vaping – which appear to be lower than smoking, but which have also led to a number of deaths and severe respiratory problems for young people – can be avoided”

There are no documented deaths from inhaling nicotine vapour and there is no evidence that vaping causes severe respiratory problems in young people.

There have been two deaths in the US from exploding unregulated ‘mechanical mods’. These fringe devices are used by a small number of hobbyists. They have no electrical protection, microchip or safety features and could never meet consumer protection standards.

There have also been very rare cases of death from accidental and deliberate nicotine overdose. However, there are no documented deaths from vaping nicotine.

Some cross-sectional studies have found an **association** between vaping in adolescents and respiratory symptoms and an increased risk of asthma (Bourke M. Paed Pulm 2021; Cho JH. Plos One 2016) Others have found no association. (Tackett A. JAMA Open 2020) However causation has not been demonstrated. Confounding by smoking status may explain some cases as may switching to vaping from smoking as a result of pre-existing respiratory symptoms (to reduce future risk as perceived by the user at least).

We are not aware of any severe respiratory problems in young people due to nicotine vaping. A teenager was diagnosed with bronchiolitis obliterans, a serious lung disease. (Landman S. CMAJ 2019) However the patient had been vaping nicotine and THC, the diagnosis was speculative and causation was not established. ([Siegel M](#))

A case of severe hypersensitivity pneumonitis in a 16-year old was attributed by the authors to vaping (Nair N. BMJ 2019). However, this very rare condition can occur spontaneously and causation was not established. ([UK Science Media Centre Nov 2019](#))

“to pursue the direction being adopted by New Zealand will inevitably lead to a large increase in vaping by people who never would have vaped [sic], and who would therefore take on the risks of vaping, without any commensurate decrease in risk from stopping smoking”

The uptake of vaping by adult non-smokers is rare in New Zealand and other countries.

Where nicotine vaping products are freely and legally available to adults, vaping is largely confined to

smokers and ex-smokers and regular use by adults who have never smoked is rare.

Vaping has been freely available in New Zealand for several years. According to the New Zealand Ministry of Health in 2020, 'Despite some experimentation with vaping products among never smokers, vaping products are attracting very few people who have never smoked into regular vaping, including young people.' ([NZ MOH 2020](#))

In New Zealand in 2016, no regular vaping was reported by adult non-smokers in the Health and Lifestyles Survey. (Oakley A. Add Behav 2019)

Public Health England reported in 2021 that only 0.2-0.6% of adults in the UK who had never smoked were currently vaping. Never-smokers vaped less frequently than current or former smokers and most (57%) tried vaping only once or twice. (PHE. 2021)

Other international surveys have found that vaping by adult non-smokers is generally less than half of one percent of the population, for example in the United States 0.3% (Zhu S. BMJ 2017); Germany 0.3% (Kotz D. DAI 2018); Iceland 0.4% ([Kyzer L. 2018](#)); and Greece 0.2%. (Farsalinos K. HRJ 2018) Current daily vaping by never-smokers in the European Union was 0.08%. (Farsalinos K. Addiction 2016)

It is theoretically plausible that some people who would never have smoked may be attracted to vaping if they perceive the potential benefits outweigh the risk of harm. This has been observed in Scandinavia for use of snus, but has not yet occurred for vaping products to any meaningful extent.

Many of the never-smoking vapers have characteristics suggesting high risk that they would have become smokers in the absence of vaping, so some proportion of the non-smoker vaper group are those protected from ever becoming smokers.

"Lack of demonstrated effectiveness of e cigarettes as a stand alone cessation tool"

There is now sufficient evidence from several different types of study that vaping nicotine helps many smokers to quit with and without behavioural support.

In its 2021 report, the UK College of Physicians concluded, 'E-cigarettes are an effective treatment for tobacco dependency and their use should be included and encouraged in all treatment pathways.' (RCP 2021)

Cohort/observational studies

Reviewer 2 relies on a meta-analysis of observational studies by Hedman as evidence that e-cigarettes are not effective. (Hedman L. Tob Prev Cess 2021) This meta-analysis is of uncertain value as the studies had different designs, user characterisations, intentions to quit (22 out of 26 studies did not report whether or not users intended to quit), outcome measures and most did not report on frequency of use or type of device. Many studies did not assess whether nicotine was used.

The selected studies were also subject to selection bias and other confounders such as differing levels of nicotine dependence (e-cigarette users are typically more nicotine-dependent).

Observational studies are prone to bias and can produce misleading results. However, two reviews of the better quality observational studies found that vaping nicotine significantly increased the chances of quitting smoking. (Glasser A. AJPM 2017; Villanti A. Addiction 2017).

Meta-analyses of RCTs

Meta-analysis of RCTs is 'more reliable in the exploration of a causal link' (Hedman L. Tob Prev Cess 2021). Meta-analyses of RCTs support the effectiveness of vaping nicotine as a quitting aid.

In Hedman's meta-analysis, there was a pooled OR of 1.78 (CI 1.41-2.25) with 'low strength of evidence' in favour of vaping. However this analysis included a study of vaping which did not use nicotine and should not have been included (Lee SH. JABFM 2019). Removing this study would increase the success rate.

The most recent Cochrane review of four studies (September 2021) concluded that vaping with nicotine liquid was 53% more effective than nicotine replacement therapy in helping smokers quit. (Hartmann-Boyce J. Cochrane Review 2021) The level of evidence was moderate. NB: This is by the stringent standards of CRCT evidence. The meta-analysis also includes earlier studies with lower delivery vaping products and there is strong evidence that these were less effective.

Two other recent analyses concluded that vaping was 69% more effective than NRT (Grabovac I. NTR 2020; [Joanna Briggs Institute 2019](#)) and a third review of seven studies by Australian academics determined that it was 49% more effective. (Chan G Addict Behav 2021)

Two other recent analyses of RCTs concluded that vaping is no more effective than NRT. (Banks E. Medrxiv 2020; Pound C. BMJ Open 2021) However, both also included the flawed study mentioned above. (Lee SH. JABFM 2019). NB: There is overwhelming evidence that NRT is an effective aid, so this is supportive of a positive effect for vaping regardless of whether it is more or similarly effective to NRT.

A further analysis of nine RCTs which also included this flawed study found that smokers using vaping products were still 55% more likely to quit than those using conventional therapies. (Wang R. AJP 2021).

Comparison to stop-smoking medicines

A network meta-analysis of 171 RCTs was recently carried out by the UK National Institute for Health Research, funded by the UK Department of Health and Social Care. (Thomas KH. HTA 2021) It found that vaping nicotine produced the best quit rates of all monotherapies. It was more effective than varenicline, NRT and bupropion. It concluded that further trials directly comparing vaping with the other medications are needed to confirm this finding.

In conclusion, there appears to be no question that vaping is at least as effective as conventional therapies for cessation, and in our view moderately strong evidence that it is more effective.

Population studies

Research in large populations has demonstrated that smokers who vape (**most without formal behavioral support**) is associated with higher quit rates than smokers who don't vape.

Two large US studies found that smokers who used a vaping device were 70% more likely to quit than those who did not vape. (Zhu S. BMJ 2017; Johnson L. Nicotine Tob Res 2018) Studies in the UK also demonstrated that smokers who vaped had significantly higher quit rates than non-vapers. (Beard E. Addiction 2019; Berry K Tob Control 2018)

Daily vaping is even more effective A recent Australian study found that daily vaping is 'strongly' associated with quitting compared to non-use (OR 2.16) (Sun T. Add Behav 2021). In studies in the US,

vapers who used their device every day were three to eight times more likely to quit than smokers who did not vape. (Giovenco D. Add Behav 2017; Berry K. Tob Control 2018)

'Accidental' quitting

A recent study confirmed that vaping nicotine can be effective for smokers who are not planning to quit. A nationally representative cohort study of 1,600 US smokers who did not plan to ever quit smoking reported that using an e-cigarettes (without behavioural support) was associated subsequently with an 8 times higher self-reported quit rate than for those who did not use e-cigarettes (aOR 8.11). (Kasza KA. JAMA 2021)

"Impact of e cigarettes on non-smoking adolescents and adults"

"Three very recent studies all demonstrating the important 'gateway' effect of e-cigs non-smoking adolescents"

Vaping is associated with later smoking but there is no good evidence that vaping is a *causal* gateway to regular smoking in young people who would not otherwise have smoked. (Chan G. Addiction 2020) In fact, vaping appears to be diverting young people away from smoking.

The 3 studies listed by the reviewer (O'Brien BMC Pub Health 2012; Martinelli T. TC 2020; Yoong Plos One 2021) confirm the well-known longitudinal **association** between adolescents trying vaping and smoking but do not demonstrate a **causal** gateway, as suggested by the reviewer.

The most plausible explanation for the association between vaping and smoking is that young people who experiment with vaping have a common liability for risk taking. (Vanyukov M. DAD 2012) Some young people are more prone to both vaping and smoking because of personal characteristics or environmental circumstances such as mental health issues, smoking parents, unfavourable home environments, peer pressure, educational under-achievement, or delinquency. Some young people are also genetically predisposed to both smoking and vaping. (Hall W. PlosOne 2021; Khouja J. PlosMed 2021) It is largely these confounders that lead to smoking, not vaping.

In the most comprehensive analysis, which adjusted for a wide range of confounders, the association between vaping and smoking was substantially reduced and almost disappeared. (Sun C. Addict Beh 2021)

This conclusion is supported by others. According to the New Zealand Ministry of Health, 'Some people worry that vaping might be a 'gateway' to smoking for young people, but there is no clear evidence for this. Smoking among young people is continuing to decline and most young people who vape are smokers or ex-smokers.' ([NZ Gov 2019](#))

Public Health England's report on youth vaping in 2018 concluded, 'Never-smokers in the UK who try e-cigarettes are more likely to have tried smoking subsequently than those who have not tried e-cigarettes. A causal link has not been established and neither has progression to regular smoking.' (PHE Review 2018)

It is quite possible that vaping may lead some non-smokers to experiment with smoking and an even smaller number may go on to become regular smokers. However, the overall effect is likely to be very small. (Kozlowski L. DAD 2017; Chan G. Addiction 2020)

Diversion from smoking

The overall evidence suggests that vaping is diverting young people **away from** smoking and reduces the risk of an adolescent becoming a smoker: the 'diversion theory'. The diversion theory is consistent with the rapid decline in youth smoking in the United States and United Kingdom since vaping became popular. (Levy D. Tob Control 2018; Selya A. Addiction 2021; Selya A. HRJ 2021; Foxon F. Addiction 2020). If there was a significant causal gateway, smoking rates would be expected to increase.

A number of recent studies have demonstrated the diversion effect. (Sun C. Add Beh 2021; Walker N. Lancet 2020). Other studies have found that students who tried vaping first (before smoking) were less likely to be smokers later than those who tried smoking first (Shahab L. Tob Control 2020; Xu S. Prev Sci 2021) and that vaping may be replacing smoking in youth who are at the highest risk of becoming smokers. (Sokol N. NTR 2021)

Further weakening the gateway theory is that most teens who try vaping are already smokers. In 2017, two in three Australian twelve to seventeen year-olds who had vaped in the last month had smoked first. (Guerin N. ASSAD 2017) Surveys in other countries have found that over three in four smoking youth had smoked cigarettes before trying vaping. (Berry K Tob Control 2018; de Lacy E. BMJ 2017; Jarvis M. Qeios 2020)

In many cases, vaping is used by Australian teens to help them quit smoking (34%), to cut down on smoking (24%), to help prevent relapse (19%) and as a safer alternative to smoking. (NDSHS 2019) If young smokers switch to vaping, that can only be a good thing.

The role of the tobacco industry.

While we are also appalled by the tobacco industry, it is unscientific to oppose a safer product just because it is associated with tobacco companies. The overriding priority of public health should be to reduce the death and disease caused by tobacco use as quickly as possible. Safer alternatives to smoking will save lives, regardless of who makes them.

Modern vaping devices were invented as a quitting aid in 2003 by a smoking Chinese pharmacist, Hon Lik. They have since been improved on, largely by small companies independent of the pre-existing tobacco industry. **Vaping is a substitute for cigarettes and is a huge, disruptive threat to the tobacco industry.** The tobacco industry has been forced to adapt and compete with the new technology or risk losing its market.

The tobacco industry first invested in vaping in 2012 and it has been trying to catch up ever since. The tobacco industry currently controls no more than 20% of the global vapour market. ([GSTHR 2020](#))

The rise in vaping has led to an unprecedented decline in the value of international tobacco stocks. Share prices fell by more than half from 2017-2020. ([Mendelsohn C. Spectator 2020](#)) Proposals to restrict vaping have been repeatedly followed by rises in tobacco stocks and increased cigarette sales. ([Imp Brands 2021](#))

Reviewer 2 raises valid concerns that tobacco companies are all about profit and about the ethics and motives of their move into reduced risk products.

However, in our view, if the tobacco industry transitions from making deadly combustible cigarettes to safer nicotine alternatives, that can only be a good thing for public health and should be encouraged. Philip Morris's smoke-free nicotine products accounted for 29% of its global net revenue in the second quarter of 2021, compared with 0.2% in 2015, and the proportion is increasing every year (includes

reduced risk heated tobacco products). ([PMI 2021](#))

The major argument put forward in the "Vaping nicotine should be part of Australia's tobacco control policy" paper is the association in two countries - UK and US – between much greater availability of e-cigarettes and faster declines in tobacco prevalence than Australia – but this is purely an association

The statement is almost certainly false. It is not possible to conclusively prove that changes in population smoking can be attributed to any one intervention. However, we believe the evidence makes a compelling case that alternatives to smoking are in all probability acting as substitutes and are an important contributor to the decline in smoking rates where they are used.

That said, we accept that the evidence is not overwhelming but it is far stronger than of the alternative position that vaping is in some way sustaining smoking or has any potential to increase overall community risk.

Vaping is the most popular quitting method in the United Kingdom (West R. Smoking Toolkit Study 2021) and the United States (Caraballo R PCD 2017) and is arguably the single most effective quitting aid. (Thomas K. HTA 2021) As a result, it is likely to have an impact on population smoking rates.

It is noteworthy that the decline in smoking in both the US and UK has accelerated over the period that vaping has become widespread and population quit rates have increased. (Zhu S. BMJ 2017; Office of National Statistics, UK)

Zhu found that quit rates increased significantly in the US after 2014-15 when vaping became popular. (Zhu S. BMJ 2017) Zhu identified no other factors such as tax rises and public health marketing which explained this change and concluded 'Given that vaping is widely used and can be effective, it is more likely than not to be contributing to this rapid decline in smoking.'

Two studies from the UK estimated that vaping prevented the premature death in 2017 alone of 50,000 smoking-related deaths. (Beard E. Addiction 2019)

Recently data from NZ shows a similar pattern to the US and UK with vaping increasing and smoking declining. ([NZ Annual Health Survey 2021](#)) This is coupled with the longer time series on snus in Scandinavia, and the evidence from Japan on the displacement of cigarettes by heated tobacco. (Cummings KM. IJERPH. 2020) Further to this, experimental behavioural economics studies have demonstrated in experimental conditions substitution effects of vaping products for cigarettes (Bickel K. Prev Med 2018).

By contrast, Australia has a low current vaping rate and the decline in smoking prevalence appears to have slowed since 2013 according to two national surveys (NDSHS 2016, 2019). This is despite Australia having among the highest priced cigarettes in the world, the introduction of plain packaging and very rigorous tobacco control laws.

The comparison between countries increases the likelihood that the differences observed are at least in part due to a positive effect of vaping on reducing smoking prevalence. (Mendelsohn C. DAR 2020)