

Evolution of tobacco products: recent history and future directions

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ABSTRACT

Declines in cigarette smoking prevalence in many countries and the consolidation of the tobacco industry have prompted the introduction of other forms of nicotine delivery. These include electronic nicotine delivery systems (ENDS), heated tobacco products (HTPs) and oral nicotine products (ONPs). Evolving over time, some of these products now deliver nicotine at levels comparable to cigarettes and may serve as effective substitutes for smokers. However, certain products, especially ENDS like JUUL, have also appealed to youth and non-smokers, prompting concerns about expanding nicotine use (and potentially nicotine addiction). The tobacco industry could shift away from primarily promoting cigarettes to promoting ENDS, HTPs and/or ONPs, though at this time it continues to heavily promote cigarettes in low and middle-income countries. Differing regulatory regimes may place upward and downward pressures on both cigarettes and these newer products in terms of population use, and may ultimately drive the extent to which cigarettes are or are not displaced by ENDS, HTPs and/or ONPs in the coming decade.

INTRODUCTION

Current tobacco use has been declining globally, with 23.5% of adults currently using tobacco in 2018, down from 33% in 2000. About one-fifth (20.9%) are expected to be tobacco users by 2025.¹ Over 80% of tobacco users are cigarette smokers,¹ making cigarettes the primary mode of tobacco consumption, though a diverse range of other combustible and non-combustible products (eg, snuff, chewing tobacco, cigars, waterpipe, pipes, bidis, kreteks) is available. Contemporaneous with, and potentially driven by,² these declines in cigarette smoking is consolidation of the tobacco industry into a handful of global players—Philip Morris International (PMI), British American Tobacco (BAT), Japan Tobacco International (JTI)—and the introduction and marketing of other forms of nicotine delivery.

BRIEF HISTORY OF TOBACCO PRODUCT INNOVATION

The global declines in smoking present challenges to cigarette manufacturers, which have tried to adjust by developing or purchasing alternative products (smokeless, heated tobacco products (HTP), e-cigarettes) to which they can attempt to migrate their customers. These efforts, arrayed as a timeline in [figure 1](#), have met with a range of success and failure.

Electronic nicotine delivery systems

In 2007, a new type of product was launched for sale—electronic nicotine delivery systems (ENDS) (also called e-cigarettes or vaping products)—a class of products that commonly contain a battery that powers a heating element to aerosolise a liquid typically containing nicotine, flavourings and humectants.³ These products have changed substantially over the past decade, starting with disposable cigalikes that resembled a cigarette, then rechargeable devices with refillable tanks and more modifiability (eg, adjustable power) and, more recently, pod-style devices like JUUL. Originally marketed by Ruyan (later NJOY), the initial offerings were slow to capture market share, but interest in ENDS rose with the marketing of blu in 2009.^{4–8} JUUL launched in 2015 and quickly became the predominant ENDS brand in the USA. In 2019, Altria purchased a stake in JUUL.^{9–10} ENDS are now the second most common tobacco product in the USA, with 4.5% of adults reporting current use.¹¹ Similar prevalence has been observed in Europe, though regional differences exist, such as higher prevalence in Eastern than Western Europe.¹² ENDS use is less common in Asia than in these other regions, with current use around 1.8% in China.¹³ ENDS also have emerged in South African market.^{14–16} ENDS use prevalence is even lower in some low and middle-income countries (LMICs) such as Bangladesh and Zambia.¹⁷ WHO recommends that ENDS be regulated to bar unproven health claims, minimise health risks, protect non-users from second-hand exposure and prevent initiation among youth (eg, by limiting advertising/sponsorship, restricting flavours), though the legal and regulatory status of these products differs widely by country. At present, 32 countries have barred the sale of ENDS, and a further 79 have enacted at least one regulation (such as use in public places, restrict advertising or include health warnings).¹⁸ For example, non-prescription ENDS with nicotine are illegal in India, Japan, Chile, Australia, among other countries. In the European Union (EU), the Tobacco Products Directive regulates the nicotine concentration (20 mg/mL maximum), liquid container volume and packaging and labelling requirements of ENDS.¹⁹ In the USA, ENDS manufacturers were required to submit premarket tobacco applications in 2020, which the Food and Drug Administration (FDA) will evaluate and use to decide whether specific vaping products should remain on the market or be removed. Publicity surrounding JUUL's appeal to youth coupled with rising youth ENDS use in the USA has led to federal, state and local restrictions



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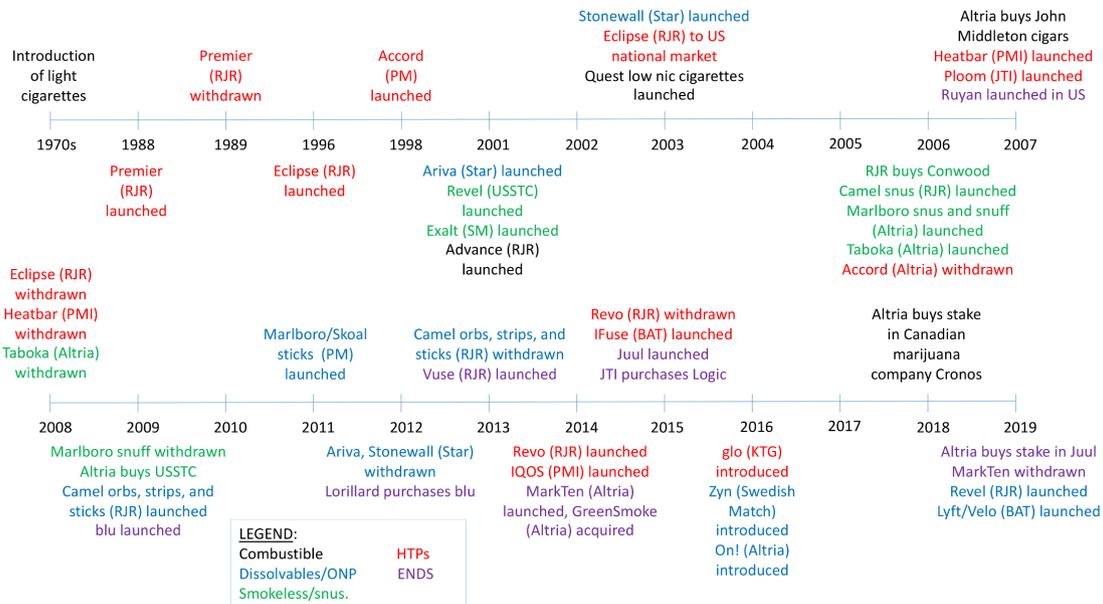


Figure 1 Timeline of new product introductions by the tobacco industry, 1970–2019. BAT, British American Tobacco; ENDS, electronic nicotine delivery systems; HTP, heated tobacco product; JTI, Japan Tobacco International; ONP, oral nicotine product; PM, Philip Morris; PMI, Philip Morris International; RJR, RJ Reynolds; SM, Swedish Match; USSTC, US Smokeless Tobacco Company.

on the sale of flavoured ENDS that appear to have reduced JUUL's overall market share and opened the door for competing products such as Puff Bar. Better monitoring of the market for these newer products is needed for tracking the industry's strategy of substituting use of these products in place of tobacco product use cessation.

Heated tobacco products

The class of HTPs, which generally heat tobacco to temperatures below combustion to generate a nicotine-containing aerosol, dates back to the introduction of Premier by RJ Reynolds (RJR) in 1988.²⁰ Lighting the charcoal tip generated heat which, when passing down the rod, formed an aerosol that released flavour and nicotine from flavour beads and a small amount of tobacco. Premier was a market failure and was withdrawn from the market in 1989.²¹ Eclipse,²² a redesign of Premier, emerged in 1996. Accord, marketed by Philip Morris (PM) in 1998, was a new design with an external heat source into which the user inserted small cigarettes with a specially formulated reconstituted tobacco mix.²³ These two approaches to HTP technology, charcoal tip and external heat source, would serve as the basic designs for Revo,²⁴ launched by RJR in 2014 and withdrawn in 2015; Heatbar,²⁵ introduced by PM in 2007 and withdrawn in 2008. These early models were withdrawn from the market within a few years of their introduction.²⁶ In more recent years, newer HTPs were met with greater receptivity among smokers, such that JTI's Ploom (launched in 2007), Philip Morris International (PMI)'s IQOS²⁷ (launched internationally in 2014 and in the USA by Altria in 2020), BAT's iFuse (launched in 2015) and KTG's glo (launched in 2016) have been able to capture a substantial global market, primarily in the WHO Western Pacific Region.^{28–29} Generally, HTPs are most popular in some Asian countries, followed by parts of Europe, USA and other regions. Current HTP use rose in Japan from 0.2% in 2015 to 10%–15% in 2019,^{30–32} and 4.4% of adults in Korea currently use an HTP.³³ Prevalence has been lower across European countries (eg, 0.1% current users in 2016–2018),³⁴ but seems to be increasing in select markets (eg, 1.1%—Italy 2019³⁵; 1.2%—England³⁶).

Current use prevalence was below 1% in other countries such as the USA, Canada and Australia,³⁶ though other estimates demonstrated current use in the USA at 1.1% in 2017, up from 0.5% in 2016.³⁷ There is limited evidence, primarily around awareness, in Mexico and Guatemala.^{38–39} The particular popularity in Japan may be ascribed to ENDS being significantly restricted in that market. In the USA, IQOS has been authorised as a modified risk tobacco product under an exposure modification order.⁴⁰ In the EU, HTPs are regulated under the Tobacco Products Directive as a novel tobacco product.

Oral tobacco products and oral nicotine products

Nicotine can be delivered in non-combusted forms, and oral delivery has been a common method, including chewing tobacco and moist snuff as used in North America, Scandinavia, Asia and Africa. For purposes of this paper, we use oral tobacco products (OTP) to refer to products that contain cut tobacco leaf material (eg, snus) and oral nicotine products (ONP) for products that do not (eg, dissolvable tablets). Smokeless tobacco (ST) companies have attempted to expand their segment of the nicotine product market—OTPs targeted toward smokers. In 2001, Swedish Match launched Exalt⁴¹ and the US Smokeless Tobacco Company (USSTC) launched Revel,⁴² both portioned snus products to try to appeal to tobacco users who were not attracted to traditional smokeless tobacco. Seeing an opportunity, US cigarette companies began to either purchase smokeless tobacco companies or market their own smokeless products. In 2006, RJR purchased Conwood⁴³ and also began to market Camel Snus.⁴² PM, leveraging the popularity of Marlboro cigarettes, launched Marlboro Snus, Marlboro Snuff and Taboka (another form of snus),⁴² before acquiring USSTC. Early ONPs also began to emerge at this time, including the 2001 launch of Ariva, a dissolvable pellet, followed by Stonewall, a larger dissolvable pellet targeted at ST users. Ariva and Stonewall left the market in 2012.⁴⁴ PM⁴⁵ and RJR⁴⁶ also ventured into this market with Camel orbs, strips and sticks (compressed dissolvable tobacco shaped and similar in size to a toothpick) launched in 2009 and withdrawn in 2013, Marlboro/Skoal sticks launched in 2011 and

Revel (now Velo) nicotine lozenges in 2019.⁴⁷ ‘Tobacco-free’ ONPs are re-emerging in the USA and Europe.^{48–49} Examples of these products include ZYN (Swedish Match), On! (Altria) and Velo (RJR Vapor), among others. In Europe, 46 brands have been identified, with 27 new brands of nicotine pouches launching in 2020.⁵⁰ These products appear to fall outside the EU ban on snus and the existing Tobacco Products Directive. German regulators ruled that they were not permitted to be sold in that country. Few studies have been published recently on these products, though one report suggests low use prevalence in the Netherlands (<1%).⁴⁸ These products have also been marketed in Pakistan, Kenya and Tanzania, though data on uptake are not published.⁵¹ Pouches are not legal for sale in Australia (except by prescription) and are permitted in New Zealand.

ADDICTIVENESS AND APPEAL OF ENDS, HTPS AND ONPS

Nicotine delivery from ENDS, HTPs and ONPs

Nicotine is a volatile chemical that is the most abundant tobacco alkaloid and the main addictive component of ENDS, HTPs and ONPs. Nicotine can be absorbed buccally, in the upper airways and in the lungs.⁵² When inhaled from ENDS and HTPs, nicotine is effectively absorbed in the lungs where it rapidly enters the pulmonary venous circulation, passes through the heart, enters arterial circulation and moves across the blood–brain barrier. Although nicotine absorption from ONP through buccal cell membranes is rapid, the rise in the brain nicotine level appears to be slower than with inhalable products. Once in the brain, nicotine binds to nicotinic acetylcholine receptors leading to the release of multiple neurotransmitters (dopamine, norepinephrine, serotonin, gamma aminobutyric acid (GABA), glutamate and endorphins) in the central nervous system.⁵³ Dopamine is the predominant neurotransmitter released, and it is associated with pleasure and appetite suppression. The release of these neurotransmitters is critical in the reinforcing and dependence-producing effects of nicotine.⁵⁴

Inhaled ENDS and HTP emissions constitute an aerosol of liquid particles (liquid phase) suspended in air (gas phase). Design characteristics of ENDS and HTPs and user behaviours (such as puffing patterns) influence nicotine yield in an inhaled aerosol and its dose delivered to the user. For example, the nicotine yield in ENDS aerosols is determined by device power, nicotine concentration and type of solvent used. Although early generations of ENDS did not effectively deliver nicotine to users, newer generations were engineered and modified to produce more aerosol and a more consistent nicotine yield.^{55–56} Studies with newer ENDS have shown that those products can generate nicotine yields comparable to, and sometimes exceeding, the nicotine yield from one tobacco cigarette (1.76–2.20 mg).^{57–59} Industry-funded studies on novel ONPs suggest that those products deliver nicotine as quickly and to a similar extent as existing smokeless products.^{60–61}

The pH of inhaled aerosol generated from ENDS and HTPs plays a large role in nicotine bioavailability. Buccal absorption of nicotine from ONPs is also highly dependent on pH of the saliva. Since nicotine is a weak base (pKa=8.0), at a higher pH, a larger portion of nicotine is unprotonated (‘free-base’) and nicotine is more volatile.⁶² Because of higher pH, a significant proportion of nicotine is present in the gas phase of inhaled aerosol. This leads to increased absorption in the oral cavity and upper respiratory tract but also causes more irritation and sensation of the unpleasant taste of nicotine. With lower pH, more nicotine is present in the liquid phase of aerosol leading to limited absorption in the upper respiratory tract but also reducing harshness

and unpleasant taste. This allows users to inhale deeply with less irritation⁶³ resulting in an increased lung deposition of the aerosol and enhanced absorption of nicotine through the lungs. Pod-based ENDS devices that were introduced in mid-2010s contain high concentrations of nicotine in its protonated form (nicotine salt liquid) which are lower in pH and consist of nicotine conjugated with a weak base (eg, benzoic acid, levulinic acid).⁶⁴ The addition of acid in nicotine salts allowed manufacturers to greatly increase the concentration of nicotine while avoiding harshness and bitterness.⁶⁵ For example, JUUL that contains 5% nicotine salt solution was introduced in 2015 and has since become the most popular ENDS brand available in the USA.⁶⁶ The availability of highly concentrated nicotine salt solutions seems to be an increasing market trend, as one recent report suggests that an online search showed more than 70 US ENDS brands containing more than 5% nicotine.⁶⁷

Consumer appeal of ENDS, HTPs and ONPs

Despite decades of research and development, the sensory properties of cigarette alternatives are still generally rated lower than cigarettes by smokers. For example, while HTPs, to some extent, suppressed urges to smoke,^{68–70} their sensory properties and ease of use are generally rated lower than conventional cigarettes.^{20–71–72} However, ENDS, HTPs and ONPs have common characteristics that may increase their appeal, particularly in high-income countries with well-established tobacco control programmes, including product regulation and public information about the risks of cigarette smoking. First, many newer products are perceived to have less severe risks than cigarettes,⁷³ making them potentially attractive to health-concerned smokers. However, consumers may falsely believe that such claims mean products are risk free or that exposure reductions can be achieved without completely quitting smoking.⁷⁴ Second, increasing restrictions on indoor use, sales, advertising and packaging have made cigarettes less attractive and convenient. For example, characterising flavours other than tobacco have been banned in cigarettes, but not in (most) other tobacco and nicotine products, in Europe, Canada and the USA.^{19–75}

While adults may use ENDS to quit or reduce smoking,^{73–76–77} adolescents and young adults often mention novelty and curiosity.^{76–78} Flavours, in particular, attract both youth and adults to use ENDS^{79–80}; they decrease harm perceptions and increase willingness to try and initiate the use of ENDS.⁸¹ Other attractive elements include variety and choice of feature (design, nicotine levels, adjustable device settings, producing ‘clouds’), packaging and price (especially relative to cigarettes), avoidance of smoking restrictions, positive sensory and other physical experiences, social acceptability and perceived safety for bystanders.^{76–78–80} Pod-style devices have become popular, especially among adolescents, with their attractive design, user-friendliness, less aversive vaping experiences, desirable flavours and discreetness.⁸²

Many of these observations about ENDS carry over to HTPs.^{26–29–74–83–84} Common terms used in marketing or promotion of HTPs include ‘reduced-risk’, ‘alternative’, ‘clean’, ‘smoke-free’, ‘innovative’, ‘chic’ and ‘pure’.^{72–84–86} HTPs are sold online and in concept stores (cf Apple stores) in high-end areas.^{87–91} HTPs in several markets are available in non-tobacco flavours.^{92–93} Other potentially attractive features of HTPs include less throat discomfort, appealing packaging, cleanliness, lack of ash and smoke and more social acceptability compared with smoking conventional cigarettes.⁷² Reported reasons to use HTPs are users’ health concerns, costs, enjoyment and satisfaction, ease of use, use practices and social aspects.^{94–95} Overall,

HTP's image is that of a high-demand, upscale product for tech-savvy users, rather different from the image of cigarettes.⁹⁰ The price of HTP tobacco inserts is similar to cigarettes,^{93 96} and the device is expensive.⁹⁰ Unlike cigarette packs (in markets where such labels are required), HTPs do not require graphic warning labels with explicit colour pictures as of yet.⁹⁰

ONPs have emerged relatively more recently, primarily marketed online as non-combustible alternatives for tobacco and nicotine products.^{97 98} Data on perceptions are limited, though a recent survey in the Netherlands showed that users perceived nicotine pouches as less harmful, but not less addictive than other tobacco and nicotine products, including cigarettes.⁹⁵ Nicotine pouches are available in fruit, mint and other flavours (eg, cinnamon and coffee),^{98 99} and they contain sweeteners.⁹⁸ Further, the product is perceived as an effective method to quit smoking, and it is easy and discreet to use, particularly in places where smoking is banned.⁹⁸ Reasons for use reported by ZYN users include reduced relative health risks, ease of use and discretion. Concerningly, 40% of never users were 'curious to see what it was like'.⁹⁸ The costs of the product are slightly lower or comparable to a pack of cigarettes in the USA.^{99 100} ONPs have the potential to displace traditional smokeless tobacco products, such as in South Asia and Africa, where they are newly marketed. Indeed, ONPs now account for approximately 4% of the total smokeless tobacco market in the USA.¹⁰¹

THE FUTURE OF TOBACCO AND NICOTINE PRODUCTS

The major multinational tobacco companies have converged on the theme of harm reduction^{102–107}; that is, moving away from combusted cigarettes and focusing on a 'smoke-free world'.¹⁰⁴ Indeed, PMI established an ostensibly independent foundation to promote the idea^{108 109} (though this foundation appears to be less independent than claimed¹¹⁰). Many leading tobacco companies have begun promoting ENDS, HTPs and ONPs that they claim to market toward smokers.^{102–107} Having learnt lessons from previously marketed products that were withdrawn, improving product appeal and expanding the market seem to be the companies' main priorities.^{102–107 111} For example, BAT plans to release Vuse Zero, an ENDS product with zero nicotine, and a variety of new strengths, flavours and formats (pouch, lozenge) for their ONP, Velo.¹⁰² In addition, they are developing a carbon tip HTP that will be known as Neo Core.¹¹¹ Similarly, PMI has four platforms of 'smoke-free' nicotine products encompassing both HTPs and ENDS designs.¹¹² Platform 1 is battery powered and heated with a ceramic heating blade (eg, IQOS and Marlboro Heatsticks).¹¹² PMI plans to expand their IQOS HTP product with the release of the IQOS ILUMA, an HTP product using Smartcore induction technology.¹⁰⁴ Platform 2 is heated with charcoal and does not require a battery source (reminiscent of RJR's Eclipse product from the late 1990s), which is planned to be branded as TEEPS.¹¹² The second two platforms are nicotine-containing ENDS that are battery powered and differ on the nicotine and heating source.¹¹² Platform 3 uses a nicotine salt and an electronically controlled heater (cf STEEM product).^{111 112} On the other hand, platform 4 uses an e-liquid (presumably free base) and an electronically controlled MESH heater, which reportedly remains in constant contact with the liquid to provide more consistent flavour.¹¹² The HTP-ENDS lines are beginning to blur as PMI promotes IQOS VEEV, an ENDS product.^{104 113} Though PMI is the least invested in the ONP product category, the PMI US subsidiary, Altria, did acquire the oral nicotine pouch, On!¹¹⁴

In addition to improving products, some companies plan to expand their market coverage. Tobacco companies strategically target various countries and populations with the most successful product. For example, Imperial plans to focus on marketing closed vapour products (ie, prefilled) in the USA, open vapour products (ie, refillable) in the UK and HTPs in Germany.¹⁰⁶ Meanwhile, Altria in the USA has marketed their HTPs, IQOS and Heatsticks within a number of US states.¹⁰⁷ IQOS is currently the only HTP approved for sale on the US market.¹¹⁵ However, there is currently a lawsuit in the USA, as well as in Germany, against PMI filed by BAT.^{115 116} Reynolds American, the US BAT subsidiary, claims that the heating technology used in IQOS is a patent infringement and is seeking an importation ban.^{115 116} They claim that PMI copied patented technology developed for BAT products, including Glo, Vuse Vibe and Vuse Solo.^{115 116} While the cases are ongoing, PMI argues that even if they are at fault, the USA should not exclude IQOS from the market because of the potential to reduce smoking.^{115 116}

The role of explicit harm reduction claims in transitioning smokers to other forms of nicotine delivery is yet to be determined. In the USA, eight snus products sold by Swedish Match were the first tobacco products to be authorised as modified risk tobacco products (MRTP).¹¹⁷ IQOS with Marlboro Heatsticks achieved a similar designation in 2020,⁴⁰ and applications are pending for Camel Snus, Copenhagen moist snuff and Moonlight low-nicotine cigarettes in the USA.¹¹⁸ As yet, no ENDS or ONPs have publicly confirmed submitting MRTP applications. ONPs, in particular, present an interesting challenge as they resemble pharmaceutical nicotine replacement products (NRT).¹⁰⁰ Superficially, oral nicotine lozenges may look like NRT lozenges, though they are often sold at higher concentrations (8 mg vs 4 mg) and with more attractive flavouring, marketing and packaging (and lacking NRT's extensive labelling of potential side effects or instructions for use). This blurring of lines may present regulatory challenges around when a product constitutes a drug. The emergence of products claiming to use synthetic nicotine also presents important questions around public perception and its impact on the regulatory process.^{119 120}

Policy developments may also intervene to shape the marketplace. For example, in April 2021, the Biden administration committed to removing menthol cigarettes (and cigars) from the US market and reintroduced plans to move forward a nicotine standard for cigarettes. This follows similar menthol bans in Canada,^{121–123} the EU and other countries.¹²⁴ Characterising flavours other than menthol have been banned in cigarettes in the EU since 2016 and menthol was added in 2020. A recent report by the Joint Action Tobacco Control concludes that menthol facilitates inhalation.¹²⁵ On this basis, some member states, such as Germany and Finland, currently prohibit use of menthol at any level (not just as a characterising flavour) based on its inhalation facilitating properties. Other tobacco products, such as cigars, cigarillos and snus, are exempt from this ban, though member states are increasingly banning flavours in ENDS. Menthol bans may shift smokers toward HTPs, ENDS or ONPs, particularly if such regulations do not apply to these products. Regulatory activities around new products have on occasion led to litigation—WHO in 2021 identified over 80 such cases.¹²⁶ Overall, WHO notes that manufacturers may challenge whether existing laws apply to their product; attempt to carve out, or have their products fall into, regulatory loopholes; and appeal to relative risk (compared with cigarettes) as a rationale to allow marketing.¹²⁷ Products claiming to contain synthetic nicotine (as opposed to nicotine derived from tobacco) have emerged in the past 2–3 years, largely in response to specific

regulatory decisions as to what constitutes a tobacco product (eg, US FDA). Depending on how the courts rule on such claims, this may present an ongoing challenge to regulation of nicotine-containing products, and testing the provenance of nicotine may become a necessary part of the regulator's toolbox.

Just because cigarette smoking is declining in high-income countries, or among high-income and educated individuals within countries, it does not mean global tobacco control is finished—cultural, regional and socioeconomic differences in tobacco use must be considered. ENDS, HTPs and ONPs are marketed primarily in high-income countries, while tobacco products such as cigarettes remain heavily promoted in LMICs.^{128 129} An important question moving forward is the extent to which ENDS, HTPs or ONPs could be attractive to users of non-cigarette, combusted tobacco products (cigars, pipes, waterpipes, bidi, kretek) and users of traditional higher nitrosamine smokeless tobacco products. This is of particular interest in markets with high use of such products (eg, India, Indonesia, Eastern Mediterranean) where their use presents a significant population health risk. It is unclear which costs, appeal or regulatory structures would create barriers to the adoption of ENDS, HTPs or ONPs in LMICs. Different orientations to policy and reasoning—harm reduction versus precautionary principle—can also inform regulatory approaches. Advocates and regulators may have priority populations or specific areas of concern—smokers versus younger people; youth addiction versus adult chronic disease outcomes; cancer versus cardiovascular disease risks (which have different dose–response effects). One country, for example, may prioritise keeping novel products out of the marketplace to forestall the expansion of overall tobacco use, while another may lower barriers to entry as part of an overall strategy to reduce smoking specifically. In either case, mechanisms for removing specific products from the market if they prove problematic should be employed as a regulatory tool.

KNOWLEDGE GAPS AND RECOMMENDATIONS FOR FUTURE RESEARCH

A key question over the next decade is how best to study such a vast and evolving marketplace. Research on specific products to aid decision makers and regulators is lacking, and such research is also difficult to undertake as products continue to evolve in design, marketing and use. Data gathering and surveillance approaches need to evolve and adapt. Anticipation (ie, what product is 'the next JUUL?') can benefit the field—the development of an early warning system, akin to structures used in drug abuse to identify misuse of medications, may be necessary. Engaging strategies used in marketing (eg, trend watching), surveillance of social media and search trend analysis also may prove valuable.^{130–132} More rapid surveillance is critical—large, national surveys with cumbersome systems for adding or changing questions are too slow to provide timely data on an actively changing marketplace. This could be particularly challenging for LMICs with limited resources for surveillance or research, and an area for technical assistance from higher income countries, civil society or WHO.

Further, the questionnaires we use and how we conceptualise tobacco use are often derived from cigarettes (eg, smokeless tobacco and early ENDS dependence questionnaires were adapted from cigarette dependence measures).¹³³ This may also need to change, as the use of new products may not be comparable—we see this already with ENDS that are puffed throughout the day rather than in discrete bouts.¹³⁴ The growth of polytobacco use (ie, regular concurrent use of two or more

tobacco products) further complicates studying product use—asking about use behaviours for three products within a survey can be time consuming, but ignoring quantity and frequency of use of multiple products within individuals may present a misleading picture of tobacco use in the population. Established knowledge and methods for cigarettes often drive content and emissions research, so new toxicants can be missed (ie, we may not know what to look for). Thus, untargeted screening is needed to address products with potential for novel contents and emissions.

Finally, with the increasing integration of technology into the tobacco market (eg, heating and vaping devices that may have Bluetooth capabilities), the collaboration of tobacco regulators with regulators of other consumer goods, as well as consideration given to potential issues of data privacy and security, may be required. Understanding how a product uses technology to interact with the product user (eg, data gathering, retention and storage; location tracking and geofencing; product 'learning') would be important for regulators to understand.

CONCLUSION

The global market in tobacco is complex, changing and expanding. Even though many tobacco companies are looking to a 'reduced-harm' future by marketing alternative nicotine sources to smokers, that is not to say that these companies are giving up on the cigarette market. JTI states that they '... believe in the freedom of adults to choose'.¹⁰⁵ In addition, Imperial Tobacco, BAT and JTI have shown revenue growth with their cigarette brands and do not appear to have plans to move to a cigarette-free future as companies such as Altria, PMI and Swedish Match have explicitly claimed.^{102 105 106} There is a fundamental need to study the impact of new and emerging products on population health in the context of different regulatory environments and across countries where the tobacco epidemic is at different stages. Full implementation of the Framework Convention on Tobacco Control (FCTC) and guarding against tobacco industry interference are important considerations.

What this paper adds

What is already known on this subject

- ▶ Over the past decade, noncigarette forms of nicotine delivery have emerged, including electronic nicotine delivery systems, heated tobacco products, and oral nicotine products.
- ▶ Certain products, especially ENDS, have gained popularity, concerningly among youth.

What this paper adds

- ▶ Differing regulatory regimes may place upward and downward pressures on use of both cigarettes and newer products, and may ultimately drive the extent to which cigarettes are displaced.

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