Nicotine policy evidence briefings

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1 Nicotine for policymakers

1.1 Key concepts

- Nicotine is the primary psychoactive agent in tobacco and alternative nicotine delivery systems (ANDS - vapes, pouches, heated and smokeless tobacco). It is a stimulant that produces subjective feelings of pleasure, reduces stress and anxiety and improves aspects of cognitive function. Its use can make people feel better and feel as though they function better. Nicotine does not cause drug effects like intoxication, oblivion, hallucinations, or violence. It may also have therapeutic benefits, showing promise for some inflammatory diseases, ADHD, and Parkinson's Disease, among others.
- The subjectively perceived positive aspects of nicotine use largely explain why people use nicotine. However, these rewards can consolidate into a physical dependence with withdrawal and craving, reinforcing nicotine use. Nicotine may provide immediate relief from stress, but its overall impact may increase stress levels physiologically and psychologically due to the cycle of use, relief, and withdrawal.
- Nicotine use is disproportionately prevalent in poorer, marginalised or otherwise disadvantaged sub-populations. Nicotine probably interacts with elevated levels of stress in these groups.
- There is no simple answer to the question, *Is nicotine addictive*? It depends on the characteristics of the user, the route of administration, and the definition of "addiction", which is an imprecise and stigmatising term. *Addiction* usually refers to compulsive behaviour *that persists in the face of significant harm caused to the user*. Cigarette smoking meets this definition, but ANDS use may not. It is better to think of physical dependence or addiction as an emergent constellation of behaviours with consequences for the individual rather than an intrinsic property of a molecule, device or liquid.
- Nicotine is not a major direct cause of smoking-related disease. Dozens of other hazardous and potentially hazardous chemicals form through combustion and constitute the particles and toxic gases of inhaled tobacco smoke. These are overwhelmingly the causes of smoking-related diseases.
- Nicotine in isolation is much less harmful than smoking but not entirely harmless. It does not cause cancer, heart disease or lung illnesses but may increase risks in people with preexisting cardiovascular conditions and can promote tumour growth in animals. Smoking causes poor pregnancy outcomes, but nicotine is unlikely to be the primary cause. Nicotine may contribute to adverse outcomes in pregnancy, and nicotine-induced constriction of blood vessels may aggravate peripheral arterial disease.
- Nicotine is the primary reason people use tobacco or ANDS, and the use of these products should be understood as *nicotine-seeking behaviour*. Within broad limits, the user, not the product, determines the dose. Users generally regulate their intake to maintain desired levels of nicotine in the body. Regulatory schemes that try to control nicotine intake through restrictions on product design are unlikely to succeed, as users titrate their nicotine intake to preferred levels, resulting in "compensation" (using the product more intensively) or switching nicotine products if compensation is not possible.
- As with other psychoactive substances – alcohol, caffeine, cannabis, etc. - the demand for nicotine is unlikely to disappear even with punitive laws. Demand is driven primarily by the real or perceived benefits experienced by those using it and, for some people, the effort required to stop.

- The main deterrent to nicotine use, the multiple health and welfare harms arising from *smoking*, is significantly reduced in smoke-free alternative nicotine delivery systems. The secondary deterrent is the effect of policies designed to control *smoking*, such as high taxes. For substantially safer alternatives, this deterrent should also significantly diminish. It is possible, therefore, that overall societal nicotine use will increase, though the total harms associated with using nicotine will substantially decline.

1.2 What is nicotine?

What is nicotine? Nicotine[1] is a naturally occurring alkaloid present in the tobacco plant, in which it functions as a botanical insecticide. It can also be made synthetically. Nicotine is also present in tea, peppers, tomatoes, potatoes, cauliflower and eggplant,[2] though dietary exposure is far lower than through tobacco use and does not have a noticeable psychoactive effect.[3] Humans have deliberately consumed nicotine, whether through pipes, cigars, chewing, snuffing, or cigarette smoking, for over 12,000 years.[4] At the levels intentionally consumed by tobacco or ANDS users, nicotine is not poisonous. For humans, it functions as a psychoactive substance[5], working as both a stimulant and an anxiolytic (i.e. with calming effects on anxiety). Unlike many drugs of abuse, nicotine does not lead to acute and often harmful effects such as intoxication, violence, oblivion, paranoia, disorientation, loss of control, or hallucinations. However, nicotine use does provide psychoactive reward and reinforcing effects. Tolerance to initial aversive effects in naive users soon develops, which frequently leads to physical dependence and unpleasant withdrawal symptoms following abstinence.

How does nicotine work as a drug? When tobacco is smoked, sucked or chewed, the nicotine is released from the tobacco or ANDS product and enters the blood via the oral cavity, airways, lungs, or nasal passages, then makes its way to the brain via the arterial circulation. Nicotine binds to receptors in the brain to release several neurotransmitters, most notably dopamine[6] and adrenaline.[7] These interactions produce feelings of pleasure,[8] increased alertness,[9] improved cognitive function,[10] [11] and mood regulation, such as reduced stress and anxiety.[12] [13] For example, research conducted through the Intramural Research Program of the U.S. National Institute on Drug Abuse concluded: [14]

> *We found significant positive effects of nicotine or smoking on six domains: fine motor, alerting, attention-accuracy and response time (RT), orienting attention-RT, short-term episodic memory-accuracy, and working memory-RT.*

This range of subjectively positive effects is important in explaining why there is *demand* for nicotine – for some people, the use of nicotine can make them feel or function better. That observation should not be understood as an endorsement of nicotine use or a recommendation, but it is an *explanation*. This range of effects also forms the basis of reward and reinforcement that lead some users to develop physical dependence and adverse withdrawal symptoms when they stop.[15] [16]

Therapeutic effects of nicotine. In some circumstances, nicotine can have anti-inflammatory or stabilising effects with potential therapeutic benefits in preventing, treating or relieving the symptoms of certain diseases. These may include Parkinson's,[17] [18] ulcerative colitis,[19] [20] ADHD,[21] [22] [23] [24] and psychosis.[25] [26] [27] [28] [29] Smokers were significantly less likely to contract COVID-19, suggesting a possible protective effect.[30] [31] However, it is unclear if this was attributable to nicotine, some other component of smoke, or a statistical artefact. Much of the discourse on therapeutic effects has been cautiously expressed because of the justifiable concern that it might encourage smoking, and the research is often suggestive, not conclusive, or has an ambiguous direction of causation. Tobacco and ANDS are not medications and should not be used to treat these conditions as an alternative to medical supervision. However, some people may be

unconsciously using nicotine to self-medicate or ease symptoms arising from these conditions. This is an *explanation*, not a recommendation.

Who uses nicotine and why? Tobacco or nicotine use is not uniformly distributed across the whole population at any given age. It is driven by various genetic and psychosocial factors (characteristics of the individual, their family, and social circumstances).[32] A 2016 study identified ninety-eight distinct predictors for smoking onset:[33]

> *An increased risk of smoking onset was consistently (i.e., in four or more studies) associated with increased age/grade, lower SES, poor academic performance, sensation seeking or rebelliousness, intention to smoke in the future, receptivity to tobacco promotion efforts, susceptibility to smoking, family members' smoking, having friends who smoke, and exposure to films.*

A 2019 study considered 13 reasons for e-cigarette use and formed these into two main factors: "alternative to cigarettes" and "larger social environment".[34] Nicotine use is disproportionately prevalent among those experiencing some form of stress, disadvantage, minority status, other forms of marginalisation, or challenging history such as neglect or abuse.[35] [36] [37] [38] [39] [40] [41] The sustained use of nicotine in these populations may be a response to the stress experienced as a result of these disparities.[42] Over time, the brain adapts to nicotine use, requiring higher doses to achieve the same calming effect, which can lead to dependence. Additionally, the withdrawal symptoms associated with nicotine, such as craving, irritability, anxiety, and difficulty concentrating, further contribute to stress when nicotine levels drop in the bloodstream. Thus, while nicotine may provide immediate relief from stress, its overall impact may increase stress levels physiologically and psychologically due to the cycle of dependence and withdrawal. However, some people remain light or non-daily nicotine users and use primarily for positive reinforcement without experiencing withdrawal symptoms.

1.3 Nicotine and addiction

Is nicotine addictive? Not always. Nicotine addiction is a *behaviour with adverse consequences for the individual* rather than a universal property of the nicotine molecule. Most of what we know about nicotine comes from studies of *smoking* behaviours. In the case of smoking, there is a clear rationale for quitting to avoid significant health and welfare detriments. Yet, many people still struggle to quit, which creates the basis for public health intervention. However, when there is much less harm, the motivation to quit is likely lower, and the consequences of not quitting are less. So, definitions of addiction tend to stress *compulsive and harmful use*, and some care is required in defining terms like addiction (see below). This is why we treat caffeine and our need for morning coffee differently – we may be dependent on it, but it does not do much harm.[43] Whether nicotine is *addictive* depends on the definition used, the characteristics of the user (e.g. genetics, stress or other factors that increase the intensity of use), the user's pattern of use, and the method of nicotine administration.

Definitions of addiction. Whether nicotine is "addictive" also depends, crucially, on the chosen definition of the term "addiction". This is a loaded, stigmatising word and is often used imprecisely.[44] Most formal definitions of addiction not only require dependent and compulsive use but also serious net harm to the user.[45] For example, the definition of addiction used in the Addiction Ontology is as follows:[46]

> *A mental disposition towards repeated episodes of abnormally high levels of motivation to engage in a behaviour, acquired as a result of engaging in the behaviour, where the behaviour results in risk or occurrence of serious net harm.*

The U.S. National Institute of Drug Use (NIDA) also includes adverse consequences within its definition:[47] [48]

> *Addiction is a chronic disease characterised by drug seeking and use that is compulsive, or difficult to control, despite harmful consequences.*

The American Psychiatric Association prefers the more clinically precise title substance use disorder (SUD) rather than addiction, though this terminology also stresses compulsive use despite harm.[49]

> *Substance use disorder (SUD) is a complex condition in which there is uncontrolled use of a substance despite harmful consequences. People with SUD have an intense focus--sometimes called an addiction--on using a certain substance(s) such as alcohol, tobacco, or other psychoactive substances, to the point where their ability to function in day-to-day life becomes impaired.*

Substance use disorder. In professional practice, the term "addiction" has been superseded by the more nuanced concept of substance use disorder, which considers different dimensions of harm. The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) refers to substance use disorder (SUD), including Tobacco Use Disorder.[50] Substance use disorders are assessed against eleven criteria,[51] which cover four broad categories of problem: impaired control, social problems, risky use, and physical dependence. Substance use disorder is graded from mild to severe according to the number of criteria met. Severe substance use disorder, involving six or more criteria, is often seen as a clinical equivalent to the more colloquial term addiction.[52] [53] Nicotine use does not generally cause impaired control or social problems, and its riskiness depends heavily on the type of product used. However, nicotine does have the potential to cause physical dependence.

Physical dependence. It is more appropriate to describe sustained nicotine use *without* severe harmful effects (e.g., via low-risk alternatives to cigarettes) as potentially causing *physical dependence,* maintained by the adverse effects of withdrawal. The AddictO ontology defines substance dependence as follows:[54]

> *…impaired functioning following reduction or termination of use of a psychoactive substance as a result of long-term physiological adaptation to that substance.*

Nicotine dependence is defined informally in this ontology as "*A tendency to experience adverse effects from reduction or termination of nicotine intake*".[55] This definition of physical dependence contrasts with an "addiction", which stresses serious harm to the user through compulsive ongoing use.

The public health significance of harm. Unless there is significant harm to the user, their family, bystanders or wider society, the case for a public health intervention to address any form of substance use or compulsive behaviour is greatly diminished. In its definition of "addiction", the Addiction Ontology provides the following rationale:

> *This entity focuses on abnormal motivation to engage in a behaviour and includes serious net harm as a feature. The reason is to limit the class to things that merit a treatment and public health response.*

This insight should drive resources to *smoking cessation* and recognition that *vaping* cessation is unlikely to be a cost-effective use of public or non-profit funds, given the respective harms. All healthcare systems ration in some way, and spending the marginal dollar on smoking cessation or other interventions with better cost-effectiveness in terms of health outcomes per dollar spent will always be better.

Other reinforcers. Though nicotine is the essential psychoactive agent in cigarette smoke, there are others, including, for example, monoamine oxidase inhibitors (MAOIs) found in smoke. MAOIs inhibit the

action of the enzyme monoamine oxidase, which breaks down dopamine and other monoamines such as serotonin, causing them to build up and persist for longer, enhancing the psychoactive effects of nicotine.[56] This may be an important consideration in explaining differences in the dependence-forming potential of different tobacco and nicotine products. Reinforcement is not just chemical; it may be driven by behavioural rituals and triggered by cues[57] [58] or marketing.[59] [60]

Nicotine and abuse liability – a regulator's dilemma. Nicotine use tends to be more strongly reinforcing when the levels of nicotine rise rapidly and peak at a high level in the brain, creating a rapid pike or "bolus". The time course of nicotine as it is absorbed in the body, carried to the brain, and then metabolised and eliminated is known as *pharmacokinetics*, often abbreviated to "PK". The PK profile is primarily determined by three interacting factors:

(1) the route of administration (e.g., via inhalation, absorption in the mouth, or through the skin),
(2) characteristics of the product or device (e.g., nicotine concentration, particle size, pH)
(3) individual user characteristics (e.g., puffing rate and depth for inhaled products or use time for oral products, which may reflect the strength of their drive to use nicotine).

Abuse liability is a concept used by regulators to address the concern that users could become dependent on a therapeutic product. For nicotine, PK studies are often used to characterise abuse liability. However, this can present a dilemma when assessing consumer-based reduced-risk alternatives to cigarettes, such as vapes or pouches. The PK profile may also reflect their efficacy as cigarette replacements, matching the PK profile experienced as a reward by smokers. Pharmaceutical regulators have generally required manufacturers of nicotine replacement therapies (NRT) to keep abuse liability low, but this has likely made NRT less effective for smoking cessation.[61] [62] [63]

1.4 The challenge of regulating nicotine exposure

Users control their nicotine exposure, and this may lead to counterintuitive effects. It is not a surprise that alcohol drinkers control the amount of alcohol they consume, drinking larger volumes of beer and smaller volumes of whiskey for the same alcohol intake. Drinkers can do this by deeper and more frequent gulps of beer and by sipping whiskey. To facilitate this, beer is served in larger glasses and usually without a straw to constrict the flow. There are equivalents for nicotine: users control or "titrate" their nicotine intake by varying their puff depth and frequency (known as "puff topography") and by their choice of product to facilitate the exposure they want without excessive effort. This creates an effect known as "compensation", in which users adjust their behaviour in response to changes in the availability of nicotine.[64] [65] It means, for example, that reducing nicotine strength may cause a greater intake of vapour aerosol to achieve the same nicotine exposure.

Attempts to measure and regulate nicotine delivery. Several ways of characterising and regulating nicotine exposure have been proposed. As discussed below, these may be ineffective and may be misleading or counterproductive.

- **Nicotine yield**. This approach was common until the 2000s, when it became no longer possible to ignore its flaws. Nicotine yield is a measure of the nicotine that is emitted from the product during use under standardised smoking regimes using a smoking machine.[66] The nicotine yield is the mass of nicotine trapped on a filter pad, reported in mg per cigarette, typically 0.1-3.0mg per stick.[67] The challenge is that people adjust their smoking behaviour ("compensation") to obtain the nicotine they want ("titration"),[68] [69] and this varies greatly between individuals and by race,[70] genetics,[71] and deprivation.[72] Further, tobacco companies designed cigarettes that would show low tar and nicotine yields on machines but made it easy for users to compensate, for example, by including filter

ventilation holes that the user could easily block. This led to falsely reassuring "light" and "mild" brands, which exploited smokers' concerns about health without doing anything to reduce risk.[73 74]

- **Nicotine content in tobacco**. There are proposals to control the addictiveness of cigarettes or tobacco by limiting the concentration of nicotine present in the tobacco itself.[75 76] Denicotinisation is feasible and can be achieved through genetic modification or by chemically lowering the nicotine to a "sub-addictive" level or levels that are too low for compensation to work. The primary health question is how users will respond to mandated low-nicotine standards: will they quit smoking, smoke very low-nicotine cigarettes, switch to safer nicotine products, access illicit nicotine cigarettes, or find workarounds? Removing most of the nicotine from cigarettes approximates to a ban on cigarettes, as most people use them. A deliberately induced *de facto* ban would present a wide range of challenges that regulators and lawmakers must consider carefully. These include public acceptability, especially among those affected, farming and supply chain disruption, enforcement, corruption and community effects, illicit trade and tax revenues. All policies to reduce smoking affect a range of interests over time, but they differ in the extent and pace of disruption.
- **Nicotine strength of e-liquids**. The European Union sets a maximum nicotine concentration for e-liquids of 20mg/ml (about 2% by volume),[77] and this regulatory approach has been used in other jurisdictions.[78] The issue is both acceptability to consumers and user compensation; people consume larger volumes of weaker liquids to achieve their preferred nicotine dose. However, that may increase exposure to contaminants and toxic products of thermal decomposition, but without doing much to change their nicotine exposure [79 80]
- **Nicotine flux.** This measures the flow rate of nicotine emitted from a product (e.g., micrograms of nicotine per second of puffing).[81 82] While intended as a proxy for nicotine delivery, parameters defining nicotine flux do not capture all factors that account for nicotine delivery to the user. The main challenge is that the *user* controls this flow by varying the puff frequency, depth and length. Proponents of this method propose to limit the effect of user behaviour by making ENDS devices function as metered-dose products, delivering a fixed or limited dose of nicotine.[83] However, in practice, the idea is unworkable and ineffective. If the dose is too low or the use of the product is frustrating or unsatisfying, users will seek alternatives, including cigarettes or vaping products that can provide the nicotine dose the user wants.
- **Nicotine "abuse liability".** This would involve placing limits on the spike ("bolus") of nicotine exposure in the brain–the peak level "C_{max}" and time to reach the peak "T_{max}" or the ratio C_{max}/T_{max}.[84] Again, these are mainly under the user's control, though they can be subject to device constraints. For low-risk products, there is ambiguity about the regulatory purpose. Should it be to reduce abuse liability to stop the products from causing dependence but risk that they will not be used as alternatives to smoking? Or should it be to match the PK profile of a cigarette and thereby provide a "satisfying" and viable, low-risk alternative to smoking that works for people who smoke but with a higher risk of dependence?

The overarching point is that trying to control nicotine use by limiting the devices or liquids through which it is consumed is likely to fail. Users will ultimately access the nicotine they want. It would be like trying to control alcohol use by limiting the size of wine glasses or making people drink through a straw.

1.5 Health effects of nicotine

Health effects of nicotine. It is now commonplace to cite Michael Russell's 1976 insight, "*People smoke for the nicotine but die from the tar*",[85] to convey the idea that it is not the nicotine that is the primary direct cause of disease and death arising from smoking. It is the reason people smoke and, as a result, expose themselves to thousands of toxicants in cigarette smoke. That insight still holds true today. U.S.

Food and Drug Administration leadership reiterated this point in 2017, setting out a strategic approach to nicotine:[86]

> *Nicotine, though not benign, is not directly responsible for the tobacco-caused cancer, lung disease, and heart disease that kill hundreds of thousands of Americans each year.*

But if nicotine itself is not directly responsible for the major smoking-related diseases, what are the residual risks? Epidemiological studies of smokeless tobacco[87] [88] [89] [90] or long-term use of nicotine replacement therapy (pharmaceutical nicotine)[91] [92] suggest that serious disease risks *attributable to nicotine* are low or arise in limited circumstances when nicotine consumption is decoupled from smoke inhalation.

- **All-cause mortality**. Long-running surveys of American exclusive smokeless tobacco (SLT) users do not show elevated mortality risks: "*SLT users, in general, did not display a significantly increased risk for all-cause mortality, all-cancer mortality, or diseases of the heart compared to never-tobacco users […] Additionally, SLT use had no discernible adverse effect on any of the nine leading causes of death and did not increase mortality risk for any of the major neoplasms often associated with SLT use*".[93]

- **Cardiovascular disease**, there is no generalised cardiovascular risk attributable to nicotine, but there may be a nicotine-specific risk to people with preexisting cardiovascular conditions:[94]

  "*the risks of nicotine without tobacco combustion products (cigarette smoke) are low compared to cigarette smoking but are still of concern in people with cardiovascular disease*.

  Studies of nicotine use without smoke exposure, for example, snus use, do not show elevated cardiovascular risk, and that "*toxic components other than nicotine appear implicated in the pathophysiology of smoking-related ischemic heart disease*"[95] and "*use of snus was not associated with the risk of stroke. Hence, nicotine is unlikely to contribute importantly to the pathophysiology of stroke*."[96] There is some suggestion of higher rates of fatality among snus users experiencing heart attacks,[97] but there are disagreements about whether this relationship is genuine and causal.[98]

- **Cancer.** The U.S. Surgeon General's Report of 2014 concluded: [99]

  "The evidence is inadequate to infer the presence or absence of a causal relationship between exposure to nicotine and risk for cancer."

  However, this report notes animal studies showing that nicotine "*is a tumor promoter in some experimental models*" but cites human epidemiological data suggesting "*that in humans nicotine may not have a strong tumor-promoting effect*". To the extent that smokeless tobacco poses any cancer risk, evidence suggests this is caused by exposure to compounds other than nicotine.[100] [101]

- **Respiratory disease**. The evidence does not support a link between systemic nicotine exposure and respiratory disease. Though there is no conclusive evidence, it is possible that direct exposure of lung cells to nicotine[102] or exposure to hazardous agents other than nicotine in an inhaled nicotine aerosol could create respiratory risk.

- **Pregnancy**. Smoking is clearly associated with a range of poor birth outcomes.[103] However, much of this is likely due to exposure to toxicants other than nicotine present in tobacco smoke. The U.S. Surgeon General concluded:[104]

  "*Evidence from studies of gene-environment interactions support the hypothesis that components of tobacco other than nicotine may contribute to tobacco-related adverse pregnancy outcomes*."

A trial of over 1,000 pregnant women who smoked found "*Regular use of e-cigarettes or nicotine patches by pregnant smokers does not appear to be associated with any adverse outcomes*."[105] While most studies find no risk from vaping, the evidence can be of poor quality and contradictory.[106]

- **Impacts on the adolescent brain**. There has been a high level of political, media and public concern about the effects of nicotine on the developing brain. The U.S. Surgeon General raised this as a significant finding in the 2016 report, *E-Cigarette Use Among Youth and Young Adults*.[107] However, the underlying evidence base is weak, based on animal models or subject to potential confounding of genetic and socioeconomic factors, the influence of other substance abuse, and the role of preexisting neuropsychiatric problems associated with youth smoking.[108] If there were noticeable impairments associated with adolescent nicotine use, these would be observable in the generations of adults who smoked as teenagers. However, there is no compelling evidence to support this: one study found that "*Past smoking was not associated with significantly poorer performance than never smokers in any cognitive domain.*"[109] Recent evidence suggests a further challenge to this argument: there are signs that differences in brain structure may *predate* and *predict* subsequent substance use initiation,[110] with exposure to environmental pollution as a possible underlying cause.[111]

- **Mental health**. There are significantly higher rates of nicotine use in populations with mental health disorders such as ADHD, anxiety disorders, and depression. It is plausible that nicotine use among affected populations is an attempt, consciously or subconsciously, to self-medicate or regulate these disorders.[112] [113] It is also possible that nicotine use could cause or intensify these disorders or that the causal relationship is bidirectional.[114] [115] It is inherently challenging to isolate the direction of any causal relationship in the association, and the evidence is currently contradictory and uncertain. [116] [117]

Public and professional perceptions of nicotine risks are grossly inaccurate. There is an extensive body of literature that supports the analysis that "People smoke for the nicotine but die from the tar" or its many variants. Yet, awareness of the basic risk concepts about nicotine is very poor. For example, in the United States, a 2022 study found that 61.2% of smokers believe nicotine causes cancer or don't know; the authors called for corrective messaging.[118] In New Zealand, proposals to lower the nicotine content of cigarettes were incorrectly understood as making the products safer.[119] In the UK in 2021, only 11% of smokers recognised that 'none' or 'a very small amount' of the health risks from smoking come from nicotine in tobacco cigarettes.[120] Several surveys show that medical professionals also share these misperceptions. For example, a 2021 U.S. study found:[121]

> *Overall, the majority of physicians "strongly agreed" that nicotine directly contributes to the development of cardiovascular disease (83.2%), COPD (80.9%), and cancer (80.5%).*

These nicotine misperceptions also underpin misperceptions of the risk of vaping and other smoke-free nicotine options, and this creates a barrier to switching from smoking to smoke-free. The problem is that false perceptions of harm influence behaviour and inhibit beneficial behaviour change, intent, and action.

1.6 Conclusion

When used as intended, nicotine is a relatively benign psychoactive substance and does not cause overdose, intoxication, hallucinations, oblivion or other more extreme drug effects. People use nicotine because it makes them feel better and feel as though they function better, and this underpins the demand for the drug. Nicotine itself does not cause the vast majority of tobacco-related harms, though it does have some adverse health effects and risks. Nicotine use may create dependence by reinforcement through positive rewards and adverse effects of temporary withdrawal and craving. Nicotine can be

challenging to quit. We may consider nicotine dependence to be an addiction if the user cannot stop *despite significant harm*, for example, through continued smoking.

For the past 100 years, nicotine has been primarily consumed by inhaling toxic tobacco smoke. However, that is changing as the world begins a transition to nicotine without smoke (vapes, pouches, heated and smokeless tobacco). This opens up a range of policy challenges and opportunities. These products can meet the nicotine demand with significantly reduced harm compared to combustible tobacco. But that also means the loss of the main deterrent to nicotine use: the harms caused by smoking. The emergence of nicotine as a relatively benign drug without major harms associated with its use demands a profound re-evaluation of the position of nicotine as a legal substance (like caffeine, alcohol and, increasingly, cannabinoids) in society.

Regulation of nicotine use is challenging because users largely control their own intake by changing behaviour, changing products, and ultimately seeking illicit supplies of the products they want. Policymakers should accept that the demand for nicotine is inevitable and likely to persist indefinitely. In that case, the policy challenge is to make nicotine available in regulated markets, with lawful suppliers meeting adult demand with safeguards to raise awareness, control marketing and branding, and limit access.

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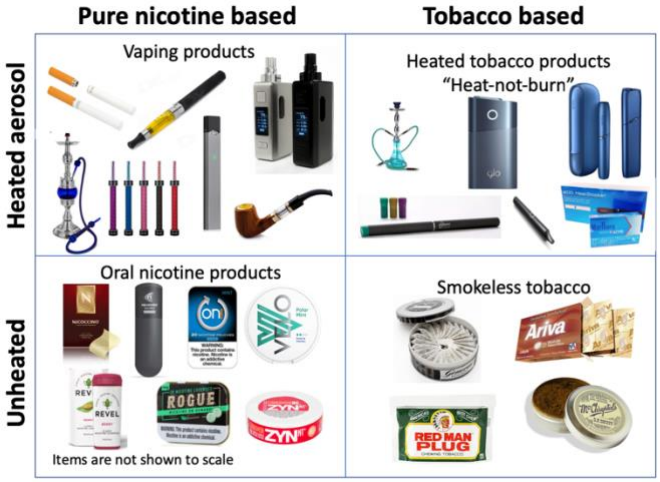
2 Smoke-free nicotine is far less harmful than smoking

2.1 Key concepts

Smoking is a uniquely harmful consumer behaviour, creating major risks for cancer and cardiovascular and respiratory disease.[1] Nearly all the risks from tobacco use arise from smoking: inhaling thousands of chemical agents, many toxic or carcinogenic, produced during the combustion of tobacco leaves in the burning tip of a cigarette.[2] *Smoking* dominates (99.4%) the global tobacco-related death toll: the Global Burden of Disease study shows 7.69 million deaths attributable to smoking annually, 1.30 million attributable to secondhand smoke, and just 55,600 attributable to smokeless tobacco.[3] This annual smoking-related death toll exceeds the annual excess mortality attributable to COVID-19 in 2020 and 2021.[4]

The imperative to stop smoking. Stopping smoking at any time reduces the risks of serious disease and premature death. Nearly all excess mortality risk is eliminated by stopping before age 40.[5] It is beyond reasonable doubt that vaping (e-cigarette or ENDS use) and the use of other smoke-free nicotine products (oral nicotine pouches, smokeless and heated tobacco) are far safer than cigarette smoking. Smoke-free products do not involve combustion or produce products of combustion. Switching from smoking to smoke-free nicotine use leads to greatly reduced exposure to the main toxicants associated with serious disease.

Four main categories of smoke-free nicotine products.



Though each non-combustion product category has a different risk profile, they are clustered closely together on a continuum of risk that has cigarettes at the opposite extreme. Most hazardous chemical agents in cigarette smoke are either not present in vape aerosol at detectable levels or at much lower levels. Similar findings apply to all the smoke-free alternatives to smoking.[6]

Chemical basis for reduced risk. Combustion of tobacco creates thousands of chemical reactions and new toxic chemicals not found in the tobacco. Tobacco smoke contains around 7,000 identifiable chemical agents, of which at least 158 are known to be toxic or carcinogenic.[7] The switch to non-combustible, smoke-free nicotine radically changes the chemical risks and demands a rethink of our whole approach to nicotine. According to independent American experts, these alternative products have "*the potential to disrupt the 120-year dominance of the cigarette*".[8]

2.2 Studies and assessments

Major assessments. Several high-quality, independent reviews conclude that exclusive ENDS use poses a small fraction of the risks of cigarettes and is likely to be at least 95% lower risk than smoking:

- *Laboratory tests of e-cigarette ingredients, in vitro toxicological tests, and short-term human studies suggest that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes.*
  National Academies of Sciences, Engineering, and Medicine, United States (2018).[9]
- *Based on the reviewed evidence, we believe that the 'at least 95% less harmful estimate' (that is, smoking is at least 20 times more harmful to users than vaping) remains broadly accurate, at least over short- and medium-term periods, but it might now be more appropriate and unifying to summarise our findings using our other firm statement: that vaping poses only a small fraction of the risks of smoking.*
  Office for Health Improvement and Disparities, England (2022).[10]
- *Vaping poses only a small fraction of the risks of smoking and switching completely from smoking to vaping conveys substantial health benefits over continued smoking. Based on current knowledge, stating that vaping is at least 95% less harmful than smoking remains a good way to communicate the large difference in relative risk unambiguously so that more smokers are encouraged to make the switch from smoking to vaping. It should be noted that this does not mean e-cigarettes are safe.*
  Public Health England (2018).[11]
- *Although it is not possible to quantify the long-term health risks associated with e-cigarettes precisely, the available data suggest that they are unlikely to exceed 5% of those associated with smoked tobacco products, and may well be substantially lower than this figure.*
  Royal College of Physicians, London (2016). [12]
- *Vaping exposes vapers to a far narrower range of toxins than does smoking cigarettes, and levels of toxins absorbed from vaping are generally low. It is therefore likely that vaping poses only a small fraction of the risk of smoking.* Royal College of Physicians, London (2024). [13]

This suggestion that vaping is at least 95% less risky than smoking has often been misunderstood: it is intended as a clear and actionable way of communicating the scale of risk reduction to consumers and professionals.[14]

Toxicants in the body. The most persuasive evidence comes from biomarker data.[15] These are measures of toxicants found in users' blood, saliva, or urine. Switching from cigarettes to ENDS,[16 17 18 19 20 21] heated tobacco,[22 23 24 25 26 27] snus,[28 29 30] or nicotine pouches[31 32 33 34] dramatically reduces the exposure to hazardous chemicals associated with smoking. Many biomarkers of exposure fall to background levels or below the limit of detection, and most others are radically reduced.[35]

Emissions toxicity. Similar findings arise from well-conducted studies of the chemical composition of aerosol emissions, including tests for cytotoxicity, mutagenicity and genotoxicity.[36] However, these studies are prone to exaggerating risk because no humans are involved. The exaggeration of risk arises because the devices can be operated in unrealistic, overheated conditions that would be

intolerable for human users. This makes the liquid prone to pyrolysis, generating excessive levels of thermal decomposition products.[37]

Health indicators. Other supportive data show improvements in health and welfare for those who switch from smoking to ENDS use completely. Studies show improvements in asthma[38], chronic obstructive pulmonary disease (COPD),[39] blood pressure,[40] lung function,[41] [42] respiratory conditions, [43] [44] [45] cardiovascular risk factors,[46] [47] and gum disease.[48] One study showed that ENDS typically has a cancer potency of just 0.4% of cigarette smoke.[49]

Public health advice. The National Health Service of the UK provides straightforward advice to smokers: "*Also known as vapes or e-cigs, they're far less harmful than cigarettes, and can help you quit smoking for good*",[50] and English authorities advertise vaping on TV as a smoking cessation strategy. New Zealand, which has seen an extremely impressive decline in smoking, has similar advice to the public: "*Vaping is not harmless, but it is much less harmful than smoking*."[51]

2.3 Proof of concept

Snus as proof-of-concept for tobacco harm reduction. The data for snus (oral tobacco) provide a powerful proof of concept for tobacco harm reduction: epidemiological evidence "*provides scant support for any major adverse health effect of snus*"[52] [53] and also that switching from cigarettes to snus reduces the risk of cancer and heart disease, and the risk in switchers being similar to that in those who quit cigarettes.[54] Through the use of snus, Sweden has the lowest smoking prevalence in the European Union (7% compared to the EU average of 23% in 2021),[55] and this is attributable to snus use displacing smoking,[56] with similar effects in Norway.[57] One estimate suggests that snus in Sweden has avoided about 3,000 deaths per year.[58] Another suggests among men over the age of 30, 355,000 lives per year could have been saved if the other European Union countries had matched Sweden's tobacco-related mortality rate.[59] The ban on snus in the European Union has no basis in science or ethics.[60] [61] Policy decisions about nicotine pouches must be informed by the experience gained with snus. We have known since at least the early 1990s that modern smokeless tobacco carries a negligible mortality penalty.[62] Yet opposition to the idea of using snus as an alternative to smoking was immediate: "*I'm not in favor of advocating use of smokeless tobacco as an approach to dealing with tobacco addiction*." (M. Fiore, 1994)[63] The opposition has persisted for thirty years and remains undimmed, denying or diverting millions of smokers from safer tobacco use and causing thousands, maybe millions, of avoidable deaths.

2.4 Concerns and misunderstandings

Common concerns. Critics of tobacco harm reduction raise a range of concerns, but these are often based on misunderstandings or poor methods.

1. **Correlation and causation**. Many studies find an association between vaping and specific health effects, yet most are deeply flawed.[64] Almost everyone who uses ENDS and is old enough to suffer serious illness has been smoking for decades. Few studies can isolate the effect of vaping from the impact of a long smoking history; some studies even counted effects associated with vaping that happened before users took up vaping.[65] [66] As noted above, studies which avoid these issues by following within-person changes when switching from smoking to ENDS show substantial reductions in harmful biomarkers and disease symptoms.

2. **"EVALI".** In 2019-2020, there was an outbreak of severe lung injuries in the United States that was misleadingly named E-cigarette or Vaping Associated Lung Injury.[67] It was not caused by ENDS, which are *electronic nicotine delivery systems*. It was caused by a thickener, Vitamin E Acetate, added to illicit cannabis (THC) liquids.[68] Nicotine vaping was not and could not have been involved in EVALI.[69] [70] The US EVALI crisis was confined in time and geography primarily to late 2019 in the United States, and it was fixed by the removal of thickeners from THC vapes. No changes were made (or necessary) to nicotine vapes. There were EVALI sufferers who claimed not to use THC. However, there have always been strong incentives not to disclose cannabis use due to consequences with law enforcement, probation, employment, education, visas and parents.

3. **"No long-term data"**. It is often asserted that we just do not know the long-term effects. While technically accurate, the point is also misleading. Toxicology has advanced dramatically since the discovery of the health risks of smoking in the 1950s, and we now know a great deal from occupational and environmental health disciplines. We cannot know everything about ENDS risks, but we already know *enough* to be confident that the risks from using smoke-free products will be *far less* than those from smoking. Also, the much simpler chemistry will more easily allow remedial action if needed (for example, removing ingredients, changing materials, or controlling temperatures). Discouraging or restricting ENDS use while we wait for detailed evidence on long-term outcomes – given that we already know they are much lower risk than smoking – allows the harms of smoking to continue.

   We should be mindful of the wise words of the great tobacco epidemiologist Austin Bradford Hill:[71]

   > *All scientific work is incomplete – whether experimental or observational. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.*

4. **"Dual use".** Some people use both cigarettes and ENDS ("dual use") and experience lower benefits or no benefits as they continue to smoke. However, many are in a gradual transition to exclusive ENDS use or to dual use with only occasional smoking. Most dual use should be seen as progress from exclusive smoking. Dual use is not the most common form of ENDS use: in the United States, just 29% of adult ENDS users were dual users in 2021.[72] In Britain, the proportion of vapers also using cigarettes has come down from around two-thirds to around one-third over the last ten years.[73] It does not appear to reduce quitting intentions.[74] More likely, it includes people who do not want to quit smoking at all but go on to become "accidental quitters".[75] [76] Some argue that dual use makes smokers worse off, as if the exposures are additive. This arises from a misrepresentation of cross-sectional studies comparing current smokers and current dual users and, therefore, does not account for differences in dependence and intensity of smoking. Studies that track individuals through smoking to dual-use show benefits.[77]

False risk perceptions. Though high-quality scientific assessments suggest vapes and other smoke-free products are much less risky than cigarettes, the public understanding of these risks is very different, and the gap between scientific evidence and public perception is deteriorating over time. In the United States, the "*Perceptions of E-cigarettes as more harmful than cigarettes doubled year on year, increasing most between 2019 and 2020 (2018: 6.8%, 2019: 12.8%, 2020: 28.3%)*",[78]

with similar findings in the UK.[79] In 2023 in the UK, an ASH survey showed that 43% of adults believed "*E-cigarettes are a lot more, more or equally harmful as cigarettes*", but only 34% believed that "*E-cigarettes are less or a lot less harmful than cigarettes*" and "*only 8% correctly state that e-cigarette use is a lot less harmful than smoking*".[80] Similar trends are evident among smokers. In all cases, the trend since 2013 has shown a deterioration.

Myth-busting. Several excellent resources have been created to tackle myths about product safety and other common concerns about ENDS use. These include:

- A consumer-orientated myth buster by the UK National Health Service[81] and myth-busting advice to health professionals from Public Health England.[82]
- A detailed myth buster by Action on Smoking and Health (UK) verified by practising scientists.[83]
- An analysis of multiple false and misleading claims made in a WHO fact sheet on ENDS.[84]
- Academic responses to flawed assessments, notably those produced in Australia[85] [86] or responses to the flawed position statements of medical associations.[87]
- Detailed methodological criticisms of misleading research on specific topics, such as carbonyl formation,[88] heavy metals migration,[89] or flawed epidemiology.[90] [91]
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3 Smoke-free nicotine use reduces smoking

3.1 Key concepts

The best way to assess the evidence that ENDS use reduces smoking is to look at all the different types of evidence together. It all points towards ENDS having a powerful effect on suppressing adult smoking via five main effects:

1. The people who use e-cigarettes are more likely to quit smoking, and success rates increase over time as smokers become familiar with e-cigarettes as an alternative.
2. More people are willing to try ENDS to quit smoking because it does not require them to give up nicotine and several other aspects of smoking to secure significant health, welfare, and economic gains. Moving from smoking to vaping is easier than moving from smoking to nicotine abstinence.
3. People who would not otherwise try to quit are drawn into smoking cessation via ENDS uptake and gradual migration away from smoking. These are known as "accidental quitters".
4. Young adults who would otherwise have become smokers are diverted into ENDS use and never started smoking.
5. Adults who may otherwise have relapsed to smoking use vaping instead.

3.2 Studies and assessments

Randomised controlled trials show ENDS to be more effective than nicotine replacement therapies and at least as good as pharmacotherapies at achieving smoking cessation in trial conditions.

- The January 2024 Cochrane review examined 88 studies and, based on seven studies that met its strict inclusion criteria, concluded that vaping nicotine was 59% more effective for quitting than nicotine patches and gum.[1]
- A review of 363 studies by the UK National Institute for Health Research found that vaping was the most effective single quitting aid.[2]
- A 2023 Cochrane review of all smoking cessation therapies concluded that nicotine ENDS and varenicline were the two most effective treatments for quitting smoking.[3]

Observational and population studies. Smokers switching to ENDS are replacing cigarettes with a much lower-risk way of taking nicotine – they are making a different consumer choice rather than taking a smoking cessation medication. Smoking cessation rates using vaping *increase* over time as smokers adjust to exclusive e-cigarette use.[4] In contrast, conventional quit approaches have *declining* quit rates over time as abstinence gives way to relapse back to smoking.[5] Vaping is associated with increased quitting in observational studies,[4 6 7] and population studies.[8-22] Significant use of ENDS policy is reflected in national smoking rates.[23 24 25]

Economic data. There is also substantial evidence from economic data that ENDS function as a cigarette substitute. In a paper for FCTC COP-7, WHO concluded, "*ENDS/ENNDS and cigarettes are substitutes*".[26] Economic evidence supports WHO's claim. There are pronounced substitution effects between combustibles such as cigarettes and smoke-free alternatives.[27-35] Substitution should be expected: both meet user demands for nicotine in a similar way, though ENDS with much

lower risk.

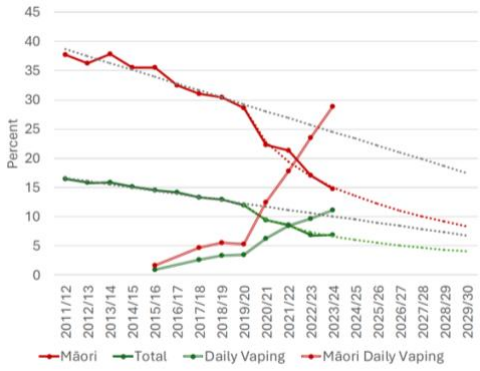
"Accidental quitters." Vaping is also the only quitting aid to assist smokers with no intention of quitting ('accidental quitters').[36] [37] [38] That is important because this group is most likely to continue smoking and, therefore, is most at risk of serious disease and premature death.

3.3 Experience and outcomes

Impact versus efficacy. Controlled trials can give insights into "efficacy" (how likely someone using the product is to quit smoking). But they can't say much about how many people will use the product. ENDS have the potential for a substantial positive public health *impact*, a function of individual effectiveness multiplied by the number of people willing to try. Switching to ENDS has become by far the most popular assisted method to quit smoking in the United States[39], England,[40] [41] and Canada.[42] There is evidence that ENDS have made such an impact at the population level in terms of sharper declines in cigarette smoking than originally expected. For example, US adult smoking prevalence is now lower than anticipated from pre-ENDS era trends – with the most significant decreases in smoking occurring in the age groups with higher uptake of ENDS (i.e., adults under 44 years of age).[43] [44] In Britain, the most significant decline in smoking between 2011 and 2023 was among young adults (age 18-24); smoking prevalence fell from 25.7% to 9.8%, and this group also had the highest uptake of vaping, reaching 15.8% by 2023 from negligible levels in 2011.[45] The most compelling example of a radical transformation of the tobacco and nicotine market is from New Zealand, in which a rapid rise in vaping has displaced smoking, including in the Māori population.

New Zealand Smoking and Vaping

Total & Māori 2011-24



Source: New Zealand Ministry of Health, Ben Youdan[46]

The impact on New Zealand Māori women was especially pronounced: between 2019-20 and 2023-24, current smoking prevalence fell by more than half from 35.0% to 16.6%, while vaping prevalence increased from 7.2% to 33.7%.[47]

Guidance for healthcare providers and the public. The UK National Centre for Smoking Cessation and Training produces high-quality guidance in the use of vaping products to quit smoking for good.[48] Academic analysis in the United States is beginning to endorse ENDS for smoking cessation in clinical settings.[49] [50] The Ministry of Health in New Zealand[51] National Health Service (England) provides plain-speaking advice to the public.[52]

User testimony. Thousands of users provide eloquent testimony of their success in quitting smoking using

ENDS. These provide compelling accounts of tobacco harm reduction at the individual level.[53] Though often dismissed as anecdotes, these first-person accounts of experience are, in fact, rich in detail and a compelling strand of evidence that triangulates well with trials, observational data, trends and economic analysis.

3.4 Heated tobacco and smoking

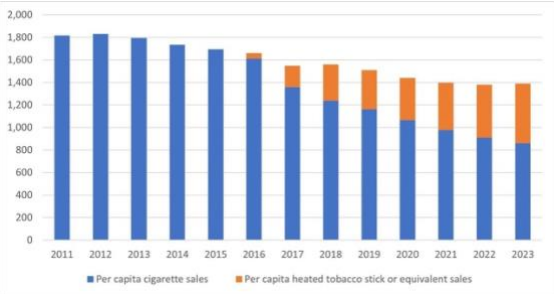
Heated tobacco products. A comprehensive review of the behavioural science related to HTPs undertaken by Imperial Brands and its consultants concluded:[54]

> *This evaluation suggests that HTP use is almost exclusively observed among those with a history of cigarette smoking, and there is a growing body of evidence for the ability of HTPs to provide support for adult smokers to transition away from cigarette smoking, in the absence of any significant "gateway" into tobacco use initiation. Many studies have reported a significant degree of dual use of cigarettes and HTPs, and efforts to assess the reasons for such patterns of use, whether these provide overall exposure reductions, and whether dual use acts as a bridge towards a complete transition away from cigarette smoking, requires further investigation.*

Heated tobacco products have been a spectacular success in reducing cigarette consumption in Japan.[55] [56] A 2024 study confirmed that cigarette sales had fallen by around half, with an accelerated downward trend since the introduction of heated tobacco products in Japan in 2016. [57]

Japan: Cigarette and Heated Tobacco Sales

Per capita, 2011-2023



Cummings et al. (2024)

3.5 Barriers to greater impact

Are ENDS as effective for smoking cessation as they could be? Since 2011, there has been significant innovation, much of which will improve the impact of vaping and smoking, and earlier data may be less relevant. However, the effect of vaping on smoking is not just a function of product design and innovation. It results from multiple influences on behaviour, including product appeal, perceptions of risk, and expected benefits and costs.

- If people believe (incorrectly) that vaping is no less harmful than smoking, they have diminished incentives to switch, and dual users would be indifferent to moving to exclusive vaping.
- If people believe (incorrectly) that nicotine vaping caused an outbreak of severe lung injuries or that "popcorn lung" is a risk, then they may be irrationally fearful about switching.
- If taxes make vapes more expensive relative to smoking, then fewer people will respond to the diminished economic incentive to switch.
- If nicotine limits, flavour bans, or plan packaging make the product less satisfying or

appealing, expect less smoking cessation.
- If doctors hesitate to recommend vaping or provide misleading information, or official healthcare advice warns against switching, then less switching will be the result.
- If ENDS advertising is banned, fewer people will be aware of the option and encouraged to switch to trusted products.

The real-world impact of ENDS on smoking is not just a function of product design but also the regulatory, fiscal, commercial, communications, and healthcare environment in which they are available to people who smoke. This environment is modifiable by governments, regulators, academics and tobacco control activists in ways that protect the cigarette trade or in ways that enhance the downward pressure on smoking and cigarettes.

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4 Smoke-free nicotine and youth

4.1 Key concepts

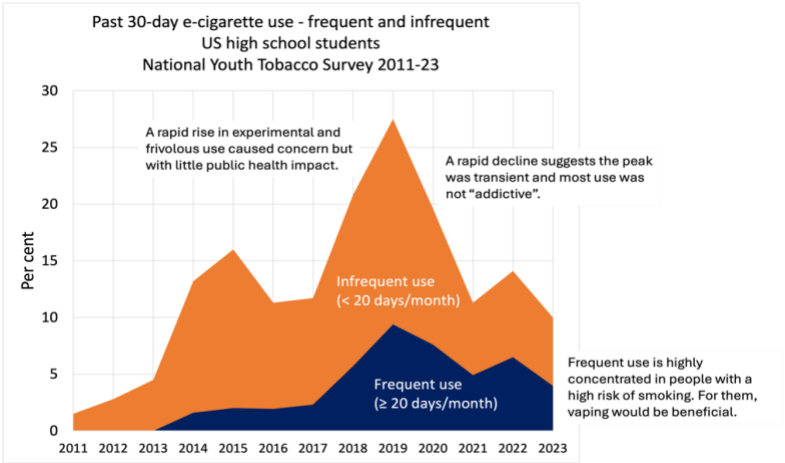
ENDS use as a youth risk behaviour. No one concerned with public health recommends or welcomes youth nicotine use. The same applies to alcohol and illicit drug use, premature or risky sexual practices, dangerous driving, and a range of other youth risk behaviours.[1] Nevertheless, such behaviours are a real part of society and require a response to reduce the harm they cause. Many are concerned about youth ENDS use, especially regarding potential "gateway" effects and signs of nicotine dependence. However, it is essential to place ENDS use in the broader context of youth risk behaviours, including smoking. For most adolescents, ENDS use would not be particularly harmful, and for some, it would be an alternative to smoking and, therefore, beneficial.

Causes of youth tobacco use. Evidence suggests that a wide range of psycho-social factors drive nicotine uptake. These factors are characteristics of the individual (genetic, mental health, rebellious outlook, delinquency, etc.) and their circumstances (household, peer group, marketing, etc). One systematic review identified *ninety-eight* conceptually different predictors of smoking onset.[2] Studies of ENDS users suggest use arises from seeking an "alternative to cigarettes", the "wider social environment",[3] and curiosity.[4]

The danger for policymakers. It is not possible (or desirable) to make straightforward cause-and-effect claims about youth smoking or vaping, such as attribution of youth use to factors such as flavours, packaging, or marketing to vaping uptake. The danger of designing policy based on a simplistic understanding of causes will leave the underlying demand intact and cause users to find alternative ways to use nicotine, including switching to smoking.[5] [6] ENDS use is one of a range of youth risk behaviours that a subset of young people will engage in, even if adults disapprove, related to substance use, violence, sexual behaviour, and risk-taking.[7] The public health challenge is to reduce the risks to these young people to the greatest possible extent, including the risks arising from the unintended consequences of poorly designed policies.

4.2 Youth vaping displaces youth smoking

Understanding youth vaping. The annotated chart below provides a basis for understanding youth ENDS use. It is based on US data from the National Youth Tobacco Survey as it developed over the last 12 years, peaking in 2019.[8] Many of the same dynamics will be common to other populations.



- **Youth ENDS use has peaked, then declined or plateaued in many countries.** In the US, the proportion of high school-aged youth who used ENDS in the past 30 days peaked in 2019 at 27.5%[9] but has since declined by almost two-thirds to 10.0%.[10] In the UK, occasional or weekly ENDS use plateaued between 2021 and 2022,[11] as did past-30-day ENDS use in Canada.[12] There may be different types of use. Firstly, relatively frivolous use based on youthful experimentation, fads, and fashion is unlikely to persist – this is of little public health consequence. Secondly, more intensive and longer-term use – but this is most likely to be displacing smoking. There is reasonable evidence to support this model.

- **Most youth ENDS use is experimental and temporary.** Most youth who ever try ENDS do not persist in using them currently. In both the US and the UK, just under half of youth who had ever tried ENDS continued to use them 1+ times in the past 30 days. [11] [13] Similarly, in the UK, over 60% of youth who used ENDS had either used them only once or twice or had used them more but discontinued them. [10] These patterns of temporary experimentation align with youths' stated reasons for *ever* using ENDS, which are most often curiosity/experimentation, boredom, and social reasons.[14] [15] [16]

- **ENDS use is concentrated in youth who had (or would have) used other nicotine products.** US youth with an *established* history of other nicotine product use were over five times as likely to have used ENDS in the past 30 days.[17] 70% of UK youth who were currently using ENDS had a history of cigarette smoking.[10] ENDS use that is frequent and/or is accompanied by nicotine dependence is even more strongly concentrated in those who had already used cigarettes or other nicotine products: approximately 98% of US youth who used ENDS frequently had used another nicotine product.[16] Youth who vape have risk factors that also predispose them to smoke cigarettes,[18] suggesting that they would have otherwise been cigarette smokers.[19]

- **Higher youth ENDS use is accompanied by larger declines in smoking, suggesting displacement rather than gateway.** If ENDS were a gateway to cigarette smoking, then youth smoking trends would be higher than otherwise expected as ENDS use increases. However, population-level studies show the opposite: youth and young adult smoking prevalence declined *faster* after ENDS use became common,[20] and this pattern is remarkably consistent across countries, including the US,[19] [21] [22] UK,[23] [24] Canada,[25] and New Zealand.[26] [27] These declines have been drastic and unexpected: in the US, youth smoking in 2020 was far lower (3.3%)[28] than what was thought possible in 2010, according to the US Healthy People target for 2020 (16%).[29] These trends are consistent with ENDS diverting youth with a predisposition for nicotine use away from more harmful combustible cigarettes.[21] [25]

4.3 The gateway effect is discredited

Evidence for the gateway hypothesis is better explained by a "common liability" to nicotine use. Claims that ENDS are a gateway to smoking are based on a misunderstanding of the evidence (i.e. that youth who use ENDS are also more likely to smoke cigarettes). Rather than ENDS *causing* youth to also smoke cigarettes (which confuses correlation and causation), it is more likely that ENDS use and smoking are both explained by pre-existing characteristics which predispose some youth to use nicotine. There are dozens of these "common liability" factors (e.g., other substance use, poor mental health, risk-seeking personality) which are not accounted for in most studies. [17] The apparent gateway association becomes successively weaker as more common liability factors are accounted for[30] [31] – in some cases becoming not statistically significant[29] [32] – suggesting that it is better explained by a pre-existing propensity to use nicotine. A 2024 analysis of the gateway effect concluded:[33]

Evidence offered in support of the gateway hypothesis does not establish that ENDS use causes youth to also smoke cigarettes. Instead, this evidence is better interpreted as resulting from a common liability to use both ENDS and cigarettes. Population-level trends are inconsistent with the gateway hypothesis, and instead are consistent with (but do not prove) ENDS displacing cigarettes. Policies based on misinterpreting a causal gateway effect may be ineffective at best, and risk the negative unintended consequence of increased cigarette smoking.

4.4 Young people have a stake in the health of adults

Young people have a stake in adult health. Young people are often discussed as if they constitute a separate population, unconnected to the adults in their lives. However, the welfare of young people is strongly connected to adults.

- Young people suffer if their parents or other significant adults are made ill or die prematurely through smoking – sadness and grief, caring burdens, and a diminished experience of parenting.[34] [35]
- Parental smoking is a strong predictor of youth smoking initiation: there may be intergenerational benefits from parents switching from smoking to vaping.[36]
- Young people are usually economically dependent on adults and are fed and clothed from a household budget that is depleted by the costs of smoking.[37]
- Secondhand smoke exposure is harmful.[38] Children may avoid secondhand smoke exposure if their parents and significant adults switch to vaping or pouches and smoking becomes denormalised in their homes and communities.
- When ENDS use displaces smoking, there are also reduced risks of household fires and resulting injuries and property loss. In March 2016, it was reported that there had been 113 fires caused by e-cigarettes in the UK over three years. There were over 16,000 smoking-related fires over the same period. [39]
- Young people grow up to be adults. ENDS create "options value" for youth who smoke – they offer the means to switch later in life before the disease risks start to build up after the 40s.[40] The availability of ENDS to adults reduces the life consequences of poor choices made as a teenager.

Adolescents account for a small minority of tobacco and nicotine users. Though much of the political and media focus is on youth vaping, the total number of adult nicotine users is likely much larger in most countries. For example, in the United States, the National Youth Tobacco Survey (2024) gives the total number of past-30-day tobacco and nicotine users in middle and high school at 2.25 million persons (2024).[41] In contrast, Altria's Adult Tobacco Consumer Tracker gives 54.8 million persons using tobacco and nicotine products (past-30-day users aged 21 or over, November 2024)[42] *twenty-four times as many adults*. It is often asserted without evidence that ENDS manufacturers "target youth". However, the addressable adult market of existing nicotine users is far larger, and adults are likely to be more intense users with more money to spend. This ratio between youth and adult users will vary between countries in response to many factors, notably demography – low- and middle-income countries have a higher proportion of younger people. However, this ratio should be a consideration in policymaking and sense-checking claims about targeting and marketing.

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5 Policies for smoke-free nicotine products

5.1 Key concepts

Policymaking for novel and emerging smoke-free tobacco products is shaped by the following:

- Non-combustible nicotine products are far safer than the dominant tobacco products (cigarettes).[1]
- These products function as substitutes for the dominant high-risk tobacco products (cigarettes).[2]
- Policies to address youth vaping can cause more harm than good, including *to young people*.[3]
- Policy must be based on insights into the dependence-forming psychoactive effects but relatively minor health impacts of nicotine, why people use nicotine, and why its use is likely to persist.[4]
- Regulatory interventions can trigger unintended responses that the regulator may not expect or want, such as users switching back to smoking, expanding illicit trade, or the use of risky workarounds.

Five questions every public health official should ask when a new nicotine policy is proposed:

1. **What problem is this policy trying to address?** Policymakers should focus on the objectives of the FCTC,[5] the SDGs,[6] and their own public health goals, such as those of the E.U.[7] or the U.K.[8] That will usually mean tackling the non-communicable disease burden, which is primarily driven by *smoking*. Strategic targets for tobacco and nicotine policy should focus on *smoking* and *achieving smoke-free status*, not on tobacco use, nicotine use or vaping. Non-combustible tobacco and nicotine products can help to attain smoke-free status, and reaching smoke-free status is the overriding public health priority.
2. **What evidence supports the proposed policy?** The WHO routinely supports prohibitions on novel and emerging tobacco and nicotine products.[9] However, there has been no reputable evaluation of this policy and its likely unintended consequences by those promoting it. Yet obvious concerns arise about illicit trade and the protection of the cigarette trade. Do flavour bans work? Do ENDS marketing restrictions protect the cigarette trade? Have the standard policymaking disciplines been applied, including impact assessment, cost-benefit analysis, risk assessment, and equity assessment?[10]
3. **What trade-offs are created by this policy?** If the policy is designed to protect youth from nicotine uptake, does it harm adults by reducing smoking cessation? Is the policy aimed at safeguarding adolescents who would never use nicotine at the expense of adolescents who would otherwise smoke? Does the policy punish disadvantaged people who continue to smoke or use nicotine, aggravating inequities? Do efforts to control access to ENDS make it relatively easier to access cigarettes?
4. **What are the foreseeable unintended consequences?** Policies do not always achieve the changes policymakers hope for, and they can make matters worse. Will the policy cause some ENDS users to return to smoking,[11] some smokers never to switch, and some young people to

smoke instead of vaping?[12] Will it trigger black-market supply[13] and draw young people into criminal networks? Will it punish people for looking after their own health at their own expense? Will it cause users or suppliers to adopt workarounds that might introduce novel risks?[14]

5. **Are distracting arguments used to justify the policy?** Are activists and bureaucrats preoccupied with policies for fighting the tobacco and nicotine industry?[15] [16] Such framing can be harmful for public health: a good idea (*making the use of nicotine much less dangerous*) does not become a bad idea because tobacco or nicotine companies align their business strategy with supplying the products that make it work. Accepting this concept does not mean embracing the views or interests of the tobacco industry but rather recognising that there is a substantial body of credible, independent public health experts who support tobacco harm reduction on public health grounds.[17] [18] [19]

An expert perspective on policy challenges. As the Royal College of Physicians (London) puts it:[20]

> *If [a risk-averse and precautionary] approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer-friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult.*

For specific policies, policymakers should be aware of the following.

5.2 Prohibitions

Prohibitions on novel and emerging products. Prohibitions trigger various responses, including illicit supply, switching to permitted products (cigarettes), and workarounds (making and selling DIY products).[21] Similar risks apply to partial prohibitions or high taxation. Australia's highly restrictive ENDS regime provides a stark lesson in unintended harmful consequences.[22] [23] [24] The United States has extremely stringent regulation imposed by the Food and Drug Administration, but this has led to unauthorised products meeting more than 90% of the demand and effectively no regulation for most of the market.[25] Illicit trade not only reaches young people as users but also involves young people in criminal supply, as the WHO was forced to admit when the ban on tobacco in Bhutan unravelled in 2020.[26] [27] According to one activist organisation, 46 countries had banned e-cigarettes by May 2025.[28] The main argument against such proposals is not merely the harmful, unintended consequences, but also the ethics of denying people at risk of serious disease the lawful right, the information, and the means to switch to much safer, smoke-free products while keeping the most dangerous products widely available on the market.[29] [30] [31] There has been minimal evaluation of these bans, yet a steady stream of press coverage about rising criminality as a response.

5.3 Taxation

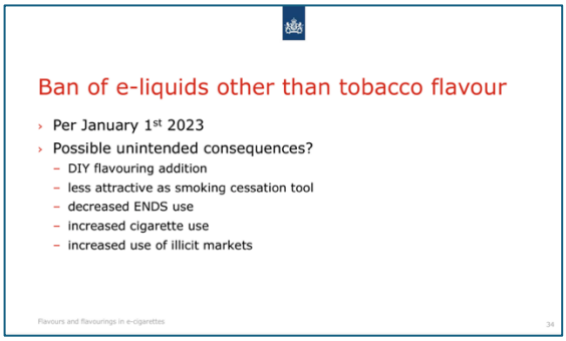
Taxing ENDS. A substantial body of evidence shows that ENDS and cigarettes behave as economic substitutes and that the demand for nicotine is more resilient than any particular way of consuming it. This means that when ENDS prices increase, the demand for ENDS falls, and the demand for cigarettes rises, all other things being equal,[32] including for youth[33] and young adults.[34] Therefore, it is impossible to analyse the impact of an ENDS tax without also accounting for the effect on alternatives to ENDS, including the impact on cigarette consumption.[35] One U.S. estimate suggested a "*proposed national e-cigarette tax of $1.65 per millilitre of vaping liquid would raise the proportion*

of adults who smoke cigarettes daily by approximately 1 percentage point, translating to 2.5 million extra adult daily smokers."[36]

5.4 Banning flavours

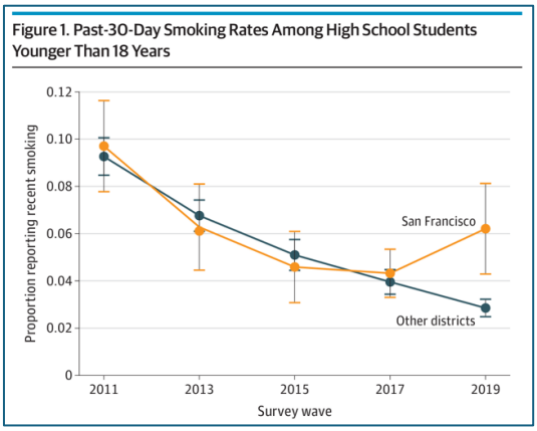
Banning flavoured ENDS. Tobacco harm reduction works by encouraging consumers of cigarettes to switch their product choice from smoking to much safer, smoke-free products. Smoke-free products must appeal to smokers to compete with cigarettes. One example of this appeal is the wide range of flavoured ENDS.[37] While banning flavours might reduce the appeal of ENDS to some users, policymakers cannot just assume that users of flavoured ENDS will become abstinent – they may respond in various ways. A ban on flavours makes alternatives to cigarettes less competitive with cigarettes and, in doing so, protects and aids the cigarette trade. There are virtually no "natural" unflavoured vape products – almost all products contain flavouring ingredients, and even tobacco flavouring is added. Only a small minority of users choose to use tobacco-flavoured vapes – and that applies to adults and youth. In contrast, most smoking products have flavours and aromas created from the combustion of tobacco without the addition of flavouring ingredients (the exception being the addition of menthol to cigarettes).

In December 2023, in a presentation on the Netherlands' approach to banning flavours, the Dutch public health agency RIVM summarised the plausible negative responses to a flavour ban (see below).[38]



The slide represents a good summary of the reasons for scepticism about flavour bans. These unintended consequences are far more significant than the intended purposes of a flavour ban. Yet the proponents of flavour bans, including RIVM, have no analysis supporting a flavour ban once these effects are included, and the Dutch government proceeded with a flavour ban, triggering a range of adaptations, including cross-border purchasing and illicit sales, with some returning to smoking.[39]

Most available evidence comes from the United States, where several flavour bans have been in place at the state and city levels since 2019. One study showed that when vape flavours were banned in San Francisco, cigarette smoking increased *among high school students*:[40]



It is essential to examine what happened when flavour bans were implemented in practice. Recent North American studies showed that ENDS flavour bans had the effect of increasing smoking:

> *In particular, we study the effect of NVP [nicotine vaping product] flavor restrictions enacted in Canada, a country with historically high tobacco regulation, through July of 2023. Using a stacked DID [difference in differences] model, we estimate that flavor restrictions increased cigarette sales by 9.6%.* (Davis et al. 2025)[41]
>
> *… state restrictions on flavored ENDS sales were associated with a 3.6–percentage point (ppt) reduction in daily vaping as well as a 2.2 ppt increase in daily smoking relative to trends in states without restrictions*." Friedman et al. (2024)[42]
>
> *We find a trade-off of 12 additional cigarettes for every 1 less 0.7 mL ENDS pod sold due to ENDS flavor restrictions*". Friedman et al. (2023)[43]
>
> *Our findings suggest that statewide comprehensive flavor bans may have generated an unintended consequence by encouraging substitution towards traditional smoking in some populations*. Saffer et al. (2025)[44]
>
> *"… we find that the adoption of an ENDS flavor restriction reduces frequent and everyday youth ENDS use by 1.2 to 2.5 percentage points. […]. However, we also detect evidence of an unintended effect of ENDS flavor restrictions that is especially clear among 18-20-year-olds: inducing substitution to combustible cigarette smoking"* Cotti et al., 2024)[45]

A survey of French consumers found that half said they would source flavours illegally, and about one-quarter said they would return to smoking.[46] Several academic studies have identified risks with flavour bans: Posner et al. (2021)[47] found that one-third of e-cigarette users would be likely to switch to cigarettes. Gravely *et al.* (2021)[48] examined possible responses to flavour restrictions in the United States, Canada, and England, finding that 28.8% would access their preferred flavours via illicit means and 17.1% would stop vaping and smoke instead.

Why flavour bans will not work. Multiple factors drive vaping uptake, not just flavours. In studies reporting the stated motivation of teenage users, *harm reduction* is an important reason for young people to use ENDS,[49] [50] [51] as well as a wide range of psychosocial factors. A flavour ban stops the lawful supply of flavoured products *but does not stop the demand*. It follows that many young people will simply find ways around the prohibition or take up smoking. Control of flavours should

focus on *descriptors* (packaging, branding, and trademarks that describe the flavour), a form of marketing. Not the flavour sensation itself.

5.5 Controls on nicotine

Controlling nicotine strength. Proposals to limit nicotine strength are based on a misunderstanding that strength reflects nicotine exposure or 'addictiveness'. In reality, *users* control their exposure to nicotine through a widely understood process known as nicotine titration.[52] Note, this also applies to alcohol – people drink smaller quantities of whiskey than beer. This titration effect has been well-documented in smokers for several decades.[53] [54] The user's puffing pattern and possibly their choice of device will change to achieve a desired nicotine intake, for example, by puffing more deeply or more often – a process known as 'compensation'. By adjusting their puffing patterns, users consume lower volumes of higher-strength liquid. But a nicotine strength limit also means that users will consume higher volumes of lower-strength liquid using more energy – potentially creating higher exposures to toxicants generated by heating liquids.[55] [56] [57] As with alcoholic spirits, the strength of nicotine in ENDS is self-limited by consumer acceptability and the excessive harshness of high-strength products. Any limits imposed on nicotine characteristics should focus on pharmacokinetics – the peak nicotine concentration in the brain (C_{max}) and how quickly it can be reached (T_{max}). As long as these characteristics show lower abuse liability (e.g. C_{max}/T_{max}) than cigarettes, there is no case for imposing controls.

5.6 Banning disposable vapes

Banning disposables. Use of disposable, single-use ENDS products has risen rapidly among adults and adolescents in several jurisdictions. However, they are still overwhelmingly used by adults: in 2023, compared to youth (11-17), around nine times as many adults (18+) use disposable vapes in Britain.[58] They have been essential in reaching poorer smokers because they are low-cost, have no upfront cost, are easy to use, and deliver an immediately satisfactory alternative to cigarettes. They offer the easiest exit route from smoking and work well for people experiencing various forms of disadvantage. In June 2025, the U.K. banned these products. A post-ban survey by Haypp Group, an online retailer, found 62.5% of vapers continued to use disposable products (82% for those aged 25-34) via illicit sources and that 6% had reverted to smoking,[59] and many may be using technically compliant reusable vapes as disposables, a workaround.[60] Because the harms of smoking are so much greater than vaping, the effect of any anti-vaping measure will be dominated by its impact on smoking. Based on this survey, the U.K. disposable ban has likely had largely adverse effects, without achieving its environmental or youth protection goals.

5.7 Controls on marketing and branding

Banning the advertising and promotion of novel and emerging products. Advertising has multiple functions, including introducing new designs and products, gaining market share, building premium brands, and raising consumer awareness. Almost all ENDS advertising functions as "anti-smoking advertising" because it is trying to draw users towards an alternative to smoking. Banning advertising favours incumbents (the cigarette trade) and penalises entrants and innovators (ENDS) who must build their competitive position against cigarettes. There is some evidence that suggests

that bans on advertising ENDS reduce the number of smokers who quit,[61] and increase demand for cigarettes.[62]

Plain packaging for ENDS. Some activists have proposed using standardised or plain packaging to reduce the appeal of e-cigarettes to youth,[63] drawing on evidence that such packaging does not affect the appeal to adults.[64] [65] Yet, this is weak evidence drawing on stated, not revealed, preferences in the contrived circumstances of an experimental study. The study did not investigate the likely behavioural response to reduced appeal to youth – it could lead to more smoking or other risky behaviours. There is also conflicting evidence that standardised packaging for ENDS can adversely change risk perceptions.[66] There is, therefore, a danger that some adults would be deterred from switching and some youth would revert to smoking. Given that smoking is far more dangerous than vaping, only a slight uptick in smoking (among adults or youth) compared to a counterfactual without standardised packaging would overwhelm any benefits from reduced youth vaping. Finally, a recent assessment of standardised *cigarette* packaging found no public health benefit.[67] Without a valid proof of concept and with the additional risk of unintended consequences, there is no credible case for standardised packaging for ENDS.

5.8 Controls on nicotine pouches

Oral nicotine pouches. Oral nicotine pouches represent the safest, low-risk nicotine product, as they do not produce inhalable aerosol or undergo chemical decomposition from heating. The risk profile for products made by reputable manufacturers is similar to that of nicotine replacement therapy.[68] However, pouches may be more effective in delivering nicotine with pharmacokinetics satisfactory to smokers and, therefore, a better approach to displacing cigarettes. Pouches follow the same harm-reduction model as snus,[69] which shows how low-risk products have driven out high-risk products in Sweden and other Nordic countries.[70] [71] As with vapes, pouch users have ways to control their nicotine exposure, for example, by where the pouch is placed, how long it is used for, and how many pouches are placed in the mouth. There is no simple relationship between the nicotine content of a pouch and its nicotine delivery,[72] [73] [74] and there is a wide range of nicotine exposures among users of the same pouch.[75] Users can control their exposure by how the pouch is placed and moved in the mouth, how long it is kept there, the choice of pouch (moist or dry, nicotine content), and, ultimately, the number of pouches used simultaneously. It will not be possible to control nicotine exposure by setting (realistic) limits on nicotine content. It may be worthwhile setting a nicotine content limit (e.g. 20mg/pouch) for safety reasons, but this should be set at a high level initially and only reduced subsequently if any unintended consequences are shown to be manageable and acceptable.

5.9 Controls on environmental exposures

Banning ENDS use in enclosed spaces. The primary policy question regarding bans on smoking or vaping in enclosed spaces turns on *who decides the policy*. Should it be up to lawmakers, enacted through generally applicable legislation, or should it be a matter for the property owner or manager to determine the policy? Typically, the case for regulatory intervention is strengthened when there is a material risk to workers or bystanders, when people have little choice but to be present, and when children are likely to be present. There is little evidence that exhaled aerosol poses a material risk. As Public Health England put it:[76]

The evidence of harm from secondhand smoke is conclusive and provides the basis for U.K. smokefree laws. In contrast, international peer-reviewed evidence indicates that the risk to the health of bystanders from secondhand e-cigarette vapour is extremely low and insufficient to justify prohibiting e-cigarettes. This evidence should inform risk assessments.

That finding does not confer a right to ENDS use in any indoor space. Instead, it suggests that the property's owner or manager should determine the policy, taking sound policy guidance into account.[77]

5.10 Protecting youth

Protecting youth. The aim of preventing youth uptake drives much ENDS policy. This aim must be placed in perspective with competing aims, including reducing adult smoking (which also has significant benefits to youth), preventing youth uptake of cigarettes, and allowing young people to switch later if they make an initial decision to smoke. Youth-oriented ENDS policies should focus on five main elements:[78]

1. ***Keeping the market mainly legal:*** regulators should aim to meet much larger legitimate adult demand without imposing excessive restrictions that trigger uncontrolled illicit trade. A large illicit market is the worst outcome for young people: it will supply any illicit product to anyone, regardless of age, and engage young people in criminal supply, introducing them to criminal networks. The focus of regulation should be on consumer protection (safety standards, product quality, accurate labelling, risk communication), which increases users' confidence in switching from smoking to ENDS. Policymakers should be cautious about regulations that aim to force behaviour change (e.g., prohibitions, product limitations, limits on access via prescription or pharmacy, taxes). This type of regulation generates a range of unintended consequences as people exercise their autonomy and respond in ways that undermine the policy goal
2. ***Candid risk communication***: Most of the control over youth risk behaviours will be self-imposed by young people acting in their own interests. Good information from trusted sources will help young people and adults make good decisions, if they want to. Being honest and respectful about the consequences of ENDS use, but without exaggeration or hyperbole, which are likely to be ineffective and degrade trust. Adults and young people must receive the same basic messaging. A good example from the U.K. National Health Service is included below.

3. ***Age-secure retailing****:* It should be difficult for young people to access any tobacco or nicotine products, though it is inevitable that some will. This means using age restrictions (up to 21), age-verification technology (that does not create an impediment to purchase and use by adults), proportionate fines and licensing, and the threat of suspension or closure. It is essential to recognise the limitations in this context, where informal economies, street traders, and limited enforcement capabilities coexist – but the alternative is illicit supply.
4. ***Control of youth-themed marketing***: The ENDS marketing proposition should not be youth-oriented (i.e. cartoons, frivolous branding, bright colours, provocative or ironic language), and a range of principles should govern advertising, promotion, and sponsorship, as well as be extended to product branding and packaging. As far as possible, this should be enforced through an industry code of marketing practice, supported by retailers, backed up by law and enforced by Trading Standards.
5. ***Control of flavour descriptors***: flavour descriptors are a particular case of marketing and branding. ENDS flavours can be conceptualised in three ways: (i) a chemical recipe, (ii) a sensory characteristic ("apple", "mint") or (iii) a descriptor and branding, including cartoons or images. Control over chemical recipes should only focus on product safety. There is no basis to allow some flavour characteristics but not others, or to permit only the flavours that users do not want. However, there is a good argument for controls over *flavour descriptors and branding*, as with other forms of marketing.

5.11 Risk proportionate regulation

The right overall approach: risk-proportionate regulation. The aim of tobacco and nicotine policy should be to realise the vast benefits of displacing cigarettes with far less risky products. Advocates of tobacco harm reduction are not opposed to the regulation of safer alternatives to nicotine. The table below provides an overview of a risk-proportionate regulatory system.

An outline of a risk-proportionate regulatory system for tobacco and nicotine

Measure	**Cigarettes, hand-rolling tobacco, and other combustibles**	**Vaping, heated and smokeless tobacco and oral nicotine**
Overall aim	Reduce appeal and deter use	Consumer protection
Taxation	Relatively high taxes	Low or zero tax (sales tax only)
Advertising	Prohibit other than within trade	Control themes and placement
Warnings	Graphic warnings depicting disease	Messages encouraging switching
Public places	Legally mandated controls	Up to the discretion of the owner
Plain packaging	Yes	No. Controls on imagery and branding
Risk communication	Major risks to health	A far safer alternative to smoking
Age restrictions	No sales to under-21s	No sales to under-18s
Flavours	Ban characterising flavours	Control flavour *descriptors*
Product standards	Control risks and reduce appeal	Control safety risks to the user

The policy aim should be to take the toughest, most restrictive measures to address the risks of smoking to the user and bystanders. The regulation of safer nicotine products should focus on consumer protection (chemical, electrical, and thermal safety, and reliable information) and on limiting youth uptake through measures to ensure responsible supply, retailing, and marketing.

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