

Flavoured Vaping Products in Tobacco Harm Reduction: A Regulatory Perspective

Ian M. Fearon¹, Matthew Stevenson², Thomas Nahde³

Review began 06/18/2025

Review ended 07/24/2025

Published 08/01/2025

© Copyright 2025

Fearon et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.89196

1. Scientific Research, whatIF? Consulting Ltd., Harwell, GBR 2. Group Science and Regulatory Affairs, Imperial Brands PLC, Bristol, GBR 3. Group Science and Regulatory Affairs, Reemtsma Cigarettenfabriken GmbH, Hamburg, DEU

Corresponding author: Ian M. Fearon, ian@whatifconsulting.net

Abstract

Reducing the harms associated with cigarette smoking is a global public health priority. Both the individual- and population-level health impacts of smoking can be reduced by novel products which deliver nicotine, but the use of which decreases user exposure to the harmful chemical toxicants responsible for smoking-related disease. Electronic vaping products (EVP) heat a flavoured liquid, most commonly containing nicotine, to generate an inhalable aerosol. Smokers who switch exclusively to using EVP reduce their exposure to the harmful toxicants found in cigarette smoke, and increasing evidence supports that EVP can help smokers quit smoking and support tobacco harm reduction (THR) efforts. However, concerns are being raised regarding the use of EVP among those for whom they are not intended, particularly youth, which could mitigate their THR potential. Some of this concern is attributed to the use of non-tobacco flavours in EVP, and there have been many calls to ban the use of such flavours. The aim of this review is to examine the recent scientific literature concerning non-tobacco flavours in EVP, focussing on the potential toxicological impact of these flavours, whether flavours affect abuse liability/dependence potential and whether they support switching away from cigarette smoking, unintended use of flavoured EVP, and the impact of existing bans and the effect of regulation. Overall, we find that non-tobacco flavoured EVP are not of a greater risk to health and have no greater abuse liability than tobacco flavoured EVP. There is some evidence that flavoured EVP may support switching among adult smokers, while unintended use may be experimental and may not translate into long-term use or act as a 'gateway' into smoking. Current flavour bans have been largely ineffective in modifying use behaviour and may have unintended consequences such as increasing smoking prevalence and promoting illicit trade. Overall, the population-level THR benefit of flavoured EVP, in terms of reducing smoking rates, largely outweighs the risks associated with unintended use. Maintaining flavour diversity is an important consideration when putting in place regulatory frameworks that aim to maximise the switching benefit for adult smokers and improve overall population-level public health.

Categories: Health Policy, Public Health

Keywords: e cigarettes, electronic vaping products, flavours, public health, tobacco harm reduction

Introduction And Background

Reducing the harms associated with cigarette smoking is a global health priority to help lower the estimated annual seven million preventable global deaths associated with smoking [1]. While nicotine in cigarette smoke is not harmless and is addictive, it is not the primary cause of the harmful effects of cigarette smoking [2-5]. Instead, smoking-related diseases are caused by smokers inhaling chemical toxicants, which are formed during the combustion and pyrolysis of tobacco [6]. Around 7,000 individual chemicals have been identified in cigarette smoke [7], and some of these have been defined by the United States (US) Food and Drug Administration (FDA) as 'Harmful or Potentially Harmful Constituents' (HPHCs) which are linked to cardiovascular disease, respiratory disease, lung cancer, and reproductive/developmental toxicity [8].

In 2001, the US Institute of Medicine (IoM) published its report on 'Clearing the Smoke-the Science Base for Tobacco Harm Reduction' [9,10] in which it outlined how novel tobacco and nicotine products could 'lower total tobacco-related mortality and morbidity even though use of that product may involve continued exposure to tobacco-related toxicants'. This suggests that while a significant proportion of individuals will continue to use tobacco and/or nicotine, tobacco harm reduction (THR) can be achieved by either decreasing the risks associated with tobacco/nicotine use, decreasing users' consumption, or decreasing the prevalence of use. This gives rise to the concept that both the individual- and population-level health impacts of smoking can be reduced by novel products which deliver nicotine but the use of which reduces user exposure to the harmful chemical toxicants responsible for smoking-related disease. Support for such an approach to THR is increasing, and several global health authorities now advocate for switching to using novel nicotine products which reduce exposure to harmful chemical toxicants and, therefore, reduce risks to health among individuals who smoke [3,4,11-13]. Calls for other global health authorities to make THR a strategy central to promoting public health have also been made [14-16]. Numerous factors are thought to be involved in determining the population-level THR potential of novel tobacco and nicotine products (Figure 1). Novel products must expose users to lower levels of toxicants than those found in cigarette smoke and therefore possess THR potential. They must be sufficiently accepted and used by adult smokers as a complete

How to cite this article

Fearon I M, Stevenson M, Nahde T (August 01, 2025) Flavoured Vaping Products in Tobacco Harm Reduction: A Regulatory Perspective. Cureus 17(8): e89196. DOI 10.7759/cureus.89196

substitute for cigarettes or as a means to substantially reduce cigarette consumption. In addition, the appeal of novel products among those for whom they are not intended must be minimised, particularly among susceptible populations such as youth and never smokers, in which novel products could pose an initiation or reinitiation risk [17,18].

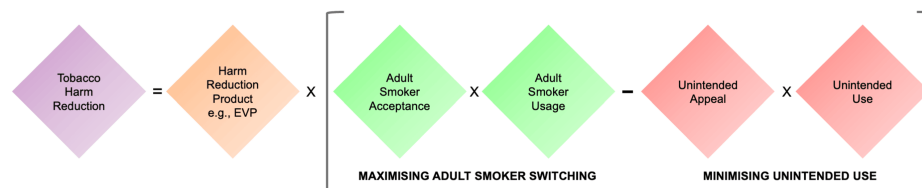


FIGURE 1: Factors determining the tobacco harm reduction potential of novel tobacco and nicotine products

EVP: electronic vaping product

Electronic vaping products (EVP), also termed e-cigarettes or electronic nicotine delivery systems, are battery-powered devices which heat a flavoured liquid solution, most commonly containing nicotine, to generate an inhalable aerosol [19]. EVP pose a potentially reduced health risk compared to cigarette smoking since their aerosols contain fewer and substantially lower levels of toxicants responsible for smoking-related disease [20–22]. This gives rise, among those smokers who switch exclusively to EVP or substantially reduce their cigarette consumption, to reduced toxicant exposure [23–27]. Increasing amounts of evidence coming from randomised controlled trials and observational studies suggest that EVP can help smokers quit smoking [28–34], and the increasingly widespread availability of EVP has been associated with reductions in smoking prevalence at the population level [35–37]. For example, analysis of US National Health Interview Survey (NHIS) data found that post-2007, a time at which EVP began to be marketed, adult smoking prevalence was significantly lower than expected based on pre-EVP era trends. These declines grew as EVP use prevalence increased and were larger in subpopulations with higher e-cigarette use, especially younger adults aged 18 to 34 [35]. Furthermore, a study which examined data from countries with historically similar smoking trajectories but differing current electronic cigarette regulations (United Kingdom (UK) and US vs. Australia, where sales of nicotine-containing EVP are banned) found that the decline in smoking prevalence seems to have been slower in Australia than in the UK overall and slower in Australia than in both the UK and the US among both young people and those in lower socioeconomic groups [36]. Both of these findings point to the THR potential of EVP. This may, however, be mitigated by the use of EVP among unintended populations such as never smokers and youth [17,18,38], and youth EVP use has been reported to be rising in many countries including those in Latin America [39], in Asia [40], and in Africa, [41], as well as in the UK [37], and in the US [42] although youth EVP use in the US does appear to be declining in more recent years [42]. Because of these increases in youth EVP use, an increasingly bright spotlight is being shone on the use of non-tobacco flavours in EVP, including fruit, sweet, and dessert flavours. It has been proposed that non-tobacco flavours may be more appealing to unintended users, including youth, than tobacco flavours [43–47], and may also elevate health risks associated with EVP use [43,44,48–50]. This has led to proposals to restrict or ban the use of non-tobacco flavours in EVP [43–45,51,52]. However, such proposals may have implications for THR. The aim of this review is to examine the recent scientific literature on EVP flavours, with a view to exploring whether flavours pose an increased health risk, and whether their availability is supportive of, or detrimental to, population-level public health and THR strategies.

Review

Do EVP flavours pose an increased health risk?

Any potential health risk assessment of EVP flavours can be determined either by undertaking desk-based quantitative risk assessments (QRAs) for individual flavour ingredients [53], by assessing the levels of toxicants in EVP aerosols and using the data generated to inform toxicological QRAs, or by conducting laboratory toxicological studies. Using analytical chemistry approaches with flavoured EVP aerosols, studies have reported the detection of metals [54–59], though in some of these studies, there was a large degree of variability between different device types and brands [58,59]. Furthermore, in two studies, tobacco-flavoured aerosols contained the highest metal concentrations [54,60], while in a further study, nickel in EVP aerosols was similar for tobacco- and mint-/menthol-flavoured EVP from one brand, lower in mint-/menthol-flavoured EVP aerosols from two brands, and higher in mint-/menthol-flavoured EVP aerosols from another brand [58]. These studies may be hampered, however, by methodological flaws, including generating EVP aerosol under unrealistic experimental conditions, which cause coil overheating or using inappropriate airflow across the coil [61]. Other studies have identified volatile organic compounds [62], carbonyls including formaldehyde, acetaldehyde, acetone and acrolein [63], other HPHCs [64], and potentially harmful flavour adducts formed by chemical interactions with the e-liquid diluents propylene glycol (PG) and vegetable glycerine (VG) [65,66], in EVP aerosols. It is notable regarding these toxicants that few studies have directly assessed differences between flavoured and unflavoured or tobacco-flavoured products in a

like-for-like comparison (i.e., assessing tobacco and non-tobacco flavours used under the same conditions and in the same device), and between-study comparisons are challenging due to differences in experimental study design as well as the products used to generate EVP aerosol. Further studies are required to address this issue and to provide specific information concerning whether the use of flavours in EVP does, in fact, change aerosol toxicant levels. Likely though, it is not a simplistic matter of one flavour type causing greater toxicant release into the aerosol than another type, but a more complex one involving flavour/device interactions as well as the individual flavour components used by different manufacturers within their flavours.

While the findings from EVP aerosol toxicant assessments may appear concerning at first sight, for each of these studies, QRAs informed by the levels of the toxicants detected, as well as estimating consumer exposures and doses at which toxicological effects are known to occur, were not conducted. In this regard, it should be noted that accurate assessment of any potential health risks is a multi-step procedure informed by identifying the hazard (toxicants), assessing a dose response, assessing the likely exposure level, and characterising the risk to determine whether it is acceptable. Carrying out such multi-step procedures is of critical importance since sensitive analytical equipment may detect potential toxicants at levels lower than those which would be of concern to health under typical patterns of EVP use, particularly for metals [67]. It is of equal importance, given that regulatory proposals aim to restrict non-tobacco-flavoured EVP, to use tobacco-flavoured e-liquids as experimental controls, and also to generate EVP aerosols under realistic conditions which equate to typical human puffing behaviour [68] and use realistic EVP power outputs which do not cause EVP coil overheating and the phenomenon known as 'dry puffing' [69-73]. In many of the studies mentioned, none of these steps was undertaken. Of additional importance, given that the intended population and the overwhelming majority of EVP users are former smokers [74,75], using cigarette smoke as an experimental control is also fundamental to inform relative risk assessments. Furthermore, some studies have assessed the impact of exposure to e-liquids on toxicological endpoints using in vitro assays [76-84]. Such experimental models do not reflect the actual route of exposure among EVP users, which is inhalational. Therefore, studies assessing toxicological impacts of flavoured EVP should use models which reflect the exposure route and expose cells in vitro to EVP aerosol or aerosol extracts [85], and again, the use of puffing regimens which reflect typical human use is paramount. In vivo animal studies have also been conducted to assess the toxicological impacts of flavours, and their use is valuable for providing evidence of biological plausibility. However, extrapolating outcomes to effects in humans is a limitation of in vivo models, and they may not accurately predict human exposure and disease risk [86]. There are also ethical concerns around tobacco product testing in animals [87,88]. Regarding methodological limitations of in vivo models, those models which assess the impact of flavours administered orally through drinking water may not reflect EVP user exposure to flavours contained within the aerosol, and as seen in some studies, may overexpose animals to the flavouring agent [89]. When examining findings from in vivo studies which have, to the extent possible, mimicked human exposure, EVP aerosol was found to be less toxic than cigarette smoke in models assessing inflammatory, respiratory, cardiovascular, gastrointestinal and renal endpoints [76,90-92], and little or no between-flavour toxicologically-relevant differences were observed [76,90,92]. Such findings concur with many other in vitro and in vivo studies [50,56,93-100]. In studies which have observed between-flavour differences, these may be confounded due to flaws in the experimental design. For example, due to the addition of flavourings at levels exceeding those found in e-liquids [76,82,101,102], cultured cells in vitro may have been exposed to a much higher level of flavouring than would occur during human aerosol exposure. Additionally, observations of flavour effects in aerosol-exposed in vitro models may be due to misuse of recommended puffing regimens, such as the CORESTA method number 81 [103]. This method stipulates a three-second puff duration with puffs taken every 30 seconds, which has been used in some studies, but for excessive numbers of puffs and with no indication of puff volume [76], both of which mean that the puffing regimen used deviated significantly from a recognised standard and typical EVP user topography. Other studies have used EVP aerosol captured by bubbling through cell culture media or phosphate-buffered saline, with some vaporising significantly more e-liquid than would be expected during typical use by an EVP user over the same period [84]. Such issues with dosimetry, along with other potential issues with the use of in vitro models [104], must be addressed in order to improve the validity of these models. This must include standardisation and rigorous reporting of the aerosol generation process [104].

While many studies have suggested a lower in vitro and in vivo toxicological impact of EVP aerosol compared with cigarette smoke, and only minor between-flavour differences, we should not disregard the fact that some flavour additives or ingredients have the potential to give rise to toxicological concern when used in EVP liquids. Various studies described above have demonstrated the potential for impacts on human health of individual flavours, although many of these studies are hampered by the experimental flaws we described previously such as the lack of a relevant control exposure, the use of experimental models not relevant to assess the potential impact of EVP use (e.g. liquid and not aerosol exposure or inappropriate experimental models used), and the lack of a rigorous stepwise health risk assessment or QRA. For example, studies in a variety of in vitro and in vivo experimental models have reported potential toxicological effects of cinnamaldehyde (a cinnamon flavouring) [79,81,105], vanillin (a sweet, vanilla flavouring) [80,106-108], benzaldehyde and other aldehyde flavourings [66,81,109], ethyl butanoate and diacetyl (butter-like flavourings) [110,111], eugenol (a spicy/clove flavouring) [112], hexyl acetate (an apple flavouring) [112], and ethyl esters (a citrus flavouring) [113]. There is also the potential for individual flavour ingredients to undergo chemical reactions with one another and with other ingredients (e.g. PG and VG) to form additional chemicals which may be of toxicological concern [49,65,66]. However, it is important to stress that due to the

large number of potential e-liquid flavour ingredients and also due to the potential for both antagonistic and synergistic effects of individual flavour ingredients, a pragmatic and holistic approach to testing may be required. This could include, for example, testing of either whole e-liquid or aerosol, which, in addition to assessing a relevant exposure article, gives the benefit of capturing any 'de novo' formation of constituents formed upon mixing or heating/vaporisation. Another potential approach is to use a 'flavour toolbox' approach in which individual flavour ingredients are assigned to groups based on structural, metabolic and toxicological similarity (read-across), from which flavour group representatives are used to create mixtures for laboratory testing [85,91,114]. Such an approach has been used by the European Food Safety Authority, among others, to assess the toxicity potential of food flavour ingredients [115,116] and could be applied to EVP.

Taking into account the literature reviewed above, overall, there is no strong indication that non-tobacco-flavoured EVP aerosols pose a greater health concern than tobacco-flavoured aerosols. Studies assessing potential health impacts of flavour components added to EVP liquids are challenging, and extreme care needs to be taken when designing experiments to assess this potential. Given the potential for the inclusion of certain flavourings to give rise to health concerns, rigorous QRAs taking a stepwise approach using both desk-based computational and laboratory-based techniques must be included in the overall process of EVP liquid development. Such assessments should identify the hazard, take into account a relevant route of exposure, include appropriate control or reference exposures, use models appropriate to reflect this exposure including the use of 3D tissue models [76,97,117-119], and where possible and relevant, take into account any dose-response and exposure levels during typical use in order to fully and accurately characterise the risk. Additionally, studies should set EVP device power conditions according to those used by EVP users, use puffing regimens that approximate normal use patterns and topography, assess the potential for the transfer of flavours from the liquid into the aerosol, and determine the potential for chemical interactions in ingredient mixtures [85,117,120]. Additionally, when potential toxicants are detected in analytical chemistry studies, the exposure level must be taken into account in order to accurately ascertain whether a human health risk exists [121]. Appropriate use of such methodologies will serve to reduce the potential for adverse effects of flavouring inclusion and help to optimise the THR potential of EVP. Fundamentally, there is an onus on manufacturers to incorporate a rigorous product stewardship approach, such as that proposed by the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) [122], into the development of e-liquid formulations to ensure product quality and consumer safety. Such an approach to e-liquid development should be mandatory for responsible e-liquid development, regardless of the flavour (tobacco or non-tobacco).

Do flavoured EVP have greater abuse liability?

The abuse liability of EVP, also termed their dependence potential, is a measure of the likelihood of a given tobacco or nicotine product to induce dependence among users. The main factors used to determine the abuse liability of tobacco and nicotine products are nicotine pharmacokinetics, principally the rate and extent of nicotine absorption into the blood [123], and subjective effects such as craving/withdrawal relief, satisfaction, liking, and intent to use again [124,125]. While EVP should ideally have an abuse liability no greater than that of conventional cigarettes, it is postulated that possessing at least some degree of abuse liability is necessary for the ability of a novel nicotine product to displace cigarettes and lead to complete switching [2,17,18,124,126]. Should EVP flavours increase the abuse liability of EVP, this may be supportive of the overall population-level THR [126]. However, EVP with too high an abuse liability may have a negative impact, by generating an initiation and/or dependence risk among non-users of nicotine, and particularly among susceptible populations such as youth [17,18].

A number of recent studies have assessed nicotine pharmacokinetics and/or subjective effects in clinical laboratory studies to determine whether flavours affect abuse liability. In studies with various pod-system EVP, including JUUL, Vuse Solo, and BIDI sticks, only minor differences were observed between flavours for both nicotine pharmacokinetics and subjective effects [127-130], although the evidence for a lack of a flavour effect is not unequivocal [131]. However, when taking the literature as a whole into account, and when considering that while flavours may influence initial appeal and other subjective effects, the speed and magnitude of nicotine delivery is likely to be the predominant factor in causing dependence [123], it is most likely that EVP flavours do not impact abuse liability to any significant degree. This conclusion is supported by studies on open-system EVP [132] as well as cross-sectional population-level assessments of the impact of flavours on EVP dependence [133,134]. However, some human studies using different methodologies, such as online purchase task measures or assessing perceptions, have reported flavour effects [135,136], while in animal studies, the impact of flavours on nicotine self-administration (a marker for abuse liability), various findings of no effect or small effects have been reported [137]. Overall, though, regardless of whether flavour effects have been reported or not for EVP, there is perhaps greater consensus that even in the presence of flavours, the abuse liability of EVP is lower, and often much lower, than that of conventional cigarettes [124,128,132,138,139]. Future research in this area needs to consider interactions between EVP flavours and other characteristics, such as nicotine concentration [126,140,141], as well as baseline characteristics at the point of EVP initiation, such as menthol or non-menthol cigarette smoking status, which can influence the relative appeal of tobacco-flavoured or non-tobacco-flavoured EVP [126]. Additionally, the downstream impact of EVP abuse liability with regard to switching potential among adult smokers also needs further assessment [142] in order to facilitate a greater understanding of the link

between EVP flavours, abuse potential, and THR.

Do flavours play a role in switching behaviour among adult smokers?

It has been posited that restricting access to non-tobacco-flavoured EVP could impede smoking cessation among adults [143] and, therefore, have a detrimental impact on public health. Central to supporting this argument would be evidence that non-tobacco-flavoured EVP are preferred by adult smokers and also evidence that they facilitate smoking cessation to a greater degree than EVP which are tobacco-flavoured. The evidence for a supportive role of flavoured EVP in supporting smoking cessation over and above that of tobacco-flavoured EVP is not unequivocal [144-150]. However, a number of studies have provided supporting evidence that non-tobacco-flavoured EVP, including mint/menthol, fruit, dessert/pastry/bakery, and candy/chocolate sweet flavours, convey a greater switching benefit in terms of either cigarette smoking reductions or complete switching [151-159] and may reduce cigarette dependence [159]. These divergent findings regarding the ability of flavoured EVP to support switching may reflect the high degree of heterogeneity between studies, and it has been suggested that further randomised controlled studies are required to delineate the presence or absence of a switching benefit of flavoured EVP [150].

It is also of note that fruit-flavoured EVP were preferred among adults trying to quit smoking [147], and greater preference for both menthol and sweet flavours was associated with lower likelihood of EVP use discontinuation, i.e., these flavours may support continued, long-term exclusive use and, therefore, prevent relapse back to cigarette smoking [149,160]. Adult EVP users, including both current and former smokers, find non-tobacco flavours more appealing and satisfying [149,161]. Flavours may play a role in EVP use initiation among current smokers [162,163], and mint and menthol flavours may be favoured by former smokers [163]. Furthermore, some evidence supports that flavour use is increasing among adults [164], and also that migration away from tobacco flavours and towards non-tobacco flavours among former-smoking EVP users occurs over time [162,165].

Other considerations regarding flavours include that menthol-flavoured EVP are favoured by menthol smokers and are more effective at reducing smoking urges in this cohort [166,167], suggesting that menthol availability may be of importance for specific segments of the smoking population. This may be particularly pertinent in reducing the disproportionate tobacco-related health disparities among certain race/ethnic groups, including Black and Hispanic/Latinx adult smokers, among whom use of menthol cigarettes is more prevalent [167]. Mint/menthol flavours may not only support menthol smokers in switching though with some evidence suggesting support for non-menthol cigarette smokers [168]. However, the recent findings that menthol or other flavours had no impact on subjective effects, behavioural intentions and craving/withdrawal compared with tobacco flavour [130,169] suggest that further research is necessary in this area to fully delineate the role of flavours in supporting switching among both menthol and non-menthol cigarette smokers.

Overall, it has been suggested that maintaining flavour diversity is an important consideration when putting in place regulatory frameworks that aim to maximise the switching benefit for adult smokers [152,158,163,169]. However, in order to determine the true THR potential of flavoured EVP, the impact of non-tobacco-flavoured compared with tobacco-flavoured EVP on smoking initiation or reinitiation among current non-smokers may require further investigation [144,153].

Do flavours increase unintended use?

As described above, the availability of non-tobacco-flavoured EVP may contribute to THR by supporting smokers in switching away from cigarette smoking, particularly in those smokers for whom flavours are appealing and satisfying. Use by those for whom they are not intended, such as youth and never-smokers, may, however, be detrimental to overall population-level health [17,18]. While adult smokers switching to exclusive EVP use undoubtedly reduces risk compared with continued smoking [11,20,22], any use of EVP among those who are either never smokers or naïve to nicotine is rightly considered to be more harmful than no nicotine use at all. Balancing these two competing impacts on public health can be challenging, but as demonstrated in the US with the recent awarding of marketing-granted orders for menthol-flavoured NJOY and JUUL EVP [47,170], this challenge is not insurmountable. There is an additional concern that EVP may act as a gateway into nicotine use and subsequently to cigarette smoking among never-smokers, including youth [171-175]. However, many studies have shown that no such gateway exists, and evidence which appears to support the gateway hypothesis may instead be explained by confounding and the presence of a 'common liability', a genetic predisposition to risk-taking, or a higher behavioural impulsivity among certain individuals [176-185]. That said, maximisation of the THR potential of EVP requires assessing unintended use with a view to minimising it. Various aspects of EVP flavours in relation to unintended use have been examined and reported upon, including the higher likelihood of multiple flavour use and switching between flavours among youth [186], the lower likelihood of EVP cessation and therefore an increased likelihood of long-term use [187], and an increased willingness to try EVP among youth [188]. However, despite the widespread availability of flavoured EVP, the use of EVP by youth is currently at low levels and declining [189]. Furthermore, although the majority of youth who use EVP use flavoured products [189], flavour availability is not a strong reason for use. Other factors such as experimentation, family or friends using them, curiosity, feeling anxious, stressed or depressed, to get a buzz from nicotine, or to reduce harms to

oneself and others around them, are commonly expressed as either equal or stronger drivers than flavours [190–193]. Some studies do suggest that banning flavours may reduce the appeal of EVP and reduce youth use [194–196]. However, other studies did not produce findings that concur with this view. One study using a life-sized model convenience store found that flavour bans did not affect intentions to use menthol/mint or sweet flavoured EVP. Conversely, removal of mint/menthol and sweet flavoured products increased intentions to use tobacco-flavoured products among those who had already started using EVP [197]. Hypothetical flavour bans may lead to continued EVP use (presumably of non-restricted flavours) and may further lead to the highly undesirable outcome of continued smoking or switching to smoking, exacerbating population health harms [198]. We can also draw upon real-world examples of flavour bans, for example, following the US Food and Drug Administration (FDA) 2020 enforcement action against flavoured pod-system EVP, which effectively banned the sale of cartridge-based (pod-system) EVP with flavours other than menthol or tobacco [199]. This led to both flavour and device-type switching, including among youth [200–202]. Consumption patterns, assessed using nicotine exposure biomarker data from the US Population Assessment of Tobacco and Health (PATH) study, were not impacted by the EVP flavour used among youth [203], a finding that counteracts the argument that flavours enhance attractiveness and increase nicotine intake/consumption [44]. Other data suggest that youth use of flavours is experimental [204,205] and such experimentation may not translate into long-term EVP use.

Overall, one of the greatest challenges of maximising the THR potential of EVP is that both adults and youth may have a preference for flavoured EVP and find them appealing [206–208]. This means that any regulatory measure to minimise unintended use by restricting the availability of flavoured EVP will likely have the unintended and detrimental consequence of removing products from markets which otherwise would have helped smokers switch [209], and consequently curtailing the declines in cigarette smoking prevalence seen in recent years [35,36].

Are flavour bans effective?

Should EVP flavours be restricted, it is important to consider the consequences, both intended and unintended and on smokers and non-users of tobacco products, in order to determine the population-level impact on public health of such action. Many proposals by various bodies have been put forward to restrict or ban the use of non-tobacco flavours in EVP [43–45,51], which variously suggest that such action will protect young people from harms associated with nicotine use by reducing EVP appeal and attractiveness [43,210,211], as well as mitigating toxicological concerns [43,44]. What these proposals often do not take into account, however, is the potential impact on adult smokers and former smokers, who, despite suggestions otherwise [43], are the predominant users of EVP [74,75]. These proposals also do not often take into account whether there is evidence base for flavour restrictions having the desired effect.

Banning non-tobacco EVP flavours has been suggested to increase cigarette sales and overall tobacco use [196,212], with one study in the US state of Minnesota finding that youth use of any tobacco product rose by up to 45% following implementation of tobacco product flavour restrictions [196]. In the US state of New York, a non-tobacco flavour ban failed to prevent more than 95% of youth EVP users from continuing to use non-tobacco-flavoured EVP [213]. This is suggestive of the development of an illicit trade in non-tobacco-flavoured EVP following this flavour ban, which may arise from retailer non-compliance and/or users procuring banned EVP from other physical and online sources, both legal and illegal. Many studies have either found evidence for, or suggested the development or presence of, an illicit trade for non-tobacco-flavoured EVP following flavour bans [209,214–224]. The availability of illicit products not only undermines the intended purpose of any regulation but also has the potential to increase health risks to users. In this regard, aerosol from ‘aftermarket’ JUUL pods (i.e., those not manufactured by JUUL but which are compatible with the JUUL device) contains higher levels of carbonyl compounds and reactive oxygen species than those pods made by the manufacturer [225]. If flavour restrictions were specific for specific device types (e.g. pod-system EVP) or flavours, some evidence suggests the users would simply switch to using non-tobacco flavours in unrestricted devices, i.e., products which fall outside of regulatory oversight [223,226–231] or ‘migrate’ to using non-restricted flavours [200,227,229]. Additionally, there is some evidence that following flavour bans, small proportions of users may mix flavoured e-liquids themselves [216,222,223], which would likely be of toxicological concern and increase potential risks to health of EVP use [232].

While some evidence suggests that EVP use may fall as a consequence of flavour restrictions [223,226,228] or that such bans would encourage at least some users to quit EVP use [209,215], other evidence suggests that flavour restrictions are perhaps largely ineffective. In the US, following the FDA’s 2020 change in enforcement discretion [199], EVP use overall was largely unaffected, among both youth and young adults [230,231,233]. Other studies have provided evidence that following implementation of restrictions, cigarette sales may increase and many EVP users may switch to, or continue, smoking [198,209,210,215,217,221,222,227,230], although some evidence suggests that switching to smoking would not necessarily occur [229,234]. There is also a concern that banning flavours could make smoking more appealing than EVP use [222], especially among youth who are more prone to partake in risky behaviours [235] which could facilitate smoking initiation or reinitiation [236]. This risk of increasing smoking rates and, therefore, overall population level health has been proposed to outweigh the potential benefits to public health of banning EVP flavours [217].

What is the overall population-level impact of EVP flavour restrictions?

The main findings of this review, placed into the context of whether implementing regulatory restrictions on non-tobacco-flavoured EVP would be supportive of, or detrimental to, THR and overall population-level public health, are presented in Figure 2. Generally speaking, there is no firm evidence that non-tobacco flavours are of risk to health, either in absolute terms or relative to tobacco flavours. While some studies have also shown that flavoured EVP may release potential toxicants into the aerosol, including metals and aldehydes, such findings are not meaningful unless the data arising from such studies are used as inputs into toxicological QRAs. This view should not be taken as meaning that all flavours are safe, and certainly some ingredients which have historically been found in flavoured EVP, such as diacetyl, are of concern and should not be present in EVP liquids which adhere to regulatory standards or which have been developed following rigorous toxicological risk assessment protocols. Such standardised toxicological QRA procedures are essential to minimise potential harms associated with EVP use, and manufacturers should take responsibility and ensure that such procedures are incorporated into product development. These procedures should take into account the route and degree of exposure, during normal and perhaps intense use, and be informed by studies which have collected aerosol chemistry data or exposed biological materials to EVP aerosol which has been generated in a manner which reflects actual use. This includes not only replicating human puffing topography but also using device settings and including flavouring ingredients at levels which accurately replicate those used by EVP users. Additionally, the use of appropriate control or reference exposures is fundamental to understanding both absolute and relative risk, taking into account that the vast majority of EVP users are former smokers.

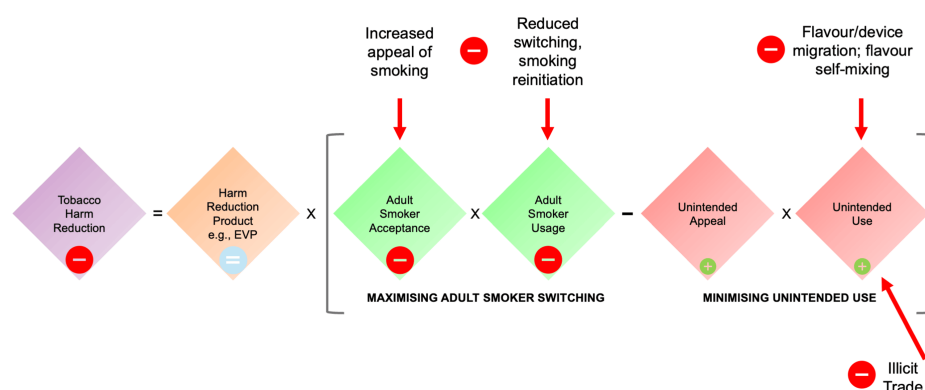


FIGURE 2: Potential impact of flavour restrictions on electronic vaping products

EVP: electronic vaping products

While flavour bans may be effective in reducing appeal and use by those for which EVP are not intended, this effect is likely to be only partial and would be offset by behavioural changes among unintended users (e.g. flavour and/or device migration, self-mixing of flavours, and obtaining EVP through illicit sources). It has also been proposed that the intended impact would be far outweighed, at the population level, by unintended and deleterious effects on adult smokers [198] such as reduced appeal of EVP and therefore reduced switching rates, leading to smoking initiation or reinitiation and increased cigarette consumption

There is also little evidence that non-tobacco-flavoured EVP possess a greater abuse liability than those which are tobacco-flavoured. What is more certain, however, is that restricting flavour choice will have a negative impact on the target population, adult smokers looking to switch to a potentially less harmful alternative to cigarettes [163]. Restricting flavours will reduce both EVP acceptance and use among adult smokers. Strong evidence supports that such regulatory action will potentially even increase the appeal of smoking, reduce switching, and encourage either smoking initiation or reinitiation, thereby creating a gateway into smoking by only allowing tobacco flavours and encouraging experimenting with the real tobacco taste from smoking cigarettes and burning tobacco. Good evidence also suggests that flavour bans have had effects opposite to those intended, including increased cigarette sales and overall tobacco product use in adults as well as youth. Such effects are undoubtedly detrimental to THR, leading to either a slowing in the declines in cigarette smoking seen in many countries, which is associated with EVP use [35], and potentially leading to a reversal in this population health-promoting trend and an increase in smoking attributable mortality [143].

Evidence supporting an overall population-health benefit of EVP flavour restrictions is weak. Little evidence supports that reducing unintended use, including among youth, is a consequence of flavour restrictions. Conversely, many studies have provided evidence for the unintended and detrimental effects of such action. These include consumers adopting behaviour changes which mitigate the effectiveness of such regulation, such as migration towards non-restricted flavours and/or EVP device types, self-mixing of EVP liquids to

include non-tobacco flavours which are of risk to health, or accessing EVP through physical and online sources, both licit and illicit. Such behaviour change not only undermines the regulatory intention, but it does so at the expense of the intended behaviour change, switching among adult smokers. Other responses to regulation may also occur, such as the inclusion by manufacturers of non-restricted flavour ingredients into EVP liquids.

Given the competing balances of THR, and trying to maximise adult switching while minimising unintended use, the question becomes how do we best achieve this? How do we continue to tap into the strong THR potential of EVP and support the continued decline of cigarette smoking, while protecting against youth use? This is a hugely important question, given that an estimated seven million smokers die each year from smoking-attributable disease [1]. The answer is not to simply restrict flavour diversity and choice for adult smokers in order to reduce youth use. The existing evidence suggests that this would be ineffectual in meeting its intended goal and runs the risk of derailing recent advances in reducing smoking prevalence and, subsequently, morbidity and mortality. The setting of regulatory policy should bear in mind that smoking-related disease and death are disproportionate and concentrated among certain race/ethnic groups, as well as the older adult population, and that current tobacco control measures have not proven successful in reducing the absolute number of smokers globally. Regulatory policy should also take into account the vast potential of EVP to help adult smokers switch to less harmful alternatives to smoking [237]. This includes maintaining flavour diversity, a supporting factor in helping adult smokers switch. The recent rises in youth EVP use, which are perhaps experimental and not sustained, can be tackled more effectively than by banning flavours, which is an overly simple solution to a much more complicated problem of public health. Greater enforcement of existing youth protection regulations is one part of a potential solution [238], which could include licensing schemes to restrict where EVP can be sold. Additional gains could be made by prohibiting products, and their marketing materials, packaging and flavour descriptors, which are overtly attractive to youth. This could be achieved, perhaps, through the implementation of responsible marketing standards. While these are more complex solutions than flavour prohibition, they would help to protect smokers' access to the diverse range of products that they currently have and which likely underpins the association of increased EVP use prevalence with smoking declines, while preventing youth access. Such approaches to EVP regulation would protect those who would benefit most from using EVP, but not to the detriment of those who would not. Hence, the overall end goal of eliminating smoking-related death and disease could remain in sight.

Conclusions

In summary, the use of non-tobacco flavours in EVP is a complex issue in which many competing factors play a role in determining the overall impact on population-level health. When setting policy, regulators should take all these factors into account, including the use of flavoured EVP by adult smokers as a means by which to quit smoking, and maintaining flavour diversity may be supportive of reducing smoking prevalence and improving public health.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Ian M. Fearon, Matthew Stevenson, Thomas Nahde

Acquisition, analysis, or interpretation of data: Ian M. Fearon

Drafting of the manuscript: Ian M. Fearon

Critical review of the manuscript for important intellectual content: Ian M. Fearon, Matthew Stevenson, Thomas Nahde

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** The writing of this paper was funded by Imperial Brands PLC. **Financial relationships:** IMF declare(s) stock/stock options from British American Tobacco. IMF declare(s) Travel expenses from Messe Dortmund GmbH. To attend and present at a tobacco expo. IMF declare(s) personal fees from Cheerain HK Ltd. IMF declare(s) personal fees from RAI Services Company. IMF declare(s) personal fees from Shenzhen Smoore Technology, Ltd. IMF declare(s) personal fees from Shenzhen JWEI Electronics Co., Ltd. IMF declare(s) personal fees from HAYPP Group, Inc. IMF declare(s) personal fees from HG Innovation Ltd. IMF declare(s) personal fees from Centre for Substance Use Research. IMF declare(s) personal fees from Russell Burnett Research and Consultancy Ltd. IMF declare(s) personal fees from Chemular. IMF declare(s) personal fees from Imperial Brands PLC. IMF declare(s) personal fees from Broughton Life Sciences. IMF declare(s) personal fees and employment from McKinney Regulatory Science

Advisors LLC. MS declare(s) employment from Imperial Brands PLC. TN declare(s) employment from Imperial Brands Reemtsma. IMF declare(s) personal fees and stock/stock options from Qnovia, Inc. IMF is a consultant to and scientific advisory board member of Qnovia, LLC, an inhaled nicotine pharmaceutical smoking cessation product manufacturer. IMF declare(s) personal fees from Tobacco and nicotine product companies, pharmaceutical companies, contract research organisations, and health advocacy groups. IMF is an independent consultant to tobacco and nicotine product manufacturers, pharmaceutical companies, contract research organisations, and health advocacy groups and provides scientific support for clinical and behavioural studies, general regulatory support, and public health advisory support. These companies/CROs/groups are unspecified for confidentiality reasons. IMF declare(s) non-financial support from Advanced Inhalation Rituals Ltd. IMF is a non-executive director at Advanced Inhalation Rituals Ltd., a manufacturer of waterpipe tobacco and electronic waterpipe products. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors thank the internal Imperial Brands PLC Reading Committee for their critical reviews and comments on this paper.

References

1. Tobacco. (2023). Accessed: November 12, 2024: <https://www.who.int/news-room/fact-sheets/detail/tobacco>.
2. Abrams DB, Glasser AM, Villanti AC, Pearson JL, Rose S, Niaura RS: Managing nicotine without smoke to save lives now: evidence for harm minimization. *Prev Med*. 2018, 117:88-97. [10.1016/j.ypmed.2018.06.010](https://doi.org/10.1016/j.ypmed.2018.06.010)
3. Royal College of Physicians: Nicotine Without Smoke: Tobacco Harm Reduction. Royal College of Physicians, London; 2016. <https://www.rcp.ac.uk/improving-care/resources/nicotine-without-smoke-tobacco-harm-reduction/>.
4. Royal College of Physicians: E-cigarettes and Harm Reduction: An Evidence Review. Royal College of Physicians, London; 2024. <https://www.rcp.ac.uk/policy-and-campaigns/policy-documents/e-cigarettes-and-harm-reduction-an-evidence-review/>.
5. Nicotine is why tobacco products are addictive . (2024). Accessed: October 11, 2024: <https://www.fda.gov/tobacco-products/health-effects-tobacco-use/nicotine-why-tobacco-products-are-addictive>.
6. Baker RR, Massey ED, Smith G: An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. *Food Chem Toxicol*. 2004, 42:53-83. [10.1016/j.fct.2004.01.001](https://doi.org/10.1016/j.fct.2004.01.001)
7. Perfetti TA, Rodgman A: The complexity of tobacco and tobacco smoke . *Beiträge zur Tabakforschung International*. 2011, 24:215-32. [10.2478/cttr-2013-0902](https://doi.org/10.2478/cttr-2013-0902)
8. Harmful and potentially harmful constituents in tobacco products and tobacco smoke; established list . (2012). Accessed: November 12, 2024: <https://www.federalregister.gov/documents/2012/04/03/2012-7727/harmful-and-potentially-harmful-constituents-in-tobacc....>
9. Institute of Medicine: Clearing the Smoke-Assessing the Science Base for Tobacco Harm Reduction. Stratton K, Shetty P, Wallace R, Bondurant S (ed): The National Academies Press, Washington, D.C; 2001. <https://nap.nationalacademies.org/catalog/10029/clearing-the-smoke-assessing-the-science-base-for-tobacco-harm>.
10. Stratton K, Shetty P, Wallace R, Bondurant S: Clearing the smoke: the science base for tobacco harm reduction-executive summary. *Tob Control*. 2001, 10:189-95. [10.1136/tc.10.2.189](https://doi.org/10.1136/tc.10.2.189)
11. Nicotine vaping in England: an evidence update including health risks and perceptions, 2022 . (2022). Accessed: November 12, 2024: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1107701/Nicotine-vapi...
12. Smokefree 2025. (2022). Accessed: November 12, 2024: <https://vapingfacts.health.nz/our-position-on-vaping.html>.
13. Vaping and quitting smoking. (2023). Accessed: November 12, 2024: <https://www.canada.ca/en/health-canada/services/smoking-tobacco/vaping/smokers.html>.
14. Beaglehole R, Bonita R: Harnessing tobacco harm reduction. *Lancet*. 2024, 403:512-4. [10.1016/S0140-6736\(24\)00140-5](https://doi.org/10.1016/S0140-6736(24)00140-5)
15. Warner KE: How to think-not feel-about tobacco harm reduction . *Nicotine Tob Res*. 2019, 21:1299-309. [10.1093/ntr/nty084](https://doi.org/10.1093/ntr/nty084)
16. Yach D: Tobacco harm reduction matters . *Lancet*. 2022, 399:1864-5. [10.1016/S0140-6736\(22\)00834-0](https://doi.org/10.1016/S0140-6736(22)00834-0)
17. Ashley DL, Spears CA, Weaver SR, Huang J, Eriksen MP: E-cigarettes: how can they help smokers quit without addicting a new generation?. *Prev Med*. 2020, 140:106145. [10.1016/j.ypmed.2020.106145](https://doi.org/10.1016/j.ypmed.2020.106145)
18. Cahn Z, Drope J, Douglas CE, Henson R, Berg CJ, Ashley DL, Eriksen MP: Applying the population health standard to the regulation of electronic nicotine delivery systems. *Nicotine Tob Res*. 2021, 23:780-9. [10.1093/ntr/ntaa190](https://doi.org/10.1093/ntr/ntaa190)
19. Breland A, Soule E, Lopez A, Ramôa C, El-Hellani A, Eissenberg T: Electronic cigarettes: what are they and what do they do?. *Ann N Y Acad Sci*. 2017, 1394:5-30. [10.1111/nyas.12977](https://doi.org/10.1111/nyas.12977)
20. 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. Public Health England, London, UK; 2018.
21. Margham J, McAdam K, Forster M, Liu C, Wright C, Mariner D, Proctor C: Chemical composition of aerosol from an e-cigarette: a quantitative comparison with cigarette smoke. *Chem Res Toxicol*. 2016, 29:1662-78. [10.1021/acs.chemrestox.6b00188](https://doi.org/10.1021/acs.chemrestox.6b00188)
22. National Academies of Sciences, Engineering and Medicine: Public Health Consequences of E-Cigarettes.

- The National Academies Press, Washington, D.C.; 2018.
<https://nap.nationalacademies.org/catalog/24952/public-health-consequences-of-e-cigarettes>.
23. Goniewicz ML, Smith DM, Edwards KC, et al.: Comparison of nicotine and toxicant exposure in users of electronic cigarettes and combustible cigarettes. *JAMA Netw Open*. 2018, 1:e185937. [10.1001/jamanetworkopen.2018.5937](https://doi.org/10.1001/jamanetworkopen.2018.5937)
 24. Cohen G, Goldenson NI, Bailey PC, Chan S, Shiffman S: Changes in biomarkers of cigarette smoke exposure after 6 days of switching exclusively or partially to use of the JUUL system with two nicotine concentrations: a randomized controlled confinement study in adult smokers. *Nicotine Tob Res*. 2021, 23:2153-61. [10.1093/ntr/ntab134](https://doi.org/10.1093/ntr/ntab134)
 25. Morris P, McDermott S, Chapman F, et al.: Reductions in biomarkers of exposure to selected harmful and potentially harmful constituents following exclusive and partial switching from combustible cigarettes to mybluTM electronic nicotine delivery systems (ENDS). *Intern Emerg Med*. 2022, 17:397-410. [10.1007/s11739-021-02813-w](https://doi.org/10.1007/s11739-021-02813-w)
 26. Shahab L, Goniewicz ML, Blount BC, et al.: Nicotine, carcinogen, and toxin exposure in long-term e-cigarette and nicotine replacement therapy users: a cross-sectional study. *Ann Intern Med*. 2017, 166:390-400. [10.7326/M16-1107](https://doi.org/10.7326/M16-1107)
 27. Smith DM, Shahab L, Blount BC, et al.: Differences in exposure to nicotine, tobacco-specific nitrosamines, and volatile organic compounds among electronic cigarette users, tobacco smokers, and dual users from three countries. *Toxics*. 2020, 8:88. [10.3390/toxics8040088](https://doi.org/10.3390/toxics8040088)
 28. Auer R, Schoeni A, Humair JP, et al.: Electronic nicotine-delivery systems for smoking cessation. *N Engl J Med*. 2024, 390:601-10. [10.1056/NEJMoa2308815](https://doi.org/10.1056/NEJMoa2308815)
 29. Lindson N, Butler AR, McRobbie H, et al.: Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev*. 2024, 1:CD010216. [10.1002/14651858.CD010216.pub8](https://doi.org/10.1002/14651858.CD010216.pub8)
 30. Meng Y, Xiang S, Qu L, Li Y: The efficacy and acceptability of pharmacological monotherapies and e-cigarette on smoking cessation: a systemic review and network meta-analysis. *Front Public Health*. 2024, 12:1361186. [10.3389/fpubh.2024.1361186](https://doi.org/10.3389/fpubh.2024.1361186)
 31. Millard PS: In adult tobacco smokers, adding e-cigarettes to standard smoking cessation counseling increased abstinence at 6 mo. *Ann Intern Med*. 2024, 177:JC70. [10.7326/ANNALS-24-00229-JC](https://doi.org/10.7326/ANNALS-24-00229-JC)
 32. Pope I, Clark LV, Clark A, et al.: Cessation of smoking trial in the emergency department (COSTED): a multicentre randomised controlled trial. *Emerg Med J*. 2024, 41:276-82. [10.1136/emmermed-2023-213824](https://doi.org/10.1136/emmermed-2023-213824)
 33. Abi Nehme AM, Lou X, Yan X, Lee JH, Salloum RG: Transition to smoking cessation among dual cigarette and e-cigarette users in the population assessment of tobacco and health study, waves 3 and 4 (2015-2017). *Addict Behav*. 2022, 129:107284. [10.1016/j.addbeh.2022.107284](https://doi.org/10.1016/j.addbeh.2022.107284)
 34. Warner KE, Benowitz NL, McNeill A, Rigotti NA: Nicotine e-cigarettes as a tool for smoking cessation. *Nat Med*. 2023, 29:520-4. [10.1038/s41591-022-02201-7](https://doi.org/10.1038/s41591-022-02201-7)
 35. Foxon F, Selya A, Gitchell J, Shiffman S: Increased e-cigarette use prevalence is associated with decreased smoking prevalence among US adults. *Harm Reduct J*. 2024, 21:136. [10.1186/s12954-024-01056-0](https://doi.org/10.1186/s12954-024-01056-0)
 36. Pesola F, Phillips-Waller A, Beard E, Shahab L, Sweanor D, Jarvis M, Hajek P: Effects of reduced-risk nicotine-delivery products on smoking prevalence and cigarette sales: an observational study. *Public Health Res (Southampt)*. 2023, 11:1-39. [10.3310/RPDN7327](https://doi.org/10.3310/RPDN7327)
 37. Moore G, Hallingberg B, Brown R, et al.: Impacts of EU tobacco products directive regulations on use of e-cigarettes in adolescents in Great Britain: a natural experiment evaluation. *Public Health Res (Southampt)*. 2023, 11:1-102. [10.3310/WTMH3198](https://doi.org/10.3310/WTMH3198)
 38. Williams PJ, Cheeseman H, Arnott D, Bunce L, Hopkinson NS, Lavery AA: Use of tobacco and e-cigarettes among youth in Great Britain in 2022: analysis of a cross-sectional survey. *Tob Induc Dis*. 2023, 21:5. [10.18332/tid/156459](https://doi.org/10.18332/tid/156459)
 39. Izquierdo-Condoys JS, Sosa KR, Salazar-Santoliva C, et al.: E-cigarette use among adolescents in Latin America: a systematic review of prevalence and associated factors. *Prev Med Rep*. 2025, 49:102952. [10.1016/j.pmedr.2024.102952](https://doi.org/10.1016/j.pmedr.2024.102952)
 40. Ko K, Ting Wai Chu J, Bullen C: A scoping review of vaping among the Asian adolescent population. *Asia Pac J Public Health*. 2024, 36:664-75. [10.1177/10105395241275226](https://doi.org/10.1177/10105395241275226)
 41. Adegbile OE, Adeniji OD, Amzat J, Kanmodi KK: E-cigarettes in Nigeria: a scoping review of evidence. *Health Sci Rep*. 2024, 7:e2074. [10.1002/hsr2.2074](https://doi.org/10.1002/hsr2.2074)
 42. Results from the annual national youth tobacco survey. (2025). Accessed: July 4, 2025: <https://www.fda.gov/tobacco-products/youth-and-tobacco/results-annual-national-youth-tobacco-survey>.
 43. Rupp A, Sommer N, Andreas S, et al.: Medical societies in Germany call for a ban on flavors in e-cigarettes-a position paper of the German Respiratory Society (DGP) in cooperation with other professional associations and organizations (Article in German). *Pneumologie*. 2024, 78:320-4. [10.1055/a-2282-9908](https://doi.org/10.1055/a-2282-9908)
 44. Sommer N, Franzen K, Andreas S, Pankow W, Kunstmann W, Hanewinkel R: Harmful health effects of flavors in e-cigarettes (Article in German). *Laryngorhinootologie*. 2025, 104:288-95. [10.1055/a-2341-0544](https://doi.org/10.1055/a-2341-0544)
 45. Council of the European Union: a call for action at the EU level to protect young people from harm caused by novel tobacco and nicotine products. (2024). Accessed: November 12, 2024: <https://data.consilium.europa.eu/doc/document/ST-10268-2024-INIT/EN/pdf>.
 46. Bansal-Travers M, Price SM, Bold KW, et al.: Common measures to evaluate flavored tobacco products: recommendations from the Tobacco Centers for Regulatory Science (TCORS) Flavored Tobacco Products Measurement Subcommittee. *Nicotine Tob Res*. 2023, 25:159-63. [10.1093/ntr/ntac171](https://doi.org/10.1093/ntr/ntac171)
 47. FDA Authorizes marketing of four menthol-flavored e-cigarette products after extensive scientific review. (2024). Accessed: July 22, 2025: <https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-four-menthol-flavored-e-cigarette-produc>....
 48. Sun Y, Prabhu P, Rahman R, Li D, McIntosh S, Rahman I: e-Cigarette tobacco flavors, public health, and toxicity: narrative review. *Online J Public Health Inform*. 2024, 16:e51991. [10.2196/51991](https://doi.org/10.2196/51991)
 49. Strongin RM, Sharma E, Erythropel HC, Kassem NO, Noël A, Peyton DH, Rahman I: Chemical and physiological interactions between e-liquid constituents: cause for concern?. *Tob Control*. 2025, 34:393-6. [10.1136/tc-2023-058546](https://doi.org/10.1136/tc-2023-058546)

50. Lamb T, Muthumalage T, Meehan-Atrash J, Rahman I: Nose-only exposure to cherry- and tobacco-flavored e-cigarettes induced lung inflammation in mice in a sex-dependent manner. *Toxics*. 2022, 10:471. [10.3390/toxics10080471](https://doi.org/10.3390/toxics10080471)
51. Pennings JL, Havermans A, Krüsemann EJ, et al.: Reducing attractiveness of e-liquids: proposal for a restrictive list of tobacco-related flavourings. *Tob Control*. 2024, 33:e41-7. [10.1136/tc-2022-057764](https://doi.org/10.1136/tc-2022-057764)
52. Reducing attractiveness of e-liquids: proposal for a restrictive list of tobacco-related flavorings . (2022). Accessed: July 22, 2025: http://2022.com/wp-content/uploads/2022/11/15_Poster-Jeroen-Pennings-RIVM1.pdf.
53. Genotoxicity hazard identification and carcinogenicity tiering of constituents in ENDS Premarket tobacco product applications. (2024). Accessed: July 4, 2025: <https://www.fda.gov/media/180609/download>.
54. Aherrera A, Lin JJ, Chen R, et al.: Metal concentrations in e-cigarette aerosol samples: a comparison by device type and flavor. *Environ Health Perspect*. 2023, 131:127004. [10.1289/EHP11921](https://doi.org/10.1289/EHP11921)
55. Schmidt C: Nicotine, flavor, and more: e-cigarette aerosols deliver toxic metals . *Environ Health Perspect*. 2024, 132:24002. [10.1289/EHP14425](https://doi.org/10.1289/EHP14425)
56. Xu T, Niu ZY, Xu J, et al.: Chemical analysis of selected harmful and potentially harmful constituents and in vitro toxicological evaluation of leading flavoured e-cigarette aerosols in the Chinese market. *Drug Test Anal*. 2023, 15:1156-63. [10.1002/dta.3337](https://doi.org/10.1002/dta.3337)
57. Kapiamba KF, Hao W, Adom S, Liu W, Huang YW, Wang Y: Examining metal contents in primary and secondhand aerosols released by electronic cigarettes. *Chem Res Toxicol*. 2022, 35:954-62. [10.1021/acs.chemrestox.1c00411](https://doi.org/10.1021/acs.chemrestox.1c00411)
58. Jameson JB, Wang J, Bailey PC, et al.: Determination of chemical constituent yields in e-cigarette aerosol using partial and whole pod collections, a comparative analysis. *Front Chem*. 2023, 11:1223967. [10.3389/fchem.2023.1223967](https://doi.org/10.3389/fchem.2023.1223967)
59. Smith C, Jamison B, Jongsma C, et al.: Harmful and potentially harmful constituents analysis of North American ENDS. *Contributions to Tobacco & Nicotine Research*. 2024, 33:189-216. [10.2478/cttr-2024-0008](https://doi.org/10.2478/cttr-2024-0008)
60. Zhao D, Ilievski V, Slavkovich V, et al.: Effects of e-liquid flavor, nicotine content, and puff duration on metal emissions from electronic cigarettes. *Environ Res*. 2022, 204:112270. [10.1016/j.envres.2021.112270](https://doi.org/10.1016/j.envres.2021.112270)
61. Soulet S, Sussman RA: A critical review of recent literature on metal contents in e-cigarette aerosol . *Toxics*. 2022, 10:510. [10.3390/toxics10090510](https://doi.org/10.3390/toxics10090510)
62. Haworth-Duff A, Parkes GM, Reed NJ: Profiling flavourings in strawberry-flavoured e-liquid using headspace-gas chromatography-mass spectrometry. *Drug Test Anal*. 2023, 15:1077-83. [10.1002/dta.3451](https://doi.org/10.1002/dta.3451)
63. Noël A, Ghosh A: Carbonyl profiles of electronic nicotine delivery system (ends) aerosols reflect both the chemical composition and the numbers of e-liquid ingredients-focus on the in vitro toxicity of strawberry and vanilla flavors. *Int J Environ Res Public Health*. 2022, 19:16774. [10.3390/ijerph192416774](https://doi.org/10.3390/ijerph192416774)
64. Kerber PJ, Duell AK, Powers M, Strongin RM, Peyton DH: Effects of common e-liquid flavorants and added nicotine on toxicant formation during vaping analyzed by (1)H NMR spectroscopy. *Chem Res Toxicol*. 2022, 35:1267-76. [10.1021/acs.chemrestox.2c00110](https://doi.org/10.1021/acs.chemrestox.2c00110)
65. Gschwend G, Jenkins C, Jones A, Kelso C, Morgan J: A wide range of flavoring-carrier fluid adducts form in e-cigarette liquids. *Chem Res Toxicol*. 2023, 36:14-22. [10.1021/acs.chemrestox.2c00200](https://doi.org/10.1021/acs.chemrestox.2c00200)
66. Kerber PJ, Peyton DH: Kinetics of aldehyde flavorant-acetal formation in e-liquids with different e-cigarette solvents and common additives studied by (1)H NMR spectroscopy. *Chem Res Toxicol*. 2022, 35:1410-7. [10.1021/acs.chemrestox.2c00159](https://doi.org/10.1021/acs.chemrestox.2c00159)
67. Farsalinos KE, Voudris V, Poulas K: Are metals emitted from electronic cigarettes a reason for health concern? A risk-assessment analysis of currently available literature. *Int J Environ Res Public Health*. 2015, 12:5215-32. [10.3390/ijerph120505215](https://doi.org/10.3390/ijerph120505215)
68. Wadkin R, Allen C, Fearon IM: E-cigarette puffing topography: the importance of assessing user behaviour to inform emissions testing. *Drug Test Anal*. 2023, 15:1222-32. [10.1002/dta.3322](https://doi.org/10.1002/dta.3322)
69. Soulet S, Sussman RA: Critical review of the recent literature on organic byproducts in e-cigarette aerosol emissions. *Toxics*. 2022, 10:714. [10.3390/toxics10120714](https://doi.org/10.3390/toxics10120714)
70. Thomson RH, Lewis PM: More on hidden formaldehyde in e-cigarette aerosols . *N Engl J Med*. 2015, 372:1575-6. [10.1056/NEJMc1502242](https://doi.org/10.1056/NEJMc1502242)
71. Bates CD, Farsalinos KE: E-cigarettes need to be tested for safety under realistic conditions . *Addiction*. 2015, 110:1688-9. [10.1111/add.13028](https://doi.org/10.1111/add.13028)
72. Farsalinos KE, Voudris V, Spyrou A, Poulas K: E-cigarettes emit very high formaldehyde levels only in conditions that are aversive to users: a replication study under verified realistic use conditions. *Food Chem Toxicol*. 2017, 109:90-4. [10.1016/j.fct.2017.08.044](https://doi.org/10.1016/j.fct.2017.08.044)
73. Farsalinos KE, Voudris V: Do flavouring compounds contribute to aldehyde emissions in e-cigarettes? . *Food Chem Toxicol*. 2018, 115:212-7. [10.1016/j.fct.2018.02.059](https://doi.org/10.1016/j.fct.2018.02.059)
74. Travis N, Knoll M, Cadham CJ, et al.: Health effects of electronic cigarettes: an umbrella review and methodological considerations. *Int J Environ Res Public Health*. 2022, 19:9054. [10.3390/ijerph19159054](https://doi.org/10.3390/ijerph19159054)
75. Mayer M, Reyes-Guzman C, Grana R, Choi K, Freedman ND: Demographic characteristics, cigarette smoking, and e-cigarette use among US adults. *JAMA Netw Open*. 2020, 3:e2020694. [10.1001/jamanetworkopen.2020.20694](https://doi.org/10.1001/jamanetworkopen.2020.20694)
76. Effah F, Adragna J, Luglio D, Bailey A, Marczylo T, Gordon T: Toxicological assessment of E-cigarette flavored E-liquids aerosols using Calu-3 cells: A 3D lung model approach. *Toxicology*. 2023, 500:153683. [10.1016/j.tox.2023.153683](https://doi.org/10.1016/j.tox.2023.153683)
77. Abou-Assali O, Ebner M, Chams J, et al.: Inhalation exposure to flavored electronic nicotine delivery systems (vaping) negatively impacts cardiac electrophysiology. *Europace*. 2024, 26:euae102.611. [10.1093/europace/euae102.611](https://doi.org/10.1093/europace/euae102.611)
78. Sabo AN, Filaudeau E, Da Silva S, Becker G, Monassier L, Kemmel V: Flavoured and nicotine-containing e-liquids impair homeostatic properties of an alveolar-capillary cell model. *Food Chem Toxicol*. 2023, 174:113650. [10.1016/j.fct.2023.113650](https://doi.org/10.1016/j.fct.2023.113650)
79. Michon M, Mercier C, Petit C, Leclerc L, Bertoletti L, Pourchez J, Forest V: In vitro biological effects of e-cigarette on the cardiovascular system-pro-inflammatory response enhanced by the presence of the

- cinnamon flavor. *Toxics*. 2022, 10:784. [10.3390/toxics10120784](https://doi.org/10.3390/toxics10120784)
80. Cox A, Brown KC, Valentovic MA: The E-liquid flavoring vanillin alters energy and autophagic pathways in human proximal tubule (HK-2) epithelial cells. *Chem Biol Interact*. 2024, 394:111003. [10.1016/j.cbi.2024.111003](https://doi.org/10.1016/j.cbi.2024.111003)
81. Winters BR, Clapp PW, Simmons SO, Kochar TK, Jaspers I, Madden MC: E-cigarette liquids and aldehyde flavoring agents inhibit CYP2A6 activity in lung epithelial cells. *ACS Omega*. 2023, 8:11261-6. [10.1021/acsomega.2c08258](https://doi.org/10.1021/acsomega.2c08258)
82. Effah F, Elzein A, Taiwo B, Baines D, Bailey A, Marczylo T: In vitro high-throughput toxicological assessment of E-cigarette flavors on human bronchial epithelial cells and the potential involvement of TRPA1 in cinnamon flavor-induced toxicity. *Toxicology*. 2023, 496:153617. [10.1016/j.tox.2023.153617](https://doi.org/10.1016/j.tox.2023.153617)
83. Richardson A, Krivokhizhina T, Lorkiewicz P, D'Souza S, Bhatnagar A, Srivastava S, Conklin DJ: Effects of electronic cigarette flavorants on human platelet aggregation ex vivo. *Toxicol Rep*. 2022, 9:814-20. [10.1016/j.toxrep.2022.04.003](https://doi.org/10.1016/j.toxrep.2022.04.003)
84. Sinha I, Goel R, Bitzer ZT, Trushin N, Liao J, Sinha R: Evaluating electronic cigarette cytotoxicity and inflammatory responses in vitro. *Tob Induc Dis*. 2022, 20:45. [10.18332/tid/147200](https://doi.org/10.18332/tid/147200)
85. Sciuscio D, Calvino-Martin F, Kumar A, et al.: Toxicological assessment of flavor ingredients in e-vapor products. *Front Toxicol*. 2022, 4:878976. [10.3389/ftox.2022.878976](https://doi.org/10.3389/ftox.2022.878976)
86. Pound P, Ritskes-Hoitinga M: Is it possible to overcome issues of external validity in preclinical animal research? Why most animal models are bound to fail. *J Transl Med*. 2018, 16:304. [10.1186/s12967-018-1678-1](https://doi.org/10.1186/s12967-018-1678-1)
87. Manuppello JR: Avoiding animal testing under the U.S. Family Smoking Prevention and Tobacco Control Act. *Appl In Vitro Toxicol*. 2017, 3:10-11. [10.1089/aivt.2016.0033](https://doi.org/10.1089/aivt.2016.0033)
88. U.S. Food and Drug Administration (FDA). (2024). Accessed: November 12, 2024: <https://www.peta.org/issues/animals-used-for-experimentation/us-government-animal-testing-programs/food-drug-administ...>
89. Akinola LS, Rahman Y, Ondo O, Cobb CO, Holt AK, Peace MR, Damaj MI: Impact of tobacco flavoring on oral nicotine consumption in C57BL/6J mice. *Drug Alcohol Depend*. 2022, 241:109685. [10.1016/j.drugalcdep.2022.109685](https://doi.org/10.1016/j.drugalcdep.2022.109685)
90. Xu A, Duan K, Yang W, et al.: The toxic effects of electronic cigarette aerosol and cigarette smoke on cardiovascular, gastrointestinal and renal systems in mice. *Sci Rep*. 2023, 13:12366. [10.1038/s41598-023-39201-7](https://doi.org/10.1038/s41598-023-39201-7)
91. Wong ET, Luettich K, Cammack L, et al.: Assessment of inhalation toxicity of cigarette smoke and aerosols from flavor mixtures: 5-week study in A/J mice. *J Appl Toxicol*. 2022, 42:1701-22. [10.1002/jat.4338](https://doi.org/10.1002/jat.4338)
92. Zhao M, Han Y, Yang Q, et al.: Evaluation of the effects of e-cigarette aerosol extracts and tobacco cigarette smoke extracts on RAW264.7 cells. *ACS Omega*. 2023, 8:29336-45. [10.1021/acsomega.3c02758](https://doi.org/10.1021/acsomega.3c02758)
93. Tellez CS, Grimes MJ, Juri DE, et al.: Flavored E-cigarette product aerosols induce transformation of human bronchial epithelial cells. *Lung Cancer*. 2023, 179:107180. [10.1016/j.lungcan.2023.107180](https://doi.org/10.1016/j.lungcan.2023.107180)
94. Bishop E, East N, Miazzi F, Fiebelkorn S, Breheny D, Gaca M, Thorne D: A contextualised e-cigarette testing strategy shows flavourings do not impact lung toxicity in vitro. *Toxicol Lett*. 2023, 380:1-11. [10.1016/j.toxlet.2023.03.006](https://doi.org/10.1016/j.toxlet.2023.03.006)
95. Wang L, Wang Y, Yang X, et al.: Cytotoxicity and cell injuries of flavored electronic cigarette aerosol and mainstream cigarette smoke: a comprehensive in vitro evaluation. *Toxicol Lett*. 2023, 374:96-110. [10.1016/j.toxlet.2022.12.012](https://doi.org/10.1016/j.toxlet.2022.12.012)
96. Czekala L, Simms L, Stevenson M, Trelles-Sticken E, Walker P, Walele T: High content screening in NHBE cells shows significantly reduced biological activity of flavoured e-liquids, when compared to cigarette smoke condensate. *Toxicol In Vitro*. 2019, 58:86-96. [10.1016/j.tiv.2019.03.018](https://doi.org/10.1016/j.tiv.2019.03.018)
97. Czekala L, Simms L, Stevenson M, Tschierske N, Maione AG, Walele T: Toxicological comparison of cigarette smoke and e-cigarette aerosol using a 3D in vitro human respiratory model. *Regul Toxicol Pharmacol*. 2019, 103:314-24. [10.1016/j.yrtph.2019.01.036](https://doi.org/10.1016/j.yrtph.2019.01.036)
98. Keyser BM, Leverette R, Wertman J, et al.: Evaluation of cytotoxicity and oxidative stress of whole aerosol from Vuse Alto ENDS products. *Toxics*. 2024, 12:129. [10.3390/toxics12020129](https://doi.org/10.3390/toxics12020129)
99. Muthumalage T, Rahman I: Pulmonary immune response regulation, genotoxicity, and metabolic reprogramming by menthol- and tobacco-flavored e-cigarette exposures in mice. *Toxicol Sci*. 2023, 193:146-65. [10.1093/toxsci/kfad033](https://doi.org/10.1093/toxsci/kfad033)
100. Bengalli R, Ferri E, Labra M, Mantecchia P: Lung toxicity of condensed aerosol from e-cig liquids: influence of the flavor and the in vitro model used. *Int J Environ Res Public Health*. 2017, 14:1254. [10.3390/ijerph14101254](https://doi.org/10.3390/ijerph14101254)
101. Morris AM, Leonard SS, Fowles JR, Boots TE, Mnatsakanova A, Attfield KR: Effects of e-cigarette flavoring chemicals on human macrophages and bronchial epithelial cells. *Int J Environ Res Public Health*. 2021, 18:11107. [10.3390/ijerph182111107](https://doi.org/10.3390/ijerph182111107)
102. Mercier C, Pourchez J, Leclerc L, Forest V: In vitro toxicological evaluation of aerosols generated by a 4th generation vaping device using nicotine salts in an air-liquid interface system. *Respir Res*. 2024, 25:75. [10.1186/s12931-024-02697-2](https://doi.org/10.1186/s12931-024-02697-2)
103. Routine analytical machine for e-cigarette aerosol generation and collection - definitions and standard conditions. (2015). Accessed: October 21, 2024: https://www.coresta.org/sites/default/files/technical_documents/main/CRM_81.pdf.
104. Smart DJ, Phillips G: Collecting e-cigarette aerosols for in vitro applications: a survey of the biomedical literature and opportunities to increase the value of submerged cell culture-based assessments. *J Appl Toxicol*. 2021, 41:161-74. [10.1002/jat.4064](https://doi.org/10.1002/jat.4064)
105. Cox A, Brown KC, Bender C, Valentovic MA: The e-liquid flavoring cinnamaldehyde induces cellular stress responses in human proximal tubule (HK-2) kidney cells. *Biomed Pharmacother*. 2024, 175:116666. [10.1016/j.biopha.2024.116666](https://doi.org/10.1016/j.biopha.2024.116666)
106. Day NJ, Wang J, Johnston CJ, et al.: Rat bronchoalveolar lavage proteome changes following e-cigarette aerosol exposures. *Am J Physiol Lung Cell Mol Physiol*. 2023, 324:L571-83. [10.1152/ajplung.00016.2023](https://doi.org/10.1152/ajplung.00016.2023)

107. Noël A, Yilmaz S, Farrow T, Schexnayder M, Eickelberg O, Jelesijevic T: Sex-specific alterations of the lung transcriptome at birth in mouse offspring prenatally exposed to vanilla-flavored e-cigarette aerosols and enhanced susceptibility to asthma. *Int J Environ Res Public Health*. 2023, 20:3710. [10.3390/ijerph20043710](https://doi.org/10.3390/ijerph20043710)
108. Goros RA, Xu X, Li G, Zuo YY: Adverse biophysical impact of e-cigarette flavors on pulmonary surfactant. *Environ Sci Technol*. 2023, 57:15882-91. [10.1021/acs.est.3c05896](https://doi.org/10.1021/acs.est.3c05896)
109. Martin A, Tempura C, Yu Y, et al.: Exposure to aldehyde cherry e-liquid flavoring and its vaping byproduct disrupt pulmonary surfactant biophysical function. *Environ Sci Technol*. 2024, 58:1495-508. [10.1021/acs.est.3c07874](https://doi.org/10.1021/acs.est.3c07874)
110. Nunes NM, do Nascimento Silva J, Conceição ML, et al.: In vitro and in vivo acute toxicity of an artificial butter flavoring. *J Toxicol Environ Health A*. 2023, 86:181-97. [10.1080/15287594.2023.2172502](https://doi.org/10.1080/15287594.2023.2172502)
111. Langel SN, Kelly FL, Brass DM, et al.: E-cigarette and food flavoring diacetyl alters airway cell morphology, inflammatory and antiviral response, and susceptibility to SARS-CoV-2. *Cell Death Discov*. 2022, 8:64. [10.1038/s41420-022-00855-3](https://doi.org/10.1038/s41420-022-00855-3)
112. Lamb T, Rahman I: Pro-inflammatory effects of aerosols from e-cigarette-derived flavoring chemicals on murine macrophages. *Toxicol Rep*. 2023, 10:431-5. [10.1016/j.toxrep.2023.04.003](https://doi.org/10.1016/j.toxrep.2023.04.003)
113. Narimani M, Adams J, da Silva G: Toxic chemical formation during vaping of ethyl ester flavor additives: a chemical kinetic modeling study. *Chem Res Toxicol*. 2022, 35:522-8. [10.1021/acs.chemrestox.1c00437](https://doi.org/10.1021/acs.chemrestox.1c00437)
114. Ho J, Sciuscio D, Kogel U, et al.: Evaluation of toxicity of aerosols from flavored e-liquids in Sprague-Dawley rats in a 90-day OECD inhalation study, complemented by transcriptomics analysis. *Arch Toxicol*. 2020, 94:2179-206. [10.1007/s00204-020-02759-6](https://doi.org/10.1007/s00204-020-02759-6)
115. Date MS, O'Brien D, Botelho DJ, Schultz TW, Liebler DC, Penning TM, Salvito DT: Clustering a chemical inventory for safety assessment of fragrance ingredients: identifying read-across analogs to address data gaps. *Chem Res Toxicol*. 2020, 33:1709-18. [10.1021/acs.chemrestox.9b00518](https://doi.org/10.1021/acs.chemrestox.9b00518)
116. European Commission: Commission Regulation (EC) no 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of regulation (EC) no 2232/96 of the European Parliament and of the Council. *OJEC*. 2000, 50:8-16.
117. Thorne D, McHugh D, Simms L, Lee KM, Fujimoto H, Moses S, Gaca M: Applying new approach methodologies to assess next-generation tobacco and nicotine products. *Front Toxicol*. 2024, 6:1376118. [10.3389/ftox.2024.1376118](https://doi.org/10.3389/ftox.2024.1376118)
118. Bishop E, Gaça M, Thorne D: Advances in whole aerosol approaches for in vitro e-cigarette testing. *Drug Test Anal*. 2023, 15:1133-44. [10.1002/dta.3471](https://doi.org/10.1002/dta.3471)
119. Li X: In vitro toxicity testing of cigarette smoke based on the air-liquid interface exposure: a review. *Toxicol In Vitro*. 2016, 36:105-13. [10.1016/j.tiv.2016.07.019](https://doi.org/10.1016/j.tiv.2016.07.019)
120. Moore MM, Abraham I, Ballantyne M, et al.: Key challenges and recommendations for in vitro testing of tobacco products for regulatory applications: consideration of test materials and exposure parameters. *Altern Lab Anim*. 2023, 51:55-79. [10.1177/02611929221146536](https://doi.org/10.1177/02611929221146536)
121. Page MK, Goniewicz ML: New analytical method for quantifying flavoring chemicals of potential respiratory health risk concerns in e-cigarette liquids. *Front Chem*. 2021, 9:763940. [10.3389/fchem.2021.763940](https://doi.org/10.3389/fchem.2021.763940)
122. Committee on Toxicity of Chemicals in Food Consumer Products and the Environment: framework for risk assessment of flavouring compounds in electronic nicotine (and non-nicotine) delivery systems (E(N)NDS-e-cigarettes). (2020). Accessed: November 12, 2024: <https://cot.food.gov.uk/sites/default/files/2020-09/COT%20E%28N%29NDS%20statement%202020-04.pdf>.
123. Henningfield JE, Keenan RM: Nicotine delivery kinetics and abuse liability. *J Consult Clin Psychol*. 1993, 61:743-50. [10.1037//0022-006x.61.5.743](https://doi.org/10.1037//0022-006x.61.5.743)
124. Fearon IM: Human abuse liability assessment of e-cigarettes: why, what and how? . *Drug Test Anal*. 2023, 15:1211-21. [10.1002/dta.3251](https://doi.org/10.1002/dta.3251)
125. Vansickel A, Baxter S, Sherwood N, Kong M, Campbell L: Human abuse liability assessment of tobacco and nicotine products: approaches for meeting current regulatory recommendations. *Nicotine Tob Res*. 2022, 24:295-305. [10.1093/ntr/ntab183](https://doi.org/10.1093/ntr/ntab183)
126. Gades MS, Alcheva A, Riegelman AL, Hatsukami DK: The role of nicotine and flavor in the abuse potential and appeal of electronic cigarettes for adult current and former cigarette and electronic cigarette users: a systematic review. *Nicotine Tob Res*. 2022, 24:1332-43. [10.1093/ntr/ntac073](https://doi.org/10.1093/ntr/ntac073)
127. Fearon IM, Gilligan K, Seltzer RG, McKinney W: A randomised, crossover, clinical study to assess nicotine pharmacokinetics and subjective effects of the BIDI(®) stick ENDS compared with combustible cigarettes and a comparator ENDS in adult smokers. *Harm Reduct J*. 2022, 19:57. [10.1186/s12954-022-00638-0](https://doi.org/10.1186/s12954-022-00638-0)
128. Goldenson NI, Buchhalter AR, Augustson EM, Rubinstein ML, Henningfield JE: Abuse liability assessment of the JUUL system in four flavors relative to combustible cigarette, nicotine gum and a comparator electronic nicotine delivery system among adult smokers. *Drug Alcohol Depend*. 2020, 217:108395. [10.1016/j.drugalcdep.2020.108395](https://doi.org/10.1016/j.drugalcdep.2020.108395)
129. Keyser BM, Hong KS, DeLuca P, et al.: Part two: an unblinded, parallel, randomized study to assess nicotine pharmacokinetics of four Vuse Solo ENDS flavors in smokers. *Sci Rep*. 2023, 13:8894. [10.1038/s41598-023-35439-3](https://doi.org/10.1038/s41598-023-35439-3)
130. Leavens EL, Lambart LM, St Helen G, et al.: Menthol versus tobacco e-liquid flavor: Impact on acute subjective effects, puff patterns, and intentions for use among Black and White menthol smokers. *Addict Behav*. 2024, 155:108038. [10.1016/j.addbeh.2024.108038](https://doi.org/10.1016/j.addbeh.2024.108038)
131. Li W, Vargas-Rivera M, Eissenberg TE, Shihadeh A, Talih S, Maziak W: Effect of menthol/mint-flavored pods on young JUUL E-cigarette users' subjective experience, puffing behavior, and nicotine exposure: a pilot study. *Drug Alcohol Depend*. 2022, 237:109516. [10.1016/j.drugalcdep.2022.109516](https://doi.org/10.1016/j.drugalcdep.2022.109516)
132. Cobb CO, Lopez AA, Soule EK, et al.: Influence of electronic cigarette liquid flavors and nicotine concentration on subjective measures of abuse liability in young adult cigarette smokers. *Drug Alcohol Depend*. 2019, 203:27-34. [10.1016/j.drugalcdep.2019.05.024](https://doi.org/10.1016/j.drugalcdep.2019.05.024)
133. Hung M, Spencer A, Hon ES, et al.: E-cigarette addiction and harm perception: does initiation flavor choice matter?. *BMC Public Health*. 2022, 22:1780. [10.1186/s12889-022-14166-w](https://doi.org/10.1186/s12889-022-14166-w)
134. Douglas AE, Childers MG, Romm KF, Felicione NJ, Ozga JE, Blank MD: Device features and user behaviors as

- predictors of dependence among never-smoking electronic cigarette users: PATH Wave 4. *Addict Behav.* 2022, 125:107161. [10.1016/j.addbeh.2021.107161](https://doi.org/10.1016/j.addbeh.2021.107161)
135. Hoetger C, Bono RS, Nicksic NE, Barnes AJ, Cobb CO: Influence of electronic cigarette characteristics on susceptibility, perceptions, and abuse liability indices among combustible tobacco cigarette smokers and non-smokers. *Int J Environ Res Public Health.* 2019, 16:1825. [10.3390/ijerph16101825](https://doi.org/10.3390/ijerph16101825)
 136. Bono RS, Barnes AJ, Lester RC, Cobb CO: Effects of electronic cigarette liquid flavors and modified risk messages on perceptions and subjective effects of e-cigarettes. *Health Educ Behav.* 2019, 46:197-203. [10.1177/1090198118806965](https://doi.org/10.1177/1090198118806965)
 137. Bagdas D, Kebede N, Zepei AM, Harris L, Minanov K, Picciotto MR, Addy NA: Animal models to investigate the impact of flavors on nicotine addiction and dependence. *Curr Neuropharmacol.* 2022, 20:2175-201. [10.2174/1570159X20666220524120231](https://doi.org/10.2174/1570159X20666220524120231)
 138. Stiles MF, Campbell LR, Graff DW, Jones BA, Fant RV, Henningfield JE: Pharmacodynamic and pharmacokinetic assessment of electronic cigarettes, combustible cigarettes, and nicotine gum: implications for abuse liability. *Psychopharmacology (Berl).* 2017, 234:2643-55. [10.1007/s00213-017-4665-y](https://doi.org/10.1007/s00213-017-4665-y)
 139. Stiles MF, Campbell LR, Jin T, Graff DW, Fant RV, Henningfield JE: Assessment of the abuse liability of three menthol Vuse Solo electronic cigarettes relative to combustible cigarettes and nicotine gum. *Psychopharmacology (Berl).* 2018, 235:2077-86. [10.1007/s00213-018-4904-x](https://doi.org/10.1007/s00213-018-4904-x)
 140. Bremner MP, Campbell AM, Xia K, Tarran R, Girdler SS, Hendershot CS: Effects of nicotine content and preferred flavor on subjective responses to e-cigarettes: a randomized, placebo-controlled laboratory study. *Nicotine Tob Res.* 2024, 26:307-15. [10.1093/ntr/ntad143](https://doi.org/10.1093/ntr/ntad143)
 141. Do EK, O'Connor K, Kreslake JM, Friedrichsen SC, Vallone DM, Hair EC: Influence of flavors and nicotine concentration on nicotine dependence in adolescent and young adult e-cigarette users. *Subst Use Misuse.* 2022, 57:652-9. [10.1080/10826084.2022.2034876](https://doi.org/10.1080/10826084.2022.2034876)
 142. Yingst J, Midya V, White A, et al.: Effects of liquid nicotine concentration and flavour on the acceptability of electronic nicotine delivery systems (ENDS) among people who smoke participating in a randomised controlled trial to reduce cigarette consumption. *Tob Control.* 2024, [10.1136/tc-2023-058282](https://doi.org/10.1136/tc-2023-058282)
 143. Friedman AS, Warner KE: The e-cigarette flavor debate-promoting adolescent and adult welfare. *N Engl J Med.* 2022, 386:1581-3. [10.1056/NEJMp2119107](https://doi.org/10.1056/NEJMp2119107)
 144. Notley C, Gentry S, Cox S, et al.: Youth use of e-liquid flavours-a systematic review exploring patterns of use of e-liquid flavours and associations with continued vaping, tobacco smoking uptake or cessation. *Addiction.* 2022, 117:1258-72. [10.1111/add.15723](https://doi.org/10.1111/add.15723)
 145. Nollen NL, Leavens EL, Ahluwalia JS, Rice M, Mayo MS, Pulvers K: Menthol versus non-menthol flavouring and switching to e-cigarettes in Black and Latinx adult menthol combustible cigarette smokers: secondary analyses from a randomised clinical trial. *Tob Control.* 2023, 32:786-9. [10.1136/tobaccocontrol-2021-057180](https://doi.org/10.1136/tobaccocontrol-2021-057180)
 146. Lindson N, Butler AR, Liber A, et al.: An exploration of flavours in studies of e-cigarettes for smoking cessation: secondary analyses of a systematic review with meta-analyses. *Addiction.* 2023, 118:634-45. [10.1111/add.16091](https://doi.org/10.1111/add.16091)
 147. Bold K, O'Malley S, Krishnan-Sarin S, Morean M: E-cigarette use patterns, flavors, and device characteristics associated with quitting smoking among a U.S. sample of adults using e-cigarettes in a smoking cessation attempt. *Nicotine Tob Res.* 2023, 25:954-61. [10.1093/ntr/ntac276](https://doi.org/10.1093/ntr/ntac276)
 148. Xu Y, Goldenson NI, Prakash S, Augustson EM, Shiffman S: Randomized trial assessing the effect of the JUUL system on switching away from cigarettes and smoking reduction among U.S. adults who smoke cigarettes. *Exp Clin Psychopharmacol.* 2024, 32:3-15. [10.1037/pha0000698](https://doi.org/10.1037/pha0000698)
 149. Gravely S, Cummings KM, Hammond D, et al.: The association of e-cigarette flavors with satisfaction, enjoyment, and trying to quit or stay abstinent from smoking among regular adult vapers from Canada and the United States: findings from the 2018 ITC four country smoking and vaping survey. *Nicotine Tob Res.* 2020, 22:1831-41. [10.1093/ntr/ntaa095](https://doi.org/10.1093/ntr/ntaa095)
 150. Liber AC, Knoll M, Cadham CJ, et al.: The role of flavored electronic nicotine delivery systems in smoking cessation: a systematic review. *Drug Alcohol Depend Rep.* 2023, 7:100143. [10.1016/j.dadr.2023.100143](https://doi.org/10.1016/j.dadr.2023.100143)
 151. 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 U.S. large, nationally representative 2018-2019 survey. *Nicotine Tob Res.* 2023, 25:541-52. [10.1093/ntr/ntac241](https://doi.org/10.1093/ntr/ntac241)
 152. Farsalinos K, Russell C, Polosa R, Poulas K, Lagoumintzis G, Barbouni A: Patterns of flavored e-cigarette use among adult vapers in the USA: an online cross-sectional survey of 69,233 participants. *Harm Reduct J.* 2023, 20:147. [10.1186/s12954-023-00876-w](https://doi.org/10.1186/s12954-023-00876-w)
 153. Friedman AS, Xu S: Associations of flavored e-cigarette uptake with subsequent smoking initiation and cessation. *JAMA Netw Open.* 2020, 3:e203826. [10.1001/jamanetworkopen.2020.3826](https://doi.org/10.1001/jamanetworkopen.2020.3826)
 154. Glasser AM, Vojjala M, Cantrell J, Levy DT, Giovenco DP, Abrams D, Niaura R: Patterns of e-cigarette use and subsequent cigarette smoking cessation over 2 years (2013/2014-2015/2016) in the population assessment of tobacco and health study. *Nicotine Tob Res.* 2021, 23:669-77. [10.1093/ntr/ntaa182](https://doi.org/10.1093/ntr/ntaa182)
 155. Russell C, Haseen F, McKeganey N: Factors associated with past 30-day abstinence from cigarette smoking in a non-probabilistic sample of 15,456 adult established current smokers in the United States who used JUUL vapor products for three months. *Harm Reduct J.* 2019, 16:22. [10.1186/s12954-019-0293-7](https://doi.org/10.1186/s12954-019-0293-7)
 156. Russell C, Haseen F, McKeganey N: Factors associated with past 30-day abstinence from cigarette smoking in adult established smokers who used a JUUL vaporizer for 6 months. *Harm Reduct J.* 2019, 16:59. [10.1186/s12954-019-0331-5](https://doi.org/10.1186/s12954-019-0331-5)
 157. Harlow AF, Fetterman JL, Ross CS, Robertson RM, Bhatnagar A, Benjamin EJ, Stokes AC: Association of device type, flavours and vaping behaviour with tobacco product transitions among adult electronic cigarette users in the USA. *Tob Control.* 2022, 31:e10-7. [10.1136/tobaccocontrol-2020-055999](https://doi.org/10.1136/tobaccocontrol-2020-055999)
 158. Li L, Borland R, Cummings KM, 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, 23:1490-7. [10.1093/ntr/ntab033](https://doi.org/10.1093/ntr/ntab033)
 159. Rest EC, Brikmanis KN, Mermelstein RJ: Preferred flavors and tobacco use patterns in adult dual users of cigarettes and ENDS. *Addict Behav.* 2022, 125:107168. [10.1016/j.addbeh.2021.107168](https://doi.org/10.1016/j.addbeh.2021.107168)

160. Pokhrel P, Kawamoto CT, Mettias H, Elwir T, Herzog T: Predictors of discontinued e-cigarette use at one-year follow-up in a sample of young adults. *Int J Environ Res Public Health*. 2023, 20:4770. [10.3390/ijerph20064770](https://doi.org/10.3390/ijerph20064770)
161. Tackett AP, Dai HD, Han DH, et al.: Appeal of e-cigarette flavors: differences between never and ever use of combustible cigarettes. *Drug Alcohol Depend*. 2023, 246:109849. [10.1016/j.drugalcdep.2023.109849](https://doi.org/10.1016/j.drugalcdep.2023.109849)
162. Russell C, McKeganey N, Dickson T, Nides M: Changing patterns of first e-cigarette flavor used and current flavors used by 20,836 adult frequent e-cigarette users in the USA. *Harm Reduct J*. 2018, 15:33. [10.1186/s12954-018-0238-6](https://doi.org/10.1186/s12954-018-0238-6)
163. 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*. 2021, 30:108-10. [10.1136/tobaccocontrol-2019-055469](https://doi.org/10.1136/tobaccocontrol-2019-055469)
164. Xu K, Lee T, Reyes-Guzman CM, et al.: Use patterns of flavored non-cigarette tobacco products among US adults, 2010-2019. *Prev Med*. 2024, 180:107870. [10.1016/j.ypmed.2024.107870](https://doi.org/10.1016/j.ypmed.2024.107870)
165. Etter JF: An 8-year longitudinal study of long-term, continuous users of electronic cigarettes. *Addict Behav*. 2024, 149:107891. [10.1016/j.addbeh.2023.107891](https://doi.org/10.1016/j.addbeh.2023.107891)
166. Bello MS, Schulte AR, Ring CR, et al.: Effects of mint, menthol, and tobacco-flavored e-cigarettes on tobacco withdrawal symptoms in adults who smoke menthol cigarettes: a laboratory pilot study. *Drug Alcohol Depend*. 2024, 256:111110. [10.1016/j.drugalcdep.2024.111110](https://doi.org/10.1016/j.drugalcdep.2024.111110)
167. Bold KW, Buta E, Simon P, et al.: Examining the potential role of e-cigarettes to reduce health disparities associated with menthol cigarette use: characterizing e-cigarette use, flavors, and reasons for use among US adults smoking menthol cigarettes. *Drug Alcohol Depend*. 2022, 236:109475. [10.1016/j.drugalcdep.2022.109475](https://doi.org/10.1016/j.drugalcdep.2022.109475)
168. Goldenson NI, Augustson EM, Shiffman S: Differences in switching away from cigarettes and JUUL use characteristics among adult menthol and nonmenthol smokers who purchased the JUUL System. *Drug Alcohol Depend*. 2022, 231:109238. [10.1016/j.drugalcdep.2021.109238](https://doi.org/10.1016/j.drugalcdep.2021.109238)
169. Dyer ML, Khouja JN, Jackson AR, Havill MA, Dockrell MJ, Munafo MR, Attwood AS: Effects of electronic cigarette e-liquid flavouring on cigarette craving. *Tob Control*. 2023, 32:e3-9. [10.1136/tobaccocontrol-2021-056769](https://doi.org/10.1136/tobaccocontrol-2021-056769)
170. FDA authorizes marketing of tobacco- and menthol-flavored JUUL e-cigarette products. (2025). Accessed: July 22, 2025: <https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-four-menthol-flavored-e-cigarette-products>
171. Chaffee BW, Watkins SL, Glantz SA: Electronic cigarette use and progression from experimentation to established smoking. *Pediatrics*. 2018, 141:e20173594. [10.1542/peds.2017-3594](https://doi.org/10.1542/peds.2017-3594)
172. Chen G, Rahman S, Lutfy K: E-cigarettes may serve as a gateway to conventional cigarettes and other addictive drugs. *Adv Drug Alcohol Res*. 2023, 3:11345. [10.3389/adar.2023.11345](https://doi.org/10.3389/adar.2023.11345)
173. Martinelli T, Candel MJ, de Vries H, Talhout R, Knapen V, van Schayck CP, Nagelhout GE: Exploring the gateway hypothesis of e-cigarettes and tobacco: a prospective replication study among adolescents in the Netherlands and Flanders. *Tob Control*. 2023, 32:170-8. [10.1136/tobaccocontrol-2021-056528](https://doi.org/10.1136/tobaccocontrol-2021-056528)
174. Chan GC, Stjepanović D, Lim C, 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, 116:743-56. [10.1111/add.15246](https://doi.org/10.1111/add.15246)
175. Conde M, Tudor K, Begh R, et al.: Electronic cigarettes and subsequent use of cigarettes in young people: an evidence and gap map. *Addiction*. 2024, 119:1698-708. [10.1111/add.16583](https://doi.org/10.1111/add.16583)
176. Delnevo CD: e-Cigarette and cigarette use among youth: gateway or common liability? *JAMA Netw Open*. 2023, 6:e234890. [10.1001/jamanetworkopen.2023.4890](https://doi.org/10.1001/jamanetworkopen.2023.4890)
177. Fearon IM, Seltzer RG, Houser TL, et al.: Curiosity and intentions to use myblu e-cigarettes and an examination of the 'gateway' theory: data from cross-sectional nationally representative surveys. *Drug Test Anal*. 2023, 15:1257-69. [10.1002/dta.3450](https://doi.org/10.1002/dta.3450)
178. Hajat C, Stein E, Selya A, Polosa R: Analysis of common methodological flaws in the highest cited e-cigarette epidemiology research. *Intern Emerg Med*. 2022, 17:887-909. [10.1007/s11739-022-02967-1](https://doi.org/10.1007/s11739-022-02967-1)
179. Hall W, Chan G: The "gateway" effect of e-cigarettes may be explained by a genetic liability to risk-taking. *PLoS Med*. 2021, 18:e1003554. [10.1371/journal.pmed.1003554](https://doi.org/10.1371/journal.pmed.1003554)
180. Lee P, Fry J: Investigating gateway effects using the PATH study. *F1000Res*. 2019, 8:264. [10.12688/f1000research.18354.2](https://doi.org/10.12688/f1000research.18354.2)
181. Selya A: The "gateway" hypothesis: evaluation of evidence and alternative explanations. *Harm Reduct J*. 2024, 21:113. [10.1186/s12954-024-01034-6](https://doi.org/10.1186/s12954-024-01034-6)
182. Tao X, Zhang J, Meng Q, et al.: The potential health effects associated with electronic-cigarette. *Environ Res*. 2024, 245:118056. [10.1016/j.envres.2023.118056](https://doi.org/10.1016/j.envres.2023.118056)
183. Davis DR, Bold KW, Morean ME, et al.: Association of youth impulsivity and use of e-cigarette devices, flavors, and frequency of use. *Addict Behav*. 2022, 134:107386. [10.1016/j.addbeh.2022.107386](https://doi.org/10.1016/j.addbeh.2022.107386)
184. Martinelli TF, De Vries H, Talhout R, van Schayck OC, Nagelhout GE: Do e-cigarettes attract youths who are otherwise unlikely to use addictive substances? Cross-sectional analyses of Dutch and Flemish secondary school students. *Tob Prev Cessat*. 2021, 7:74. [10.18332/tpc/144181](https://doi.org/10.18332/tpc/144181)
185. Selya A, Gitchell JG: Commentary on Conde et al.: evidence and gap map offer an important opportunity for dialogue and refinement of the gateway hypothesis controversy. *Addiction*. 2024, 119:1709-10. [10.1111/add.16645](https://doi.org/10.1111/add.16645)
186. Bansal-Travers M, Rivard C, Silveira ML, et al.: Factors associated with changes in flavored tobacco products used: Findings from wave 2 and wave 3 (2014-2016) of the population assessment of tobacco and health (PATH) study. *Addict Behav*. 2022, 130:107290. [10.1016/j.addbeh.2022.107290](https://doi.org/10.1016/j.addbeh.2022.107290)
187. Steeger CM, Harlow AF, Barrington-Trimis JL, Simon P, Hill KG, Leventhal AM: Longitudinal associations between flavored tobacco use and tobacco product cessation in a national sample of adults. *Prev Med*. 2022, 161:107143. [10.1016/j.ypmed.2022.107143](https://doi.org/10.1016/j.ypmed.2022.107143)
188. Chaffee BW, Couch ET, Wilkinson ML, et al.: Flavors increase adolescents' willingness to try nicotine and cannabis vape products. *Drug Alcohol Depend*. 2023, 246:109834. [10.1016/j.drugalcdep.2023.109834](https://doi.org/10.1016/j.drugalcdep.2023.109834)
189. Results from the annual National Youth Tobacco Survey. (2025). Accessed: July 22, 2025:

- https://www.fda.gov/tobacco-products/youth-and-tobacco/results-annual-national-youth-tobacco-survey.
190. Gentzke AS, Wang TW, Cornelius M, et al.: Tobacco product use and associated factors among middle and high school students-National Youth Tobacco Survey, United States. *MMWR Surveill Summ*. 2022, 71:1-29. [10.15585/mmwr.ss7105a1](https://doi.org/10.15585/mmwr.ss7105a1)
191. Xiao C, Heley K, Kennedy RD, Lagasse L, Moran MB: Sociodemographic differences in reasons for ENDS use among US youth within Wave 2 of the PATH study. *Tob Induc Dis*. 2019, 17:4. [10.18332/tid/99879](https://doi.org/10.18332/tid/99879)
192. Lindpere V, Winickoff JP, Khan AS, Dong J, Michaud TL, Liu J, Dai HD: Reasons for e-cigarette use, vaping patterns, and cessation behaviors among US adolescents. *Nicotine Tob Res*. 2023, 25:975-82. [10.1093/ntr/ntac278](https://doi.org/10.1093/ntr/ntac278)
193. Patrick ME, Miech RA, Carlier C, O'Malley PM, Johnston LD, Schulenberg JE: Self-reported reasons for vaping among 8th, 10th, and 12th graders in the US: nationally-representative results. *Drug Alcohol Depend*. 2016, 165:275-8. [10.1016/j.drugalcdep.2016.05.017](https://doi.org/10.1016/j.drugalcdep.2016.05.017)
194. Merz L, Puhon MA, Serra-Burriel M: A discrete choice experiment on price and flavour effects on the appeal of nicotine products: a pilot study among young adults in Switzerland. *Swiss Med Wkly*. 2023, 154:3733. [10.57187/s.3733](https://doi.org/10.57187/s.3733)
195. Satchell T, Diaz MC, Stephens D, Bertrand A, Schillo BA, Whitsel LP: The impact of two state-level approaches to restricting the sale of flavored tobacco products. *BMC Public Health*. 2022, 22:1799. [10.1186/s12889-022-14172-y](https://doi.org/10.1186/s12889-022-14172-y)
196. Olson LT, Coats EM, Rogers T, et al.: Youth Tobacco use before and after local sales restrictions on flavored and menthol tobacco products in Minnesota. *J Adolesc Health*. 2022, 70:978-84. [10.1016/j.jadohealth.2022.01.129](https://doi.org/10.1016/j.jadohealth.2022.01.129)
197. Dunbar M, Setodji CM, Martino SC, Jensen D, Li R, Bialas A, Shadel WG: An experimental evaluation of the effects of banning the sale of flavored tobacco products on adolescents' and young adults' future nicotine vaping intentions. *Addict Behav*. 2023, 145:107784. [10.1016/j.addbeh.2023.107784](https://doi.org/10.1016/j.addbeh.2023.107784)
198. Tam J, Jimenez-Mendoza E, Buckell J, Sindelar J, Meza R: Responses to real-world and hypothetical e-cigarette flavor bans among US Young adults who use flavored e-cigarettes. *Nicotine Tob Res*. 2024, 26:1113-7. [10.1093/ntr/ntad258](https://doi.org/10.1093/ntr/ntad258)
199. Enforcement priorities for electronic nicotine delivery systems (ENDS) and other deemed products on the market without premarket authorization (revised): guidance for industry. (2020). Accessed: November 12, 2024: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-d...>
200. Borowiecki M, Kim Y, Emery S: A patchy prohibition: product and flavor substitution after the Food and Drug Administration's prioritized enforcement policy on flavored e-cigarettes. *Nicotine Tob Res*. 2024, 26:527-35. [10.1093/ntr/ntad212](https://doi.org/10.1093/ntr/ntad212)
201. Selya A, Shiffman S, Hannon MJ: Youth patterns of use of electronic nicotine delivery systems (ENDS), population assessment of tobacco and health (PATH) waves 4-5.5. *Addict Behav*. 2023, 145:107783. [10.1016/j.addbeh.2023.107783](https://doi.org/10.1016/j.addbeh.2023.107783)
202. Kasza KA, Hammond D, Reid JL, Rivard C, Hyland A: Youth use of e-cigarette flavor and device combinations and brands before vs after FDA enforcement. *JAMA Netw Open*. 2023, 6:e2328805. [10.1001/jamanetworkopen.2023.28805](https://doi.org/10.1001/jamanetworkopen.2023.28805)
203. Dai HD, Michaud T, Guenzel N, Morgan M, Cohen SM: Biomarker assessment of nicotine exposure among adolescent e-cigarette users: 2018-2019. *Pediatrics*. 2024, 153:e2023062424. [10.1542/peds.2023-062424](https://doi.org/10.1542/peds.2023-062424)
204. Ruokolainen O, Ollila H, Karjalainen K: Correlates of e-cigarette use before and after comprehensive regulatory changes and e-liquid flavour ban among general population. *Drug Alcohol Rev*. 2022, 41:1174-83. [10.1111/dar.13435](https://doi.org/10.1111/dar.13435)
205. Shamblen SR, Abadi MH, Thompson KT, García-Ramírez G, Richard BO: Changes in the patterns and characteristics of youth ENDS use over time. *Int J Environ Res Public Health*. 2022, 19:8120. [10.3390/ijerph19138120](https://doi.org/10.3390/ijerph19138120)
206. Jongenelis MI: E-cigarette product preferences of Australian adolescent and adult users: a 2022 study . *BMC Public Health*. 2023, 23:220. [10.1186/s12889-023-15142-8](https://doi.org/10.1186/s12889-023-15142-8)
207. Donaldson CD, Couch ET, Hoeft KS, et al.: Flavored tobacco and nicotine use among California Adolescents: preferences by use experience and survey format effects. *J Adolesc Health*. 2023, 73:753-60. [10.1016/j.jadohealth.2023.05.012](https://doi.org/10.1016/j.jadohealth.2023.05.012)
208. Kaplan B, Hardesty JJ, Welding K, Breland AB, Eissenberg T, Cohen JE: Electronic nicotine delivery system flavor use over time by age group in the US: a longitudinal analysis. *Tob Induc Dis*. 2023, 21:67. [10.18332/tid/162365](https://doi.org/10.18332/tid/162365)
209. Cadham CJ, Liber AC, Sánchez-Romero LM, Issabakhsh M, Warner KE, Meza R, Levy DT: The actual and anticipated effects of restrictions on flavoured electronic nicotine delivery systems: a scoping review. *BMC Public Health*. 2022, 22:2128. [10.1186/s12889-022-14440-x](https://doi.org/10.1186/s12889-022-14440-x)
210. Cotti C, Courtemanche C, Liang Y, Maclean JC, Nesson E, Sabia JJ: The effect of e-cigarette flavor bans on tobacco use. *J Health Econ*. 2025, 102:103013. [10.1016/j.jhealeco.2025.103013](https://doi.org/10.1016/j.jhealeco.2025.103013)
211. King BA: Flavors remain a major driver of youth e-cigarette use . *Am J Public Health*. 2022, 112:999-1000. [10.2105/AJPH.2022.306895](https://doi.org/10.2105/AJPH.2022.306895)
212. Xu Y, Jiang L, Prakash S, Chen T: The impact of banning electronic nicotine delivery systems on combustible cigarette sales: evidence from US state-level policies. *Value Health*. 2022, 25:1352-9. [10.1016/j.jval.2021.12.006](https://doi.org/10.1016/j.jval.2021.12.006)
213. Schneller LM, Kasza KA, Hammond D, Bansal-Travers M, O'Connor R, Hyland A: E-cigarette and tobacco product use among NYS youth before and after a state-wide vaping flavour restriction policy, 2020-2021. *Tob Control*. 2022, 31:s161-6. [10.1136/tobaccocontrol-2022-057450](https://doi.org/10.1136/tobaccocontrol-2022-057450)
214. Freitas-Lemos R, Stein JS, Tegge AN, et al.: Illegal experimental tobacco marketplace ii: effects of vaping product bans-findings from the 2020 International Tobacco Control Project. *Tob Control*. 2022, 31:s214-22. [10.1136/tc-2022-057515](https://doi.org/10.1136/tc-2022-057515)
215. Gravely S, Smith DM, Liber AC, et al.: Responses to potential nicotine vaping product flavor restrictions among regular vapers using non-tobacco flavors: findings from the 2020 ITC Smoking and Vaping Survey in

- Canada, England and the United States. *Addict Behav.* 2022, 125:107152. [10.1016/j.addbeh.2021.107152](#)
216. Yang Y, Lindblom EN, Ward KD, Salloum RG: The impact of flavored e-cigarette bans on e-cigarette use in three US states. *medRxiv.* 2023, [10.1101/2023.05.19.23290249](#)
217. Yang Y, Lindblom EN, Ward KD, Salloum RG: Reactions to hypothetical flavor bans among current users of flavored e-cigarettes. *Transl Behav Med.* 2023, 13:533-8. [10.1093/tbm/ibac109](#)
218. Yang Y, Lindblom EN, Ward KD, Salloum RG: Would banning menthol cigarettes, flavored cigars, and flavored e-cigarettes prompt users to seek illicit channels for obtaining them in the United States?. *Prev Med.* 2024, 183:107954. [10.1016/j.ypmed.2024.107954](#)
219. Yan D, Wang Z, Laestadius L, et al.: A systematic review for the impacts of global approaches to regulating electronic nicotine products. *J Glob Health.* 2023, 13:04076. [10.7189/jogh.13.04076](#)
220. Donaldson SI, Beard TA, Colonna R, Andersen-Rodgers E, Wipfli HL, Ribisl KM, Allem JP: Online purchase attempts of flavored e-cigarettes to minors in California before and after Senate Bill 793. *JAMA Netw Open.* 2023, 6:e2348749. [10.1001/jamanetworkopen.2023.48749](#)
221. Weng X, Song CY, Liu K, Wu YS, Lee JJ, Guo N, Wang MP: Perceptions of and responses of young adults who use e-cigarettes to flavour bans in China: a qualitative study. *Tob Control.* 2024, [10.1136/tc-2023-058312](#)
222. Khouja JN, Dyer ML, Havill MA, Dockrell MJ, Munafò MR, Attwood AS: Exploring the opinions and potential impact of unflavoured e-liquid on smoking cessation among people who smoke and smoking relapse among people who previously smoked and now use e-cigarettes: findings from a UK-based mixed methods study. *Harm Reduct J.* 2024, 21:90. [10.1186/s12954-024-01003-z](#)
223. Bold KW, Krishnan-Sarin S, O'Malley S, Morean ME: Examining associations of e-cigarette flavour restrictions with e-cigarette use and success quitting smoking among US adults. *Tob Control.* 2022, 31:s184-6. [10.1136/tobaccocontrol-2022-057458](#)
224. Silver N, Kucheralapaty P, Kostygina G, Tran H, Feng M, Emery S, Schillo B: Discussions of flavored ENDS sales restrictions: themes related to circumventing policies on Reddit. *Int J Environ Res Public Health.* 2022, 19:7668. [10.3390/ijerph19137668](#)
225. Talih S, Karaoghlanian N, Salman R, et al.: Effects of aftermarket electronic cigarette pods on device power output and nicotine, carbonyl, and ROS emissions. *Chem Res Toxicol.* 2023, 36:1930-7. [10.1021/acs.chemrestox.3c00213](#)
226. Schillo B, Seaman EL, Cuccia A, Ali FR, Cordova J, Mills S, Kreslake J: Early evidence of flavored tobacco product restrictions in Massachusetts and New York State. *Tob Induc Dis.* 2023, 21:140. [10.18332/tid/172000](#)
227. Li D, Ossip DJ, Bansal-Travers M, Xie Z: Impact of the FDA flavour enforcement policy on flavoured electronic cigarette use behaviour changes. *Tob Control.* 2022, 31:s176-83. [10.1136/tc-2022-057492](#)
228. Kasza KA, Rivard C, Seo YS, et al.: Use of electronic nicotine delivery systems or cigarette smoking after US Food and Drug Administration-prioritized enforcement against fruit-flavored cartridges. *JAMA Netw Open.* 2023, 6:e2321109. [10.1001/jamanetworkopen.2023.21109](#)
229. Gravely S, Meng G, Hammond D, et al.: Electronic nicotine delivery systems (ENDS) flavours and devices used by adults before and after the 2020 US FDA ENDS enforcement priority: findings from the 2018 and 2020 US ITC Smoking and Vaping Surveys. *Tob Control.* 2022, 31:s167-75. [10.1136/tobaccocontrol-2022-057445](#)
230. Romm KF, Henriksen L, Huang J, et al.: Impact of existing and potential e-cigarette flavor restrictions on e-cigarette use among young adult e-cigarette users in 6 US metropolitan areas. *Prev Med Rep.* 2022, 28:101901. [10.1016/j.pmedr.2022.101901](#)
231. Hammond D, Reid JL, Burkhalter R, et al.: E-cigarette flavors, devices, and brands used by youths before and after partial flavor restrictions in the United States: Canada, England, and the United States, 2017–2020. *Am J Public Health.* 2022, 112:1014-24. [10.2105/AJPH.2022.306780](#)
232. El-Hellani A, Soule EK, Daoud M, et al.: Assessing toxicant emissions from e-liquids with DIY additives used in response to a potential flavour ban in e-cigarettes. *Tob Control.* 2022, 31:s245-8. [10.1136/tc-2022-057505](#)
233. McCauley DM, Gaiha SM, Lempert LK, Halpern-Felsher B: Adolescents, young adults, and adults continue to use e-cigarette devices and flavors two years after FDA discretionary enforcement. *Int J Environ Res Public Health.* 2022, 19:8747. [10.3390/ijerph19148747](#)
234. Brown EM, Rogers T, Spinks JG, Gammon D, Nonnemaker J, Farrelly MC: Changes in sales of vaping products and cigarettes associated with the New York state flavored vaping product sales restriction. *Nicotine Tob Res.* 2024, 26:135-41. [10.1093/ntr/ntad158](#)
235. Cheng HG, Lizhnyak PN, Knight NA, Vansickel AR, Largo EG: Youth susceptibility to tobacco use: is it general or specific?. *BMC Public Health.* 2021, 21:1913. [10.1186/s12889-021-11956-6](#)
236. Siegel M, Katchmar A: Effect of flavored e-cigarette bans in the United States: what does the evidence show?. *Prev Med.* 2022, 165:107063. [10.1016/j.ypmed.2022.107063](#)
237. Balfour DJ, Benowitz NL, Colby SM, et al.: Balancing consideration of the risks and benefits of e-cigarettes. *Am J Public Health.* 2021, 111:1661-72. [10.2105/AJPH.2021.306416](#)
238. Ball J, Katoa L, Hoek J: Specialist vape store audit reveals poor compliance with new e-cigarette regulations. *N Z Med J.* 2024, 137:72-85. [10.26635/6965.6507](#)