

Briefing: Nicotine for policymakers

Summary and key insights

- 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.

What is nicotine?

What is nicotine? Nicotine¹ 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 substance⁵, 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 dopamine⁶ 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.

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}

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.

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 nicotine¹⁰² 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.

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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