

A critical analysis of ‘Electronic cigarettes and health outcomes: Systematic review of global evidence’

1 | INTRODUCTION

The Australian Department of Health recently funded a review of vaping by Banks and colleagues that aimed to examine the ‘contemporary evidence on the health outcomes of nicotine and non-nicotine e-cigarette use’ and integrate this with ‘systematic reviews on smoking uptake and cessation’ to guide the formulation of evidence-based policy and practice [1].

In our view, the review failed to achieve its aims because it did not compare the relative risk of the harms of vaping to conventional cigarettes; it did not consider the net public health impact of vaping; it ignored evidence that vaping is effective in smoking cessation; and it confused causation and correlation in interpreting the association between youth vaping and cigarette smoking.

Banks et al. also used evidential double standards: they were prepared to accept a causal interpretation for the gateway hypothesis based on an association in observational studies but rejected similar evidence from observational studies of cessation. More importantly, they adopted a sceptical attitude towards the findings of randomised controlled trials showing that vaping is effective in assisting smoking cessation.

In this analysis, we summarise evidence that is inconsistent with the main findings of the review.

2 | VAPING AND SMOKING CESSATION

The Banks review concludes that ‘There is limited evidence that, in the clinical context, freebase nicotine e-cigarettes may be more efficacious for smoking cessation than existing NRT [nicotine replacement therapy]’ [1].

The most recent Cochrane review of randomised controlled trials (RCT) of electronic cigarettes versus nicotine replacement therapy (NRT) concluded that ‘There is moderate-certainty evidence that electronic cigarettes with nicotine increase quit rates compared to NRT (RR 1.53)’ [2]. Other meta-analyses report that electronic

cigarettes are superior to placebo and NRT but the authors differ in their confidence in the results [3–5].

Modern vaping devices may be even more effective than the cigalikes used in earlier trials [6]. A recent RCT in smokers unable to quit using conventional methods found that vaping was six times more effective than NRT at 6 months (relative risk 6.4, $p = 0.01$, 95% confidence interval 1.5–27.3) [7].

A recent network meta-analysis of 171 RCTs of all smoking cessation medications concluded that vaping was the most effective monotherapy, followed by varenicline and NRT [8]. The width of the confidence interval indicates the need for larger trials.

In assessing the effectiveness of vaping, the review also disregarded supportive evidence from observational studies, population studies and declines in national smoking rates. ‘Triangulation’ of all data provides a more accurate picture than relying on RCTs alone and increases confidence that vaping is an effective quitting aid [9].

Observational cohort studies have had mixed results, but two reviews of higher-quality studies found that vaping nicotine was significantly associated with an increased chance of an individual quitting smoking [10, 11].

Surveys in Australia, the United States and the UK have found that smokers who used a vaping device were significantly more likely to quit than those who did not vape [12–14]. Daily vaping delivers more effective nicotine replacement and is associated with higher quit rates than less frequent use. Those who vape daily are two to eight times more likely to quit smoking than smokers who do not vape [14–16]. Accelerated declines in adult smoking rates have been seen in the UK and United States where vaping rates are much higher than in Australia.

3 | VAPING AS A GATEWAY TO SMOKING

The Banks review claims that ‘there is strong evidence that e-cigarettes increase combustible smoking uptake in

Smoking and Vaping, US High schoolers

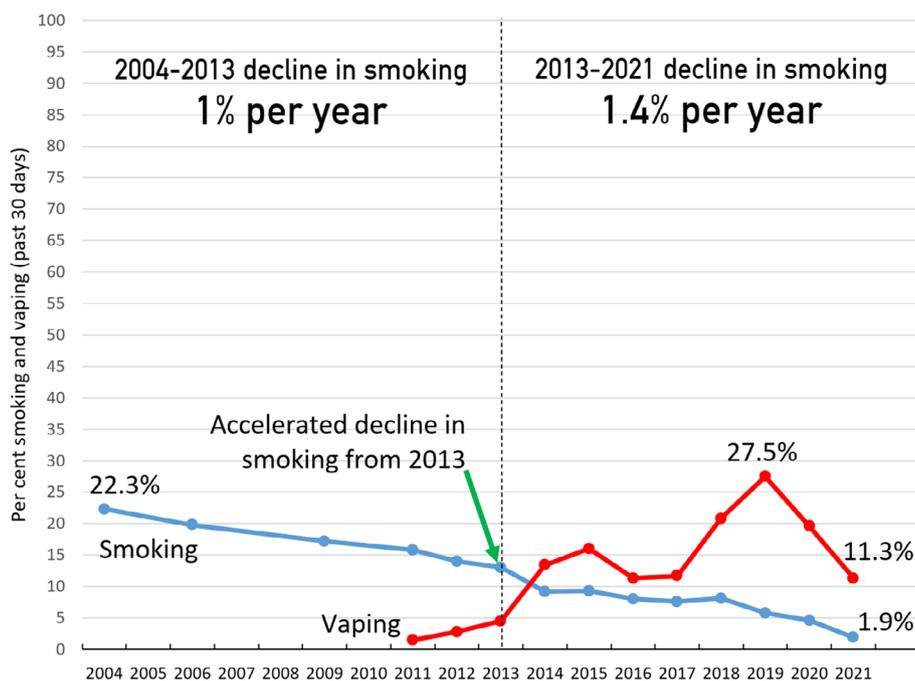
National Youth Tobacco Surveys (CDC)
Grades 9-12, ages 15-18 | Past 30-day use

FIGURE 1 Accelerated decline in youth smoking in the United States as vaping rates increased [24]

non-smokers, particularly youth'. However, in making this claim they confuse evidence of association for causation.

There is an association between vaping and smoking, but the most likely explanation is a common liability for risk taking, that is, that young people who experiment with vaping are more prone to take risks for personal, environmental or genetic reasons [17]. More rigorous prospective studies that adjust for a wide range of common risk factors for smoking and vaping (confounders) have found that the association between vaping and smoking largely disappears, as predicted by the common-liability model [18].

Evidence from population studies also suggests that vaping more likely diverts young people from smoking than encourages them to smoke [19–22]. Indeed, declines in youth and young adult smoking rates in the United States accelerated from around the time vaping became popular [23]. This population finding is the opposite of that predicted by the gateway hypothesis (Figure 1).

Most young people who vape have first smoked cigarettes [25]. Most vaping by never-smokers is experimental and transient, and regular vaping is rare [25, 26].

Regular vaping is rare in adult never-smokers. In Australia in 2019, less than 1 in a 100 adult never-smokers vaped once or more in the previous 12 months [27].

4 | COMPARATIVE HARMS OF VAPING AND SMOKING

The Banks review does not address the critical issue of relative risk. A meaningful assessment of the risk from vaping nicotine should compare it to the enormously greater risk of continuing to smoke tobacco.

The vast majority of frequent vapers are current or former smokers who have been unable to quit smoking using other methods.

Harm reduction from vaping is based on the substantially reduced exposure to toxins and carcinogens in vapour compared to smoke [28, 29] and is confirmed by a considerable reduction in biomarkers of harm in the blood, urine and saliva of smokers who switch to vaping [30, 31].

Smoke contains over 7000 toxic chemicals and solid particulate matter. Vaping liquid aerosols generally have fewer than 100 detectable chemicals, most in far lower concentrations [29].

Some additional chemicals not found in smoke are present in vapour but these do not appear to pose a significant hazard when inhaled [32]. The effect of inhaled food flavourings is largely unknown and could have potential risk. No harms from flavourings have been demonstrated so far but ongoing monitoring is needed [33].

Most of the cardiovascular effects of vaping are consistent with the known effects of nicotine [34]. These include transiently raised pulse and blood pressure, cardiac contractility and arrhythmogenesis. Nicotine may pose some risk in people with pre-existing cardiovascular disease [34]. Cardiotoxic constituents of smoke are either absent from vapour or are present in much lower levels [34].

Human studies on cardiovascular outcomes are limited. However, two studies showed a significant and sustained reduction in blood pressure in smokers who switched to vaping [35, 36]. Another study demonstrated substantial improvements in vascular function in smokers who switched to vaping after 4 weeks [37].

Vaping is also likely to be far less harmful to the lungs than smoking [38]. Human respiratory studies have demonstrated improved pulmonary health in smokers who switch to vaping, including improved respiratory symptoms and lung function [39]; asthma [40]; chronic obstructive pulmonary disease [41]; muco-ciliary clearance [42]; and fewer respiratory infections [43].

In vitro and animal studies have found that harmful cardiovascular and respiratory effects from vapour are generally far less than from tobacco smoke [39, 40, 44, 45].

It is highly implausible that nicotine vaping was a cause of the EVALI outbreak (E-cigarette, or vaping, product use-associated lung injury) in the United States in 2019. This condition was strongly linked to vitamin E acetate added to black-market tetrahydrocannabinol (THC) vaping oils and disappeared after vitamin E acetate was removed from the illicit supply chain [46]. The observation that 14% of EVALI patients denied using THC and had been vaping nicotine does not prove a causal link with nicotine vaping products. Many patients who denied vaping THC were subsequently found to have done so, and no other causal agent has been identified in nicotine e-liquids [47, 48].

Based on the substantial reduction in the number and dose of carcinogens in vapour, the lifetime cancer risk from vaping has been estimated to be less than 0.5% of the risk from smoking [49, 50].

The Cochrane Review did not detect evidence of harm in studies up to 2 years, although the number of studies was small and longer studies are needed [2].

5 | NET PUBLIC HEALTH EFFECTS OF VAPING

The key public health question is whether the net effect of vaping is beneficial or harmful at a population level. The net effect is a function of the harm differential between vaping and smoking, its effectiveness as a cessation aid and uptake by smokers and non-smokers.

Vaping is the most popular quitting aid in Australia [27] and is arguably the most effective monotherapy for quitting [8]. Regular use by adult and youth never-smokers is rare [26, 27]. As a result, vaping has the potential to reduce smoking prevalence more than any other intervention.

Numerous modelling studies (with one exception) [51] have concluded that the overall benefits of vaping are considerably greater than the harms and are likely to improve public health [52–54]. These have evaluated the net effects under a wide range of assumptions about rates of uptake among non-smokers, cessation rates and reduction in harm compared to smoking.

One study estimated that under current patterns of vaping and substitution in the United States, nicotine vaping will translate into 1.8 million premature smoking- and vaping-attributable deaths avoided and 38.9 million life-years gained between 2013 and 2060 [54].

Beard estimated that 50,000 additional smokers stopped smoking in the UK with a vaping product in 2017 who would otherwise have continued smoking [14].

6 | CONCLUSION

Contrary to the conclusions of the Banks review, the evidence suggests that vaping nicotine is an effective smoking cessation aid; that vaping is substantially less harmful than smoking tobacco; that vaping is diverting young people away from smoking; and that vaping by smokers is likely to have a major net public health benefit if widely available to adult Australian smokers.

CONFLICT OF INTEREST

Dr Colin Mendelsohn was a Board Member of the Australian Tobacco Harm Reduction Association (ATHRA), a registered health promotion charity, from October 2017 to January 2020 and Dr Alex Wodak is a Board Member of ATHRA. ATHRA accepted unconditional seed funding from the vape retail industry to get established. Funding ceased in March 2019. Drs Colin Mendelsohn and Alex Wodak were Directors of ATHRA in March 2018 when it received a donation from Knowledge Action Change Communications, a private sector public health agency in the UK. The donation was sourced from a surplus arising from the Global Forum on Nicotine conference in May 2017. Knowledge Action Change Communications is legally separate from Knowledge Action Change (KAC). KAC has received two grants from tobacco companies: (i) In 2012, KAC received a small development research grant from Nicoventures (owned at the time by British American Tobacco) for evaluating the use of a nicotine delivery device in Scottish Prisons. The study was conducted in conjunction

with the Scottish Prison Service. This funding was publicly declared. (ii) In 2018, The Foundation for a Smoke-Free World provided a grant specifically for the preparation of The Global State of Tobacco Harm Reduction report, an international review of tobacco harm reduction and the regulations involved. The Foundation for a Smoke-Free World is funded by an annual grant from Philip Morris International. Under the Foundation's bylaws and pledge agreement, Philip Morris International and the tobacco industry are precluded from having any influence over how the Foundation spends its funds or focuses its activities. Dr Colin Mendelsohn is the author of Aurora Press, *Stop Smoking Start Vaping*. He has never received payments from electronic cigarette or tobacco companies. Dr Alex Wodak has never received payments from electronic cigarette or tobacco companies. Professors Wayne Hall and Ron Borland have no interests to declare.

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