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Commentary What are the harms of vaping in young people who have never smoked?



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Recent increases in nicotine vaping by adolescents have understandably alarmed parents and school communities. Concerns have been greatest about the uptake of vaping by young people who have never smoked.

A reasonable fear is that vaping by people who have never smoked may cause potential new harms, such as nicotine dependence, effects on the developing brain and a transition to cigarette smoking, the most harmful way of obtaining nicotine. Vaping among young people who already smoke may be beneficial if it diverts them away completely from cigarette smoking.

Youth vaping is the key driver of media debates and vaping policy in many countries, such as Australia and the United States. An objective assessment of the risks and benefits of vaping in young people is important to understand its impact on public health and inform evidencebased policy. This requires an analysis of the prevalence of vaping by young people who have never smoked and a review of the evidence on the risks it poses to health.

How common is frequent vaping in never-smokers?

Most vaping by never-smoking adolescents is occasional and transient (Action on Smoking and Health UK, 2022; ASH New Zealand, 2022; Glasser, Johnson, Niaura, Abrams, & Pearson, 2021; Hammond et al., 2019; Jarvis, Jackson, West, & Brown, 2020; NHS Digital, 2022). Frequent vaping by young people who have never smoked is uncommon in western countries with a prevalence mostly under 2%. (Table 1) Vaping rates are substantially higher in current or former smokers, ranging from 18-89% (Action on Smoking and Health UK, 2022; ASH New Zealand, 2022; Glasser et al., 2021; Hammond et al., 2019; Jarvis et al., 2020; NHS Digital, 2022).

The most detailed data on youth vaping are from England and demonstrate a strong association between vaping and smoking (NHS Digital, 2022) (Table 2). In 2021, only 1% of 11-15-year-olds who had never smoked cigarettes vaped regularly (once or more weekly), although a proportion of these may take up smoking later. In comparison, 61% of those who smoke regularly (at least one cigarette per week) also vaped regularly.

Measures of lifetime vaping ("even a puff") or current vaping (at least once in the past 30-days) overestimate the prevalence of frequent vaping by those who have never-smoked because they include experimental and infrequent vaping which is the most common pattern of use in this group (Action on Smoking and Health UK, 2022; Glasser et al., 2021; Hammond et al., 2019; Jarvis et al., 2020).

Does vaping increase the risk of taking up smoking?

It is well established that young people who try vaping are more likely to later try smoking (Soneji et al., 2017). There is a tendency in policy discussions to assume that this association is causal (the gateway hypothesis) (Chan et al., 2021). However, it is not the only possible or the most plausible explanation. A more likely explanation is that the association is explained by shared risk factors for vaping and smoking, such as a genetic liability to develop nicotine addiction (Hall & Chan, 2021) and environmental, psychological and social causes e.g., peer group or parental smoking (Cambron & Thackeray, 2022) that create a 'common liability' for risk taking (Vanyukov et al., 2012). In studies that adjust for these confounders, most of the association between vaping and subsequent smoking has disappeared (Kim & Selya, 2019; Lee, Coombs, & Afolalu, 2018; Sun, Mendez, & Warner, 2022).

The gateway hypothesis also predicts that increased vaping will increase cigarette smoking among youth. However, increases in youth vaping have been accompanied by an accelerated decline in smoking since vaping became popular in the US, UK and New Zealand, suggesting either no overall gateway effect or at most, a small gateway effect that is outweighed by the much larger number moving from smoking to vaping (Centers for Disease Control and Prevention, 2021; Levy et al., 2019; Meza, Jimenez-Mendoza, & Levy, 2020; NHS Digital, 2022) (Fig. 1).

Population and modelling studies also suggest that vaping and smoking are substitutes and that vaping is displacing smoking at a population level (Foxon & Selya, 2020; Selya & Foxon, 2021; Sokol & Feldman, 2021; Walker et al., 2020). Studies of the effects of tax increases on vaping products also support a diversion effect. Higher taxes on vapes are associated with increased cigarette smoking while higher cigarette prices are associated with increased vaping (Abouk et al., 2023; Cantrell et al., 2020; Chan et al., 2022; Pesko & Warman, 2022), (Fig. 2).

Bans or purchasing restrictions on the sale of vapes to teens are also associated with increased adolescent smoking (Dave, Feng, & Pesko, 2019; Friedman, 2015; Pesko, Hughes, & Faisal, 2016). One study estimated that establishing a minimum legal sale age for e-cigarettes in

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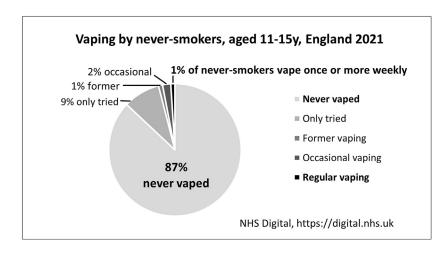
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Table 1

	Frequent of	or daily	vaping	by	never-smoking	youth.
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Country	Vaping frequency	Year	Never smokers	Current smokers	Age	Ref
England	\geq once weekly	2021	1%	61% of regular smokers (at least one cigarette per week) were regular vapers	11-15	(NHS Digital, 2022)
	> once weekly	2022	0.5%	55.4% of current smokers (occasional or more frequent) were current vapers	11-17	(Action on Smoking and Health UK, 2022)
	\geq 15 days in the last 30	2018	0.1%	13.4% of current smokers (at least 100 cigarettes in lifetime and smoked in past 30 days) vaped frequently	16-19	(Hammond et al., 2019)
United States	\geq 20 days in the last 30	2018	0.4%	88.9% of frequent vapers were current (smoked in the past 30 days) or past smokers	9-19	(Glasser, Johnson, Niaura, Abrams, & Pearson, 2021)
		2019	2.1%	48.8% of frequent vapers had smoked >100 cigarettes	14-18	(Jarvis, Jackson, West, & Brown, 2020)
	\geq 15 days in the last 30	2018	1.5%	23.4% of current smokers (at least 100 cigarettes in lifetime and smoked in past 30 days) vaped frequently	16-19	(Hammond et al., 2019)
Canada	\geq 15 days in the last 30	2018	0.6%	18% of current smokers (at least 100 cigarettes in lifetime and smoked in past 30 days) vaped frequently	16-19	(Hammond et al., 2019)
New Zealand	Daily	2022	4.3%	86.6% of daily smokers vaped daily	15	(ASH New Zealand, 2022)



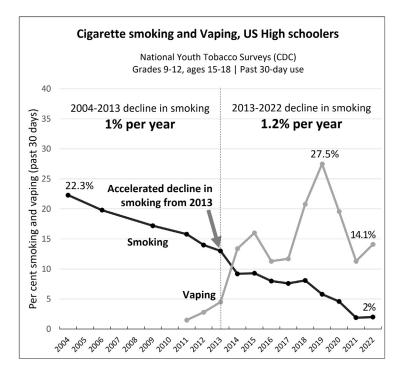


Fig. 1. Vaping by never-smokers, aged 11-15y, England 2021.

Fig. 2. Decline in youth smoking in the US as vaping increased (Centers for Disease Control and Prevention, 2021).

the US between 2010-2016 reduced e-cigarette use but increased daily smoking by approximately 35% (Pesko, 2023).

Approximately 25-50% of adolescents who experiment with vaping are non-smokers at the time (Legleye, Aubin, Falissard, Beck, & Spilka, 2021; Mus, Monzon, Islam, Thrasher, & Barnoya, 2023; Shahab, Beard, & Brown, 2021; Watts et al., 2022). There is growing evidence that those who vape first (before smoking) are less likely to smoke later, compared to those who smoke first (Chyderiotis, Benmarhnia, Beck, Spilka, & Legleye, 2020; Legleye et al., 2021; Mus et al., 2023; Shahab et al., 2021; Sokol & Feldman, 2021; Xu et al., 2022).

Importantly, in cross-sectional (Kim & Selya, 2019; Levy et al., 2019; Shahab et al., 2021) and longitudinal studies (Sun, Méndez, & Warner, 2023) it does not appear that youth vaping leads to increases in sustained cigarette use which is the major public health concern. Studies that measure experimentation with smoking overestimate smoking uptake because only a small fraction of ever or infrequent cigarette smokers progress to become persistent lifetime users (Glasser et al., 2021).

What are the known health effects of vaping by never-smokers?

Young people who have never smoked should not vape as this exposes them to toxic chemicals and unnecessary health risks. The precise long-term effects of vaping nicotine will not be fully known for decades. Effects from long-term vaping may include cardiovascular (Benowitz & Fraiman, 2017) and respiratory effects (Polosa, O'Leary, Tashkin, Emma, & Caruso, 2019). Ongoing monitoring and long-term studies are essential to detect any problems that may arise in the future, particularly from sustained frequent vaping.

Furthermore, most vaping by young people who have never smoked is infrequent and short-term (Action on Smoking and Health UK, 2022; Glasser et al., 2021; Hammond et al., 2019; Jarvis et al., 2020). This pattern is associated with lower levels of toxic exposure and so is likely to have fewer adverse health effects than frequent or sustained use. The most commonly reported adverse short-term effects of vaping are throat and mouth irritation, headache, cough and nausea, effects which tend to dissipate with continued use (Hartmann-Boyce et al., 2022).

Vaping has been associated with respiratory symptoms in young people in cross-sectional studies, but many young people who vape have also smoked tobacco so the significance of these findings is uncertain (McConnell et al., 2017; Schweitzer et al., 2015; Wang, Ho, Leung, & Lam, 2016). Other studies have found no functionally-important respiratory symptoms in young people who vape after account is taken of past cigarette smoking (Stevens et al., 2022; Tanski et al., 2022). A metaanalysis of ten cross-sectional studies found an association between vaping and asthma in young people but it was unclear if the association is causal (Li et al., 2022). A large, longitudinal study found that exclusive e-cigarette use was not associated with the onset of asthma (Mattingly et al., 2023).

There is evidence from animal studies that high doses of nicotine cause harmful effects on the adolescent brain but it is uncertain if these findings can be extrapolated to adolescent humans (Balfour et al., 2021). Studies have not found large difference in IQ (Wennerstad et al., 2010), educational achievement (Treur et al., 2015) or cognitive abilities (Corley, Gow, Starr, & Deary, 2012) in adulthood between those who have smoked in the past and those who have never smoked.

There is some evidence that nicotine may in the short-term improve attention, memory (Heishman, Kleykamp, & Singleton, 2010) and cognitive function (Gil & Metherate, 2019), relieve anxiety (Morissette, Tull, Gulliver, Kamholz, & Zimering, 2007) and improve mood (Picciotto, Brunzell, & Caldarone, 2002).

Nicotine itself represents minimal risk of serious harm in the doses commonly used in vaping (McNeill, Brose, Calder, Bauld, & Robson, 2018; McNeill et al., 2022). Nicotine does not cause cancer (International Agency for Research on Cancer, 2012) or lung disease (US Department of Health and Human Services, 2014) and it has only a minor role in cardiovascular disease (Benowitz & Burbank, 2016). A recent meta-analysis of 42 studies with a median duration of 10 weeks found with moderate certainty that there are no significant associations between the use of nicotine and the risk of clinically diagnosed adverse cardiovascular events (Kim et al., 2023).

However, nicotine withdrawal can cause short-term symptoms such as irritability, restlessness, anxiety, difficulty concentrating and depression (Benowitz, St Helen, & Liakoni, 2021).

To date, there have been no identified health risks of passive vaping to bystanders due to the low levels of toxicants emitted (McNeill et al., 2018; Royal College of Physicians, 2016).

There is no evidence that vaping nicotine causes the serious lung disease E-cigarette or Vaping Associated Lung Injury (EVALI) (Mendelsohn, Wodak, & Hall, 2023) or seizures (Benowitz, 2020) EVALI was caused by vaping illicit cannabis oils contaminated with vitamin E acetate (Krishnasamy et al., 2020). There is a rare risk of burns and injuries from lithium-battery explosions, but none have been reported from disposables, the most popular type of device used by young people (Tattan-Birch, Jackson, Kock, Dockrell, & Brown, 2022; Watts et al., 2022).

Vaping is likely to be far less harmful than smoking (Committee on Toxicity of Chemicals in Food Consumer products and the Environment (COT), 2020; McNeill et al., 2018; McNeill et al., 2022; National Academies of Sciences Engineering and Medicine, 2018; Royal College of Physicians, 2016). There are substantially fewer harmful and potentially harmful constituents (HPHC) in vapour than in tobacco smoke and those that are present occur at far lower concentrations (McNeill et al., 2022). Further research is needed to assess the potential toxicity of inhaled flavoring additives and their thermal degradation products (Committee on Toxicity of Chemicals in Food Consumer products and the Environment (COT), 2020).

Do never-smokers who vape become dependent on nicotine?

Vaping can cause nicotine dependence in some young people who have never smoked. The evidence suggests however, that this is a minority of cases, not, as the media often claim, a "new generation addicted to nicotine" (Jackson, Brown, & Jarvis, 2021).

An analysis of the 2018 US National Youth Tobacco Survey found that <4% of young people who had vaped in the past 30 days but had never smoked had signs of nicotine dependence (Jarvis et al., 2020). This low incidence is consistent with the dominant pattern of occasional and short-term use of vapes.

Nicotine dependence is concentrated in young people who have previously or currently smoke (Hammond et al., 2019; Jackson, Kotz, West, & Brown, 2019; Liu, Wasserman, Kong, & Foulds, 2017). In the US, there was a 50% decline in youth vaping from 2019-2021 suggesting that many young people who vaped were readily able to stop. This period included the COVID pandemic, although its influence on this decline is unclear (Chen-Sankey, Bover Manderski, Young, & Delnevo, 2022) (Fig. 1).

Nicotine dependence in the US youth population has not increased overall from 2012-19 despite the rise in youth vaping (Jackson et al., 2021). This may be partly attributable to a shift away from cigarettes (on which users are most dependent) to vaping products (on which users are less dependent).

Not all young people who vape use nicotine. Thirty to fifty percent report not using nicotine, or not knowing if they had used it or not (Gorini et al., 2020; Miech, Johnston, O'Malley, Bachman, & Patrick, 2019; Watts et al., 2022).

As with adults, nicotine dependence is lower in young people who vape compared to those who smoke (Hammond et al., 2021; Jarvis et al., 2020). Some young people may need support to stop vaping using strategies such as counselling, a gradual reduction in nicotine concentration or abrupt cessation, switching to a nicotine replacement product and re-

lapse prevention (National Centre for Smoking Cessation and Training, 2022).

The development of nicotine dependence in adolescence is unlikely to increase the risk of later use of other drugs (Lynskey & Agrawal, 2018). However, research has not been able to discount the possibility of a causal link.

What about the risks for young smokers who take up vaping?

The vast majority of young people who experiment with both vaping and smoking had smoked before they tried vaping (Berry et al., 2019; Chyderiotis, Spilka, & Beck, 2019; de Lacy, Fletcher, Hewitt, Murphy, & Moore, 2017; Jarvis et al., 2020). Many teens who smoke use ecigarettes to quit smoking or as a safer alternative (Australian Institute of Health and Welfare, 2020; Camenga, Kong, Cavallo, & Krishnan-Sarin, 2017; Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2015). However, studies so far have not found an association between e-cigarette use and subsequent smoking cessation in this population (Lin et al., 2022; Saller, Agaku, & Filippidis, 2022; Wang, Li, Wu, Lam, & Chan, 2017).

There is also little evidence of effectiveness of nicotine replacement therapy for adolescent smoking (Myung & Park, 2019) which may be partly explained by poor compliance (Scherphof, van den Eijnden, Lugtig, Engels, & Vollebergh, 2014).

Vaping is not harmless, but is likely to be far less harmful than smoking and those who switch from smoking to vaping are likely to see health benefits (McNeill et al., 2022). Switching to exclusive vaping is recommended for optimal benefit as dual use (vaping and smoking) is associated with greater toxicant exposure than vaping alone and greater health risk (Anic et al., 2022).

Modelling studies suggest a net benefit from vaping to population health under all plausible scenarios. These models take into account harms from vaping (uptake by never-smoking youth and adults, the potential to increase smoking, inhibit smoking cessation and promote relapse) and benefits (cessation of smoking and diversion of those who would have otherwise have taken up smoking) (Levy et al., 2021; Summers, Ait Ouakrim, Wilson, & Blakely, 2022).

Policy measures to reduce youth vaping

Vaping policy needs to balance the substantial and more immediate benefits for adults who smoke against the smaller and delayed risks of uptake among non-smoking youth (Balfour et al., 2021). A tightly regulated, risk-proportionate consumer model with strict age verification would make regulated vaping products more available for adults who smoke, reduce illicit sales and reduce youth access (Mendelsohn, Wodak, & Hall, 2023). Nicotine liquids should be available from licensed retail outlets, such as specialist vape shops, pharmacies and general retail outlets, as for cigarettes and alcohol. Strict age verification at the time of purchase should be required with harsh penalties for breaches such as fines and loss of licence. Consideration could be given to mandatory CCTV recording of sales as a condition of a sales licence. Some leakage to youth through social sources is inevitable and controlling this would need further regulatory measures.

Strict age verification at the time of sale is essential and can be enforced under a licensing scheme for retail outlets. Breaches of age-of-sale limits should result in severe penalties and loss of licence. A third-party verification service is required for online purchases with age verification on delivery.

We need to recognize that overly restrictive policies intended to reduce youth vaping can have counterproductive results. Vaping products and cigarettes are substitutes among nicotine users. Restrictions on youth access to e-cigarettes are associated with higher adolescent cigarette smoking (Dave, Feng, et al., 2019; Friedman, 2015; Pesko et al., 2016). Young people enjoy flavored products and longitudinal studies have found that the initial use of flavors is associated with continued vaping (Notley et al., 2022). Flavors may also contribute to the diversion of young people from smoking and as an aid to smoking cessation. There is no evidence to date that flavored e-liquid use specifically is associated with tobacco smoking uptake or cessation (Notley et al., 2022) but more research is needed to clarify the overall impact of flavors.

Flavor bans can also have unintended harmful effects. A ban on flavored tobacco and vaping products in San Francisco in 2020 was associated with a more than doubling of cigarette smoking by high school students relative to concurrent changes in other districts (Friedman, 2021). A ban on flavors in pod-based products other than tobacco and menthol in the US resulted in a shift to disposable products by adolescents. Vaping and smoking behaviours remained unchanged (Hammond et al., 2022). The effects of these policies need further evaluation. However, flavor names that specifically appeal to young people should be prohibited.

Taxation should be kept to a minimum and proportionate to risk to incentivize switching by adults who smoke (Royal College of Physicians, 2016). Increased taxation of vaping products to reduce youth vaping is associated with increased smoking by youth (Abouk et al., 2023; Pesko & Warman, 2022) and shifts the source of vapes from retail to social sources (Abouk et al., 2023).

Disposable devices are popular with young people (Tattan-Birch et al., 2022). However, a disposable ban could simply similarly shift usage from disposables to another nicotine product (Khouja & Munafò, 2022). Disposables also play an important role as a transition model for adults who smoke and a ban may have unintended consequences for adults (Russell, McKinney, & Fearon, 2023).

Advertising to adults who smoke at the point-of-sale helps raise awareness of vaping as a safer alternative and may encourage them to switch (Dave, Dench, Grossman, Kenkel, & Saffer, 2019). There is also an association between viewing advertisements and youth vaping (Dai & Hao, 2016; Padon, Lochbuehler, Maloney, & Cappella, 2018). It is not clear if this association is causal or if adolescents who are interested in vaping are more likely to notice advertisements (attentional bias) (Dai & Hao, 2016). The impact of advertising on adolescents can be minimised by enforcing socially responsible advertising and controlling the content and placement of advertisements (UK Advertising Code, 2016).

Packaging should not include images that appeal to youth. However, the one study of graphic images found that they were not effective in deterring youth vaping (Wojtecka et al., 2023). A recent study found that adolescents considered their peers would be less interested in plain, standardised green packs for vape products compared to fully branded packaging (Taylor et al., 2023). Plain packaging is appropriate for smoking products but in our view may be disproportionate to the risk involved from vaping.

Australia's current prescription-only model for vaping has primarily been justified to minimise youth uptake of vaping (Therapeutic Goods Administration, 2022). However, since the introduction of this policy in October 2021, the illicit vaping market has grown rapidly and probably contributed to a significant increase in youth vaping (Watts et al., 2022).

Strategies to reduce youth vaping are listed in (Table 2).

Table 2

- · Legal vaping products sold only from licensed retail outlets
- Strict age verification at the time of sale

Policy measures to reduce youth vaping.

- · A third-party age verification service for online purchases and on delivery
- Advertising restricted and regulated to prevent marketing to adolescents
- Substantially increased fines and loss of licences for illegal sales
- · Banning flavour names, images and packaging which appeal to young people
- Education programs for young people should provide accurate information about the absolute and relative risks of vaping and smoking.

Conclusion

Frequent vaping of nicotine by young people who have never smoked is uncommon and there is limited evidence so far that vaping has caused significant harms in this population. At a population level, the net benefits of vaping to adult and youth who smoke are likely to outweigh the feared harms of vaping to youth.

Very few nicotine-naïve young people who vape develop nicotine dependence. There is weak evidence that vaping leads to smoking. In fact, the evidence suggests that vaping is diverting more young people away from smoking. It is also likely to be beneficial to young people who smoke who switch to vaping.

A balanced, risk-proportionate approach to regulation is needed to restrict the uptake of vaping by young people who do not smoke while allowing easier access for adults who smoke, for whom it is an effective and popular quitting aid.

Author contributions

Each author certifies that their contribution to this work meets the standards of the International Committee of Medical Journal Editors.

Ethics approval

The authors declare that the work reported herein did not require ethics approval because it did not involve animal or human participation.

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Declaration of Competing Interest

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Colin Paul Mendelsohn

C.P.M. was an unpaid board member of the Australian Tobacco Harm Reduction Association (ATHRA), a registered health promotion charity, from October 2017 to January 2021. ATHRA accepted unconditional seed funding from the vape retail industry to become established. Funding ceased in March 2019. C.P.M. was a Director of ATHRA in March 2018 when it received a donation from KAC Communications.

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C.P.M. is the author of *Stop Smoking Start Vaping*, published by Aurora Press. C.P.M. has never received payments from electronic cigarette or tobacco companies.

Wayne Hall

No competing interests.

CRediT authorship contribution statement

Colin Paul Mendelsohn: Conceptualization, Project administration, Writing – original draft, Writing – review & editing. **Wayne Hall:** Writing – review & editing.

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