Potential reforms to the regulation of nicotine vaping products

Submission

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3 I am responding as an individual

4 n/a

5 n/a

6 Registered healthcare practitioner

7 Medical practitioner

8 Yes

9 I have never received payments from electronic cigarette or tobacco companies.
I 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 get established. Funding ceased in March 2019.

10 No

11 Yes. Uploaded document

Introductory statement

Regulation of vaping should aim to optimise the net public health impact. The current regulations focus on reducing youth access. However, in doing so they have reduced legal availability to adult smokers.

The harm to young people from vaping is relatively minor and distant (see below), but the potential benefit to adult smokers is substantial, immediate and can be life-saving. Regulation should balance concerns about the risks to young people with the potential health benefits for adult smokers. [1]

There is compelling evidence that e-cigarettes are effective quitting aids and are substitutes for smoking. [2] The evidence from randomised controlled trials, observational studies, and population data converges on NVPs displacing smoking and having a beneficial impact on public health. [3]

Regulation of NVPs should be **proportionate to risk** which is substantially lower than for smoking. [4] Harsh regulations support the tobacco industry and promote smoking. A light touch regulatory model for vaping will achieve the best public health outcomes.

Harsh regulation which could have the unintended consequences of making smoking relatively more attractive and making switching to NVPs more difficult, less appealing or more expensive.

The current prescription-model amounts to a de facto prohibition and has not achieved its two stated aims [Link]

1. "Prevent adolescents and young adults from taking-up nicotine vaping products while
2. allowing current smokers to access these products for smoking cessation with appropriate medical advice."

This failure was also acknowledged by the Deputy Secretary of the Therapeutic Goods Administration (TGA) at the Senate Estimates hearing on 10 November 2022, [5] (page 54, 57)

There is very little support from doctors and pharmacies for the prescription-only model. As of October 2022, only 243 of Australia's 130,000 doctors were publicly listed as Authorised Prescribers for nicotine. [6] Over 90% of vapers do not have a prescription [7]and current smokers are rarely getting "appropriate medical advice". Very few pharmacies stock the products because of low demand. Only 2% of vapers purchase nicotine from pharmacies with a prescription. [8]

It is difficult for adult smokers to legally access nicotine liquid for vaping, creating a thriving black-market which also sells unregulated disposable nicotine vapes freely to young people. As a result, there has been a substantial and unacceptable increase in youth vaping over the last 12 months.

There has also been very poor compliance by adult vapers with the current model. Vapers consider nicotine liquid to be a consumer product, a substitute for an existing consumer product, combustible cigarettes. Many vapers do not know that a prescription is required.

Doubling down on this model will only make this worse.

The Royal College of Physicians (London) in its 2016 report highlighted this danger:

> "However, if [a risk averse and precautionary] approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult" (Nicotine without Smoke: tobacco harm reduction, Section 12.10 page 187 – link)

Youth vaping

There is growing media attention about youth vaping which is a concern for parents and school communities. Young people should not vape or smoke. However, the relatively small harms from youth vaping are exaggerated.

Frequency of vaping by never-smokers

The group of most concern is young people who have never smoked and who vape frequently. Regular vaping exposes this group to new, potential harms from inhaled toxicants and there is a risk of developing nicotine dependence.

However, most use by never-smokers is experimental and short term and is of little concern to public health. Frequent use by young never-smokers is rare and is mostly ≤1.5% in western countries.

Country	Frequency	Never smokers	Current and former smokers	Age	Reference
England	> once weekly	0.5%	30.5%	11-17	ASH 2022
	≥ 15 days in the last 30	0.1%	13.4%	16-19	Hammond 2019
	≥ once weekly	1%	Current smokers 61% Former smokers 30%	11-15	NHS Digital 2021
US	≥ 20 days in the last 30	0.4%	3%	9-18	Glasser 2020
		1%	n/a	9-18	Jarvis 2019
		0.7%	15%	12-18	Polosa 2022
	≥ 15 days in the last 30	1.5%	23.4%	16-19	Hammond 2019
Canada	≥ 15 days in the last 30	0.6%	18%	16-19	Hammond 2019
New Zealand	Daily	4.3%	86.6% (of daily smokers)	15	ASH 2022

Table 1. Frequent or daily vaping by never-smoking youth

Some never-smokers who vape would have become smokers if vaping was not available.

The most detailed data is available from England and demonstrates the low prevalence of regular vaping by never-smokers. (Figure 1) Regular smoking and vaping are defined as once or more weekly. In 2021, only 1% of never-smokers aged 11-15 years were regular vapers and 61% of regular smokers vaped regularly.

		E-cigarette use				
		Never used	Only tried	Former users	Occasional user	**Regular user**
Smoking	**Regular**	8%	5%	14%	12%	**61%**
	Occasional	4%	11%	7%	25%	**53%**
	Ex-smoker	12%	10%	22%	25%	**30%**
	Tried smoking	21%	35%	9%	19%	**15%**
	Never	87%	9%	1%	2%	**1%**

Figure 1. E-cigarette use by smoking status, ages 11-15 years, England 2021 [NHS Digital]

The gateway theory

Evidence suggests that vaping is reducing smoking overall by **diverting young people** from smoking. [9-12] As youth vaping rates have increased, the decline in youth smoking rates has accelerated.

There is no good evidence that vaping causes young people who would not otherwise have smoked **to progress to regula**r smoking ('gateway theory'). [13-15]

The gateway hypothesis predicts that an increase in the uptake of e-cigarettes by youth will be followed by an increase in cigarette smoking. However, increases in youth vaping have been accompanied by declines in youth smoking which have accelerated from the time that vaping became popular. [16-18]

Known harms from youth vaping in never-smokers

Frequent vaping of nicotine by young people who have never smoked is rare and there is little evidence that vaping causes significant harms in this population.

There are substantially fewer toxicants in vapour than in tobacco smoke and those present are at far lower concentrations. [4] Low levels of additional chemicals in vapour not found in smoke are also present particularly from flavouring chemicals. However, so far there is "no clear evidence that specific flavourings pose health risks". [19]

The most commonly reported adverse effects are throat and mouth irritation, headache, cough and nausea which tend to dissipate with continued use. [2]

Vaping has been associated with respiratory symptoms in young people in cross-sectional studies, however, there is no evidence of causation. [20-22]

Other studies have found no evidence of functionally-important respiratory symptoms from vaping in young people after correcting for past smoking. [23, 24]

A meta-analysis of ten studies found an association between vaping and asthma in young people but a causal link could not be demonstrated. [25]

Some young people who have never smoked become nicotine-dependent from vaping. However, most do not. [26-28]

There is no evidence that nicotine is harmful to the adolescent human brain. Adverse effects have been found in animal studies but extrapolation to humans is speculative. [1] There is also **no long-term evidence** of impaired brain function in the hundreds of millions of adults who smoked as adolescents and then stopped.[29]
Studies of young people who smoked have not found any difference in **IQ**, [30] **educational achievement** [31] or **cognitive abilities** [32] in adulthood compared to non-smokers.
In spite of claims to the contrary, nicotine improves attention and memory. [33-35] It also relieves anxiety [36] improves mood [37] and improves cognitive function. [38]

Nicotine "represents minimal risk of serious harm" in the doses used in vaping. [4, 19] Nicotine does not cause cancer [39] or lung disease [40] and has only a minor role in cardiovascular disease. [41]

The harm from youth vaping is relatively minor compared to the much greater harm from other risks such as smoking, binge drinking, drink driving and illicit drug use.

Nicotine dependence

Vaping likely causes nicotine dependence in some young never-smokers. However, the evidence suggests that this is occurring in a small minority of cases[42]

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. [43, 44]

An analysis of the 2018 US National Youth Tobacco Survey found that very few never-smokers who had vaped in the past 30 days developed signs of nicotine dependence - 3.8% reported cravings and 3.1% reported wanting to vape withing 30 minutes of waking. [26] This low incidence is consistent with the finding that most vaping by never-smokers is occasional and short-term.

Exclusive use of e-cigarettes is associated with lower nicotine dependence than smoking and most dependence is concentrated in users who were already smokers. [45, 46]

In the US, there was a 50% decline in youth vaping from 2019-2021, suggesting that significant nicotine dependence was unlikely to be an issue for many users. This decline also raises the possibility that e-cigarette use may be a passing adolescent fad, like fidget spinners and Pokémon.

Policy measures

Measures to reduce youth access to vaping under a consumer model include

- Legal vaping products sold only from licensed retail outlets
- Strict age verification at the time of sale
- A third-party age verification service for online purchases and age verification on delivery
- Advertising restricted and regulated to prevent marketing appealing to adolescents
- Substantially increased fines and loss of licence for illegal sales to act as a deterrent
- Banning flavour names, images and packaging which appeal to young people. However, widespread flavour bans could reduce the appeal of vaping as an adult quitting aid

  Education programs for young people should inform them with accurate information about the risks. It is then up to the adolescent to decide what to do. There is no place for exaggeration, alarmist messages and harsh sanctions

Options for border control

12. Which border control option for regulating NVPs is preferred by you? Why?

Make no changes to the current regulatory framework

The current flood of illegal, unregulated imports is a consequence of the prescription-only model which was introduced formally on 1 October 2021. This has substantially reduced access for adult smokers and vapers and has created a high demand for illegal products from the black-market.

These illegal products are labelled nicotine-free to avoid detection. False labelling is misleading for potential buyers who may not realise the addictive potential of the products.

The Australian Border Force does not have the resources to intercept more than a tiny fraction of illicit products.

The solution is a tightly regulated consumer model under which

- Low concentrations of nicotine liquid for vaping (up to 20mg/mL freebase nicotine and 50mg/mL nicotine salt) are exempt from the Poisons Standard and regulated as consumer products by the Australian Competition and Consumer Commission (ACCC)
- Adults can access regulated nicotine liquid as a consumer product (without a prescription) from pharmacies, licensed specialist vape shops and licensed general retail outlets
- Youth access is restricted by strict age verification, severe penalties and loss of licence for underage sales

This model would also benefit the legitimate vape industry, increase government revenue (GST and stimulation from a growing industry) and save costs to Medicare.

13. Would any of these options have an impact on you? How?

As a clinician who sees patients for smoking cessation, this will allow me to recommend a wide range of vaping products for smoking cessation. A wide range of products is needed as different devices suit different smokers.

Under the consumer model, my patients will also be able to access expert advice from vaping shops which sell nicotine liquid and hardware.

It will also dramatically reduce the need for illegal products. The black-market will diminish, and enforcement will be simplified.

14. If the border control regulations are changed, how much time would you require, if any, to become familiar with the reforms, and to organise procurement of compliant products as necessary, before the reforms come into effect?

Not applicable

Options for pre-market assessment of NVPs by TGA

15. Which option (for pre-market assessment of NVPs) do you prefer? Why?

Other option

- A streamlined **pre-market notification** of nicotine liquids under which manufacturers notify the regulator that their products are compliant with Australian standards and provide confirmatory data before marketing is allowed. This model is used in
  - New Zealand. All products are registered with the Ministry of Health's Vaping Regulatory Authority's Health Advisory and Regulatory Platform (HARP). All notified products are recorded in a publicly available searchable database, the HARP database [link]
  - United Kingdom. Under the TPD, 6 months prior to marketing, producers must supply a list of all ingredients in the product (e-liquid); Emissions from the product; Toxicological data, including health and addictive effects; Nicotine dose and uptake when consumed; Components of the product; Production process details.

- Post-market surveillance and reporting of adverse events eg the Yellow Card reporting system in the UK, the Vaping Regulatory Authority in New Zealand [link] and the FDA Safety Reporting Portal in the US [link]

Under consumer regulation by the **Australian Competition and Consumer Commission** (ACCC), products would **not** need to be listed on the ARTG.

Pre-market authorisation of every product by the TGA or ACCC would be an onerous, expensive and time-consuming process and **is not recommended**. This process is used by the US FDA has been very problematic. Pre-market authorisation discriminates against reduced-risk products compared to cigarettes which require no such assessment. It would be a barrier to entry and innovation for manufacturers of NVPs and would favour tobacco companies who have the resources for these submissions.

Excessive regulation imposes high costs, burdens and restrictions, slows innovation, delays the availability of lifesaving products and drives good products and firms out of the market through 'regulatory barriers' to entry.

16. Would any of these options have an impact on you? How?

No

17. If changes are made to pre-market assessment of NVPs by the TGA, how much time would you require, if any, to become familiar with the reforms, and to organise procurement of compliant products as necessary before the reforms come into effect? What impact would any requirement to pay a fee have on you?

Time required before reforms come into effect (in months)
6-12 months to give manufacturers time to prepare documentation and upload product details.

Fees for this process should be minimal as very little government oversight is needed.

Minimum quality and safety standards for NVPs

18. Which option to restrict flavours in NVPs do you prefer? Why?

Make no change to the list of currently restricted flavouring agents in NVPs .

Recommendation for flavours

- Simple descriptions of flavour profiles only eg 'mint', 'blueberry', 'tobacco', 'vanilla tobacco'
- Prohibit descriptive flavour names that specifically appeal to youth eg 'dragon vomit'
- Prohibit flavours found to have a material risk to health

Flavours are an integral part of the appeal of vaping for **adult smokers** and play an important role in the **initiation** of vaping for current smokers. [47] Restricting flavours would reduce the appeal of vaping and lead to more smoking and smoking-related death and disease.

Flavoured e-liquids also **increase quit rates** compared to non-flavoured or tobacco flavours and reduce the rate of relapse. [48-50] Those who vape with flavours also have **higher odds of making a quit attempt**. [50]

Flavour bans would also lead to increased black-market supplies and dangerous home mixing, with **little effect on youth uptake**. [51]

19. Do you think any other ingredients should be restricted in addition to those currently restricted? If so what ingredients?

Yes
TPD/UK list of banned chemicals [link]

Restriction should focus on hazardous agents in quantities that pose a material risk to users and psychoactive agents other than nicotine.

20. Do you support introducing plain packaging requirements for NVPs? If so, should this entail packaging similar to other prescription-only medicines, or should additional measures be considered?

No
Plain packaging for NVPs would send a signal to smokers that vaping is as harmful as smoking and would reduce switching to the safer product. The public health goal should be to encourage smokers who are unable to quit to switch to vaping, a far safer alternative.

Plain packaging for combustible products is intended to discourage smoking due to the high risk of harm to health. No such justification applies to vaping products as vaping is around 95% less harmful than smoking.

21. Do you support introducing additional warning statements for NVPs? If so, which warning statements should be included? How would this align with the treatment of NVPs as a prescription-only medicine?

Yes
Sensible relative risk health warnings comparing the risks to smoking, for example

- "This product may be addictive but is a far less harmful alternative for adult smokers"
- "If you are a smoker, switching completely to vaping is a much less harmful option"
- "Completely replacing your cigarette with a vaping product will significantly reduce your exposure to numerous toxic and cancer-causing substances"
- "No nicotine product is safe, but this product presents substantially lower risks to health than cigarettes."

22. Do you support restricting nicotine concentrations in NVPs to 20mg/mL (or base form equivalent concentration for nicotine salt products)? If not, what alternative do you support?

No
I support an upper limit of 20mg/mL for freebase nicotine and 50mg/mL for nicotine salt.

If the guidelines refer to nicotine base **only**, I would recommend 30mg/mL which would allow up to 50mg/mL nicotine salt and 30mg/mL freebase nicotine

Nicotine salt is mostly used in popular disposable and more compact pod devices. Because of the low battery power, these devices require a higher concentration of nicotine to deliver a satisfying

dose of nicotine to the user. The smaller size, convenience and nicotine delivery of these devices has made them very popular as transition models.

Higher concentrations of nicotine are safer than low concentrations as they generate smaller vapour volume, with a corresponding reduction in toxicants. [52-55] Furthermore, users titrate their nicotine intake to control their exposure. The same amount of nicotine is absorbed by the user from smaller devices with high nicotine level as from larger devices with low nicotine levels. [56]

Excessively low doses of nicotine will lead to lower rates of switching. [57] Smokers often need higher doses of nicotine in the early stages of switching or while they are learning to vape. Heavier or more dependent smokers may find e-cigarettes unsatisfying with low dose nicotine liquids– so those most at risk are denied the products more likely to work.

23. Do you support limiting the maximum volume of liquid NVPs? If so, what maximum volume should be specified?

Yes and no
I support a **maximum amount of nicotine per container** rather than a maximum bottle size. The New Zealand limit of 1800mg nicotine per container is a sensible compromise. [link] This would be 100mL of 18mg/mL or 36mL of 50mg/mL.

Over-restriction of bottle sizes increases waste and environmental pollution. All bottles should have child-proof caps, and be leak proof, unbreakable (PET plastics) and have anti-spill protection making accidental poisoning very unlikely. Small bottles are also less convenient and make vaping less attractive, with a greater risk of running out of supplies and relapse to smoking.

24. Do you support preventing access to disposable NVPs?

No
Disposable vape devices are a popular aid for adults transitioning from smoking as they are convenient, easy-to-use, require no maintenance or charging and provide good nicotine delivery. They are especially useful for elderly, disabled and non-technical users.

Disposable models are the most appropriate device for a hospital, inpatient or criminal justice settings as they require no refilling or recharging and are tamper proof.

These devices are increasingly popular in Australia and other western countries and the demand is likely to continue to rise. [58] A ban on disposables may have unintended consequences. It may simply result in users switching to other products or may act as a barrier to switching for adult smokers. [59] It will not prevent continued illegal importation and sales of unregulated products from the black-market.

Regulated disposable devices should be mandated to not appeal to young people, for example no bright colours or youth-appealing flavour names and images.

25. Would any of the options set out in questions 18 to 24 have an impact on you? How?

Yes
See question 13 above

26. If changes to product quality and safety standards are made, how much time would you require, if any, to become familiar with the reforms, and to organise the procurement of compliant products as necessary, before the reforms come into effect?

6 months

27. Are there any other potential minimum requirements for unregistered NVPs that the TGA should consider including in TGO 110?

Yes

- Minimum standards for the manufacture and safety of vaping liquids
- Standardised testing regimes
- Purity standards for ingredients
- Extended blacklist or dose limits on problematic ingredients
- Laboratory testing of liquids
- Emission testing

Clarifying the status of NVPs as 'therapeutic goods'

28. Do you support regulating NVPs that contain nicotine, but are not labelled as containing nicotine, under the therapeutic goods framework?

No. Vaping products with or without nicotine are adult consumer products and should be regulated by the Australian Competition and Consumer Commission (ACCC).

Vaping products are consumer products and should be regulated by the ACCC which provide strong protection for consumers. The ACCC ensures that products are safe, fit for purpose, of merchantable quality and comply with all legal requirements under the Competition and Consumer Act 2010.

Vaping products should not be regulated by the Therapeutic Goods Administration (TGA). The TGA is responsible for regulating medicines and medical devices which make therapeutic (medicinal) claims, such as ‘this product can help you quit smoking’. Nicotine vaporisers are consumer products used almost exclusively as a less harmful substitute by smokers who can’t or won’t quit smoking or consuming nicotine.

No western country requires vaping products to undergo medicines regulation or requires a doctor’s prescription. It makes no sense to require the highest standards of research and quality for nicotine vaporisers when they are replacing a far more harmful product, lethal cigarettes, which are virtually unregulated.

One of the purposes of the medical model was to give smokers the opportunity to receive appropriate advice from a doctor. However, this has not occurred. **Very few patients are getting advice from doctors**. Doctors know very little about vaping and most Australian GPs do not even know how to write a nicotine prescription.

A systematic review of 25 studies of the knowledge, attitudes and beliefs of general practitioners found that [60]

- The majority … did not agree that e-cigarettes should be recommended as a smoking cessation treatment

- **Most GPs believed they had insufficient knowledge around e-cigarettes and lacked information they needed to confidently provide advice and guidance to their patients on e-cigarettes as a smoking cessation aid.**
- Most were reluctant to recommend e-cigarettes due to insufficient research around the safety and long-term health effects.
- GPs were adamant the only way they would recommend or prescribe e-cigarettes for smoking cessation and take responsibility for their action, is if it has been approved by a regulatory authority

Australian doctors are discouraged from supporting vaping by repeated negative messaging from the Health Department, AMA and many health and medical organisations.

30. To proceed, please select from the options below how you would like the TGA to deal with your submissions:

I agree to the TGA publishing my response in full.

References

1. Balfour DJK, Benowitz NL, Colby SM, Hatsukami DK, Lando HA, Leischow SJ, et al. Balancing Consideration of the Risks and Benefits of E-Cigarettes. Am J Public Health. 2021:e1-e12.
2. Hartmann-Boyce J, Lindson N, McRobbie H, Butler AR, Bullen C, Begh R, et al. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews; 2022.; 2022. [accessed 2022 November 19]. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010216.pub7/full
3. Mendelsohn C, Hall W, Borland R. Could vaping help lower smoking rates in Australia? Drug Alcohol Rev. 2020;39(4):415-8.
4. McNeill A, Simonavicius E, Brose LS, Taylor E, East K, Kuilova E, et al. Nicotine vaping in England: an evidence update including health risks and perceptions, September 2022. A report commissioned by the Office for Health Improvement and Disparities. London: Office for Health Improvement and Disparities. 2022. [accessed 2022 Nov 7]. Available from: https://www.gov.uk/government/publications/nicotine-vaping-in-england-2022-evidence-update
5. Commonwealth of Australia. Community Affairs Legislation Committee, Senate Estimates Hearing, 10 November. 2022.
6. Therapeutic Goods Administration. Authorised Prescribers of unapproved nicotine vaping products. 2022. [accessed 19 November 2022]. Available from: https://www.tga.gov.au/resources/resource/guidance/authorised-prescribers-unapproved-nicotine-vaping-products
7. Mendelsohn C. How many adult Australians vape? ; 2022. [accessed 19 November 2022]. Available from: https://colinmendelsohn.com.au/number/
8. Australian Association of Convenience Stores. Nicotine Vaping Product Usages and Change. 2022. [accessed 2023 January 3]. Available from: https://aacs.org.au/wp-content/uploads/2022/08/AACS-CMA-Research-Attachment.pdf
9. Sun T, Lim CCW, Stjepanović D, Leung J, Connor JP, Gartner C, et al. Has increased youth e-cigarette use in the USA, between 2014 and 2020, changed conventional smoking behaviors, future intentions to smoke and perceived smoking harms? Addict Behav. 2021;123:107073.
10. Walker N, Parag V, Wong SF, Youdan B, Broughton B, Bullen C, et al. Use of e-cigarettes and smoked tobacco in youth aged 14-15 years in New Zealand: findings from repeated cross-sectional studies (2014-19). Lancet Public Health. 2020;5(4):e204-e12.

11. Sokol NA, Feldman JM. High School Seniors Who Used E-Cigarettes May Have Otherwise Been Cigarette Smokers: Evidence From Monitoring the Future (United States, 2009-2018). Nicotine Tob Res. 2021;23(11):1958-61.
12. Selya AS. Reducing the smoking-related health burden in the USA through diversion to electronic cigarettes: a system dynamics simulation study. Harm Reduct J. 2021;18(1):36.
13. Chan GCK, Stjepanovic D, Lim C, Sun T, Shanmuga Anandan A, Connor JP, et al. Gateway or common liability? A systematic review and meta-analysis of studies of adolescent e-cigarette use and future smoking initiation. Addiction. 2021;116(4):743-56.
14. Mendelsohn CP, Hall W. Does the gateway theory justify a ban on nicotine vaping in Australia? Int J Drug Policy. 2020;78:102712.
15. Sun R, Mendez D, Warner KE. Is Adolescent E-Cigarette Use Associated With Subsequent Smoking? A New Look. Nicotine Tob Res. 2022;24(5):710-8.
16. Levy DT, Warner KE, Cummings KM, Hammond D, Kuo C, Fong GT, et al. Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. Tob Control. 2019;28(6):629-35.
17. NHS Digital. Smoking, Drinking and Drug Use among Young People in England, 2021. 2022. [accessed 2022 Nov 7]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/smoking-drinking-and-drug-use-among-young-people-in-england/2021
18. Meza R, Jimenez-Mendoza E, Levy DT. Trends in Tobacco Use Among Adolescents by Grade, Sex, and Race, 1991-2019. JAMA Netw Open. 2020;3(12):e2027465.
19. McNeill A, Brose LS, Calder R, Bauld L, Robson D. Evidence review of e-cigarettes and heated tobacco products 2018. A report commissioned by Public Health England. London: Public Health England. 2018. [accessed 2022 Nov 7]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/684963/Evidence_review_of_e-cigarettes_and_heated_tobacco_products_2018.pdf
20. Schweitzer KS, Chen SX, Law S, Van Demark M, Poirier C, Justice MJ, et al. Endothelial disruptive proinflammatory effects of nicotine and e-cigarette vapor exposures. Am J Physiol Lung Cell Mol Physiol. 2015;309(2):L175-87.
21. Wang MP, Ho SY, Leung LT, Lam TH. Electronic Cigarette Use and Respiratory Symptoms in Chinese Adolescents in Hong Kong. JAMA Pediatr. 2016;170(1):89-91.
22. McConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, Unger J, et al. Electronic Cigarette Use and Respiratory Symptoms in Adolescents. Am J Respir Crit Care Med. 2017;195(8):1043-9.
23. Stevens ER, Xu S, Niaura R, Cleland CM, Sherman SE, Mai A, et al. Youth E-Cigarette Use and Functionally Important Respiratory Symptoms: The Population Assessment of Tobacco and Health (PATH) Study Waves 3 and 4. Int J Environ Res Public Health. 2022;19(22).
24. Tanski S, Halenar MJ, Edwards KC, Emond J, Woloshin S, Brunette M, et al. Tobacco product use and functionally-important respiratory symptoms among US adolescents/young adults. Acad Pediatr. 2022.
25. Li X, Zhang Y, Zhang R, Chen F, Shao L, Zhang L. Association Between E-Cigarettes and Asthma in Adolescents: A Systematic Review and Meta-Analysis. Am J Prev Med. 2022;62(6):953-60.
26. Jarvis M, Jackson S, West R, Brown J. Epidemic of youth nicotine addiction? What does the National Youth Tobacco Survey 2017-2019 reveal about high school e-cigarette use in the USA? Qeios 2020. Available at: https://www.qeios.com/read/745076.5/pdf
27. Action on Smoking and Health UK. ASH brief for local authorities on youth vaping. 2022. [accessed 2022 December 11]. Available from: https://ash.org.uk/wp-content/uploads/2022/08/ASH-brief-for-local-authorities-on-youth-vaping.pdf

28. Jackson S, Kotz D, West R, Brown J. Moderators of real-world effectiveness of smoking cessation aids: a population study. Addiction. 2019.
29. The health consequences of smoking: a report of the Surgeon General. [Atlanta, Ga.]: Dept. 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; Washington, D.C., 2004.
30. Wennerstad KM, Silventoinen K, Tynelius P, Bergman L, Kaprio J, Rasmussen F. Associations between IQ and cigarette smoking among Swedish male twins. Soc Sci Med. 2010;70(4):575-81.
31. Treur JL, Willemsen G, Bartels M, Geels LM, van Beek JH, Huppertz C, et al. Smoking During Adolescence as a Risk Factor for Attention Problems. Biol Psychiatry. 2015;78(9):656-63.
32. Corley J, Gow AJ, Starr JM, Deary IJ. Smoking, childhood IQ, and cognitive function in old age. J Psychosom Res. 2012;73(2):132-8.
33. Majdi A, Sadigh-Eteghad S, Gjedde A. Effects of transdermal nicotine delivery on cognitive outcomes: A meta-analysis. Acta Neurol Scand. 2021;144(2):179-91.
34. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. Psychopharmacology (Berl). 2010;210(4):453-69.
35. Levin ED, Conners CK, Silva D, Hinton SC, Meck WH, March J, et al. Transdermal nicotine effects on attention. Psychopharmacology (Berl). 1998;140(2):135-41.
36. Morissette SB, Tull MT, Gulliver SB, Kamholz BW, Zimering RT. Anxiety, anxiety disorders, tobacco use, and nicotine: a critical review of interrelationships. Psychol Bull. 2007;133(2):245-72.
37. Picciotto MR, Brunzell DH, Caldarone BJ. Effect of nicotine and nicotinic receptors on anxiety and depression. Neuroreport. 2002;13(9):1097-106.
38. Gil SM, Metherate R. Enhanced Sensory-Cognitive Processing by Activation of Nicotinic Acetylcholine Receptors. Nicotine Tob Res. 2019;21(3):377-82.
39. International Agency for Research on Cancer. Tobacco smoking and carcinogenic risk to humans. IARC Monograph 100E 2012. Available at: http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E-6.pdf
40. US Department of Health and Human Services. The health consequences of smoking - 50 years of progress. A report of the Surgeon General.; 2014. [accessed 2022 Nov 7]. Available from: https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf
41. Benowitz NL, Burbank AD. Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. Trends Cardiovasc Med. 2016;26(6):515-23.
42. Jackson SE, Brown J, Jarvis MJ. Dependence on nicotine in US high school students in the context of changing patterns of tobacco product use. Addiction. 2021;116(7):1859-70.
43. Watts C, Egger S, Dessaix A, Brooks A, Jenkinson E, Grogan P, et al. Vaping product access and use among 14-17-year-olds in New South Wales: a cross-sectional study. Aust N Z J Public Health. 2022.
44. Gorini G, Gallus S, Carreras G, De Mei B, Masocco M, Faggiano F, et al. Prevalence of tobacco smoking and electronic cigarette use among adolescents in Italy: Global Youth Tobacco Surveys (GYTS), 2010, 2014, 2018. Prev Med. 2020;131:105903.
45. Hammond D, Reid JL, Rynard VL, Fong GT, Cummings KM, McNeill A, et al. Prevalence of vaping and smoking among adolescents in Canada, England, and the United States: repeat national cross sectional surveys. BMJ. 2019;365:l2219.
46. Liu G, Wasserman E, Kong L, Foulds J. A comparison of nicotine dependence among exclusive E-cigarette and cigarette users in the PATH study. Prev Med. 2017.
47. Gendall P, Hoek J. Role of flavours in vaping uptake and cessation among New Zealand smokers and non-smokers: a cross-sectional study. Tob Control. 2020.
48. Glasser A, Vojjala M, Cantrell J, Levy DT, Giovenco DP, Abrams D, et al. Patterns of e-cigarette use and subsequent cigarette smoking cessation over two years (2013/2014 to

2015/2016) in the Population Assessment of Tobacco and Health (PATH) Study. Nicotine Tob Res. 2020.
49. Li L, Borland R, Cummings KM, Fong GT, Gravely S, Smith DM, et al. How Does the Use of Flavored Nicotine Vaping Products Relate to Progression Toward Quitting Smoking? Findings From the 2016 and 2018 ITC 4CV Surveys. Nicotine Tob Res. 2021;23(9):1490-7.
50. Mok Y, Jeon J, Levy DT, Meza R. Associations between e-cigarette use and e-cigarette flavors with cigarette smoking quit attempts and quit success: Evidence from a US large, nationally representative 2018-2019 survey. Nicotine Tob Res. 2022.
51. Buckell J, Marti J, Sindelar JL. Should flavours be banned in cigarettes and e-cigarettes? Evidence on adult smokers and recent quitters from a discrete choice experiment. Tob Control. 2018.
52. Kosmider L, Kimber CF, Kurek J, Corcoran O, Dawkins L. Compensatory puffing with lower nicotine concentration e-liquids increases carbonyl exposure in e-cigarette aerosols Nicotine Tob Res. 2017.
53. Dawkins L, Cox S, Goniewicz M, McRobbie H, Kimber C, Doig M, et al. 'Real-world' compensatory behaviour with low nicotine concentration e-liquid: subjective effects and nicotine, acrolein and formaldehyde exposure. Addiction. 2018;113(10):1874-82.
54. Talih S, Salman R, El-Hage R, Karam E, Karaoghlanian N, El-Hellani A, et al. Might limiting liquid nicotine concentration result in more toxic electronic cigarette aerosols? Tob Control. 2020.
55. Kimber C, Zaidell L, Hunter S, Cox S, Notley C, Dawkins L. Comparing the Effects of the EU-Versus the US-JUUL Pod in a Sample of UK Smokers: Nicotine Absorption, Satisfaction and Other Nicotine-Related Subjective Effects. Nicotine Tob Res. 2022.
56. Benowitz NL, St Helen G, Liakoni E. Clinical Pharmacology of Electronic Nicotine Delivery Systems (ENDS): Implications for Benefits and Risks in the Promotion of the Combusted Tobacco Endgame. J Clin Pharmacol. 2021;61 Suppl 2:S18-s36.
57. Goldenson NI, Ding Y, Prakash S, Hatcher C, Augustson EM, Shiffman S. Differences in Switching Away From Smoking Among Adult Smokers Using JUUL Products in Regions With Different Maximum Nicotine Concentrations: North America and the United Kingdom. Nicotine Tob Res. 2021;23(11):1821-30.
58. Tattan-Birch H, Jackson SE, Kock L, Dockrell M, Brown J. Rapid growth in disposable e-cigarette vaping among young adults in Great Britain from 2021 to 2022: a repeat cross-sectional survey. Addiction. 2022.
59. Khouja JN, Munafò MR. Commentary on Tattan-Birch et al.: How might the rise in popularity of disposable vapes among young adults impact policy in the United Kingdom? Addiction. 2022.
60. Selamoglu M, Erbas B, Kasiviswanathan K, Barton C. General practitioners' knowledge, attitudes, beliefs and practices surrounding the prescription of e-cigarettes for smoking cessation: a mixed-methods systematic review. BMC Public Health. 2022;22(1):2415.