



CROSSTALK

CrossTalk proposal: The benefits of e-cigarettes outweigh the harms

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Tobacco use kills over 8 million people annually and costs billions in healthcare worldwide (World Health Organization, 2019). Addiction to smoking explains why smoking persists into adulthood, with 96% of unaided attempts to quit ending in failure (Hughes *et al.* 2004). Treatment, pharmacotherapy and behavioural support, can increase success rates severalfold (Stead *et al.* 2016). Countries such as the UK that have made such treatment available advertise this to the public and clinicians refer to such services. Despite this, the uptake of e-cigarettes eclipsed the uptake of known effective and safe options, even before big business moved into the e-cigarette industry and advertised the products. It is this ability to provide an attractive alternative to smoking that creates the potential for e-cigarettes to improve public health.

When cigarettes were first discovered to be harmful, most adults had smoked for many years and epidemiology was able to estimate the risks. In a world in which nearly everyone who vapes has smoked or currently smokes, and where people who vape have

done so for <10 years, epidemiology will not be able to assess long-term risks. Here we argue that it is possible from appropriately conducted toxicological studies and emerging epidemiological data to conclude that e-cigarettes are substantially less risky than smoking, even if the precise risks remain uncertain. In light of evidence that e-cigarettes promote switching *from* smoking and not *to* smoking, we argue that the benefits outweigh the harms.

Vaping is comparatively less harmful than smoking

There is overwhelming evidence that smoking causes substantial harm to smokers and bystanders. In smokers, smoking increases the risk of heart disease and stroke 2–4 times, respiratory disease 12–13 times, and lung cancer 25 times (US Department of Health & Human Services, 2014). The corollary of this is that stopping smoking reduces the risk of developing serious illnesses and disease progression, even in those who have smoked for >40 years (Critchley & Capewell, 2003).

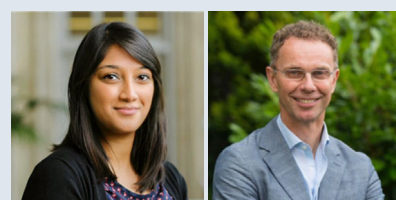
There are now many toxicological studies of the effects of e-cigarettes. A common trope is to apply e-liquid (the liquid used to fill an e-cigarette) to a cell culture and incubate, find abnormalities, and then publish a paper and press release claiming that e-cigarettes are toxic. A systematic review concluded that, while most *in vitro* studies suggest e-cigarettes are toxic, they are less toxic than comparable use of cigarettes or solutions (Wang *et al.* 2019) – the relevant comparison for most vapers. The key overarching conclusion was that the field desperately needs standards to define the dose of e-liquid components applied and the relevant cell cultures they are applied to, developing study paradigms that mimic the repetitive but intermittent exposures relevant to human vaping. Even

in vivo studies of e-cigarettes vaped in laboratory studies can mislead. One study raised concerns that concentrations of toxic aldehydes, including formaldehyde, acrolein and acetaldehyde, were higher from vaping than from smoking (Jensen *et al.* 2015). However, a replication study involving human vapers showed that such concentrations only occur under 'dry puff' conditions, in which overheated e-liquid produces a foul taste that all vapers recognised and avoided. At tolerable vaping conditions, aldehyde concentrations were low (Farsalinos *et al.* 2015b, 2017).

Tobacco cigarette smoke contains thousands of toxic chemicals, many of which are carcinogenic and are present in tobacco or derived from its combustion. In contrast, e-cigarettes do not contain tobacco, nor do they involve combustion, and so many toxins present in cigarette smoke are either absent or occur at much lower concentrations in e-cigarette aerosol (Goniewicz *et al.* 2014; Hajek *et al.* 2014). Biomarker of exposure studies have found that, compared to smokers, long-term e-cigarette users had substantially reduced their exposure to tobacco-specific nitrosamines, particularly metabolites of the lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (Shahab *et al.* 2017). E-liquids contain nicotine of varying strengths; while some concerns lie in its addictive potential, nicotine itself does not significantly contribute to smoking-related disease (Benowitz, 1997) and it is widely accepted and effective in the form of nicotine replacement therapy as a substitute for smoking.

Additional concerns have been reported for toxins released from flavoured e-liquids, including diacetyl and acetyl propionyl. These compounds have been associated with bronchiolitis obliterans, but no cases have been reported due to e-cigarette use and the concentrations are hundreds of

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times lower than observed in tobacco smoke (Farsalinos *et al.* 2015a). Heavy metals in e-cigarette aerosol have also caused alarm, given that inhalation in larger quantities may cause respiratory diseases; however, the levels detected in e-cigarette aerosols are, again, considerably lower than that found in cigarette smoke (Farsalinos & Rodu, 2018). As e-cigarette technology improves, emissions could be reduced (Royal College of Physicians, 2016).

Limited clinical data show no cause for concern in people vaping after stopping smoking for up to 2 years (Hartmann-Boyce *et al.* 2016). Most commonly reported adverse events are throat or mouth irritation and dry cough (Hajek *et al.* 2014), with recent trial evidence showing a greater decline in the incidence of cough over a 1 year period in smokers who had switched to e-cigarette use compared to those using nicotine replacement therapy (Hajek *et al.* 2019). People with asthma and chronic obstructive pulmonary disease have generally shown improvements in respiratory health, rather than a worsening, following a sustained switch to e-cigarettes from smoking (Polosa *et al.* 2016, 2018). A recent trial found that smokers who switched to e-cigarette for 1 month showed significant improvements in endothelial function, arterial stiffness and systolic blood pressure compared with continuing smoking (George *et al.* 2019).

The recent outbreak of severe lung injury in predominantly young men in the USA has been clearly associated with vaping vitamin E acetate, a product used in illegal cannabis vaping products (Blount *et al.* 2019; Hartnett *et al.* 2020). It is not relevant to people vaping to stop or reduce their smoking.

E-cigarettes are a useful tool for helping people to stop smoking

Randomised controlled trials indicate that e-cigarettes support smokers to quit, something expected from their ability to provide nicotine, doubling the rate of long-term abstinence (Hartmann-Boyce *et al.* 2016). A recent randomised controlled trial involving nearly 900 participants found that alongside behavioural support, e-cigarettes were nearly twice as effective at helping smokers quit compared with nicotine replacement therapy at 1-year follow-up (Hajek *et al.* 2019).

While e-cigarettes have rapidly grown in popularity both in the UK and USA, smoking prevalence has declined (Wang *et al.* 2018; Office for National Statistics, 2019). In the UK, data from a time series analysis found that an increase in the use of e-cigarettes by smokers in England was positively associated with an increase in overall quit rates and quit success rates (Beard *et al.* 2020). These findings are supported by a population-level survey in the USA showing a significant increase in smoking cessation rates among e-cigarette users (Zhu *et al.* 2017). Although these data are observational and cannot show causality, they do add to evidence that e-cigarettes are not undermining the decline in smoking prevalence. There is no evidence that e-cigarette use is slowing the rate of decline in smoking among young people (Bauld *et al.* 2017), despite the rise in uptake and experimentation in both the UK and USA. In fact, smoking rates in US adolescents have decreased more rapidly since e-cigarettes became popular (Jamal *et al.* 2017). Never-smokers who take up vaping do expose themselves to avoidable health risks, but less than 1% of never-smokers become regular vapers in the UK (Action on Smoking & Health, 2019).

Closing remarks

E-cigarettes help people stop smoking and while some vapers continue vaping long-term, the harm they experience from this is likely to be substantially less than that from smoking. While it may seem natural to urge caution, Sweden shows the dangers of over-zealous 'cautious' regulation. When Sweden joined the EU, snus, a nicotine-containing oral tobacco pouch, was used commonly by men. The EU banned snus use everywhere but exempted Sweden. In Sweden, oral tobacco use prevalence is high (20%) but Sweden has the lowest rates of daily cigarette use in the EU (5% compared to the EU 24%) (The European Commission, 2017). Swedish men have the lowest rates of tobacco-related mortality and lung cancer in Europe (Ramström & Wikmans, 2014), while snus use poses only a fraction of the risk of smoking (Gartner *et al.* 2007). This example highlights the danger of over-regulation of harm-reduction products, which appear to be able to break the tenacious hold that smoking has on

many people and substantially reduce avoidable morbidity and mortality.

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Additional information

Competing interests

None.

Author contributions

Both authors have contributed to the conception or design of the work and drafting the work or revising it critically for important intellectual content. Both authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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