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IM - REVIEW

Nicotine pouches: an aid in smoking cessation, or a new public health hazard?

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Abstract

Tobacco harm reduction strategies aim to reduce the devastating health burden of smoking by providing lower-risk alternatives to those unable or unwilling to quit combustible cigarettes. Nicotine pouches have recently emerged as a novel, tobacco-free oral product category, evolving from the concept of Swedish snus but eliminating the tobacco leaf entirely. This narrative review assesses the current scientific evidence regarding the chemical composition, toxicological profile, nicotine delivery and smoking cessation efficacy, and potential public health impact of nicotine pouches. Chemical analyses and biomarker studies consistently demonstrate that these products occupy the lowest end of the toxicant risk continuum, with harmful constituents such as tobacco-specific nitrosamines being largely undetectable or present at negligible levels compared to snus and combustible cigarettes. Consequently, smokers who switch to nicotine pouches experience reductions in toxicant exposure comparable to complete smoking cessation. While specific long-term epidemiological data are currently unavailable, the extensive evidence on Swedish snus, which has not been linked to lung cancer or significant cardiovascular disease, provides a compelling "bridging" argument for the safety of these tobacco-free derivatives. Still, product-specific research and epidemiological surveillance is needed to confirm their long-term safety/risk profile, and healthcare professionals should consider recording the use of nicotine pouches in the medical history of patients. Furthermore, pharmacokinetic profiles suggest that modern pouches can deliver nicotine efficiently enough (although at a much slower rate than smoking) to alleviate cravings and displace combustible tobacco. There are some regulatory challenges that need to be explicitly addressed concerning labeling consistency, flavoring additives, and maximum nicotine limits. Current population data suggest they are unlikely to become a gateway to smoking, but continuous monitoring is warranted. In conclusion, nicotine pouches could represent a promising harm reduction tool with a risk profile likely adjacent to pharmaceutical nicotine replacement therapies, and could be considered by clinicians as substitutes for smoking in smokers unable or unwilling to quit with currently approved methods.

Keywords Smoking · Nicotine · Tobacco · Nicotine pouches · Tobacco harm reduction

Introduction

Smoking remains a substantial global public health concern and the leading cause of preventable death. According to the World Health Organization (WHO), tobacco kills more than 8 million people each year [1]. Despite decades of anti-smoking initiatives, it is estimated that there are still approximately 1.3 billion tobacco users worldwide [2]. If current trends continue, the death toll is projected to rise, with a significant burden falling on low and middle income countries. In the United States, cigarette smoking is responsible for more than 480,000 deaths annually, including nearly one in five deaths [3]. Similarly, in the European region, tobacco use remains the single largest avoidable health risk [4]. Consequently, intensive tobacco control efforts to reduce uptake and convince established smokers to quit have been undertaken over the past decades.

Tobacco control measures, including campaigns, heavy taxation, smoking restrictions, and organized smoking cessation services have been used widely for many years. Acknowledging the global burden of smoking, in 2005 the

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Framework Convention on Tobacco Control (FCTC) came into force, with the main goal of providing guidance and evidence-based strategies to reduce tobacco demand and supply. The MPOWER represents a comprehensive package of six high-impact, cost-effective tobacco control measures designed to help countries implement the FCTC: Monitor tobacco use and prevention policies, Protect people from tobacco smoke, Offer help to quit, Warn about the dangers, Enforce bans on advertising, promotion and sponsorship, and Raise taxes [5]. Although these efforts have substantially reduced smoking prevalence in many high-income countries, the decline has slowed in recent years, and smoking remains a persistent public health crisis in many regions of the world.

Smoking-cessation pharmacological interventions have been available for decades. Initially, nicotine replacement therapies (NRTs) such as gums and patches were developed, and subsequently oral medications such as bupropion, varenicline and cytisine became available. While these medications increase the odds of smoking cessation compared to placebo and are generally considered safe [6–8], their real-world success rates remain modest. Nicotine replacement therapies, for instance, often demonstrate low long-term abstinence rates, partly because they fail to replicate the pharmacokinetic delivery profile and the sensory rituals associated with smoking [9, 10]. Consequently, a substantial proportion of smokers fail to quit using approved pharmaceutical aids, leading to a growing interest in the strategy of tobacco harm reduction. Added to this, many smokers are reluctant to ask for professional help and use smoking cessation medications.

Harm reduction is a strategy of reducing the adverse health consequences of recreational drug use, or any other risky behavior, to those who cannot or are not willing to achieve complete abstinence. A harm reduction strategy for smoking has been proposed for decades, related to the use of lower-risk alternatives to combustible cigarettes. The basis for this approach relies on the observation that while nicotine is the dependence agent, it is the combustion process and the inhalation of smoke that are responsible for the vast majority of smoking-related diseases [11]. A strong proof of concept exists in Sweden, where the widespread use of snus (a pasteurized oral tobacco product) among men has replaced cigarette smoking. As a result, Swedish men have the lowest rates of tobacco-related mortality and lung cancer in Europe [12, 13]. This phenomenon is confined to men because of the lower and slower adoption of snus among women, who have higher smoking rates in Sweden compared to men. However, unlike pharmaceutical NRTs, tobacco harm reduction products often face regulatory hurdles and skepticism within the public health community.

Nicotine pouches are a relatively new category of oral nicotine products that have evolved from the concept of Swedish snus but differ in a fundamental way: they are tobacco-free. The precursor of nicotine pouches can be dated in a patent applied in 1993 by a pharmaceutical company, which involved creating a powdery composition comprising nicotine incorporated in degradable starch microspheres that could be delivered both nasally and orally [14]. However, the first patent that presents nicotine pouches in their current form was submitted in 2003, presenting a nicotine-containing particulate material comprising a microcrystalline cellulose into which nicotine or a pharmaceutically acceptable salt, complex or solvent can be incorporated [15]. The first product was registered in 2008 as a nicotine replacement therapy. In the United States, tobacco-free nicotine pouches became available in 2016 [16]. Like snus, they are placed under the upper lip, between the lip and the gum, with nicotine being absorbed through the oral mucosa. They were developed to provide the nicotine delivery and sensory experience of snus without the inclusion of tobacco leaf, thereby potentially eliminating tobacco-specific impurities. Since their wider market introduction in the late 2010 s, the popularity of nicotine pouches has grown rapidly, particularly in the United States and Europe.

This rapid expansion has resulted in a heated debate about the potential public health effects of nicotine pouch use. One part of the public health community views nicotine pouches as a promising evolution of harm reduction—a product likely cleaner than snus and infinitely safer than combustible cigarettes—that could accelerate the obsolescence of smoking [17]. Another part considers them a new threat, raising concerns about the wide variety of flavors appealing to youth, the potential for nicotine dependence in non-users, and the lack of long-term epidemiological data [18, 19]. These contrasting views are similar to those expressed for e-cigarettes [20]. The present analysis will discuss the main factors that determine the public health impact of nicotine pouches and present a brief overview of the evidence related to each factor: (1) their safety/risk profile, both relative to smoking and in absolute terms; (2) their potential effectiveness in smoking displacement; and (3) the patterns of use by different population subgroups, specifically focusing on youth uptake and use by never-smokers. Finally, the review highlights the clinical utility of these findings for internal medicine and primary care practitioners, offering practical considerations for counseling smokers regarding relative risk, dosing safety, and the avoidance of dual use.

Factors determining the public health impact of nicotine pouches

The overall influence of nicotine pouches on population health is complex, relying on the interplay between benefits for existing smokers and potential risks for non-users (Table 1). To quantify whether the introduction of these

Table 1 Main factors determining the public health impact of nicotine pouches

Factor	Description and public health implication
Relative risk profile	The magnitude of harm reduction compared to combustible cigarettes. Given the absence of combustion and tobacco leaf, pouches must demonstrate a toxicological profile significantly lower than smoking to provide a public health benefit for switchers
Absolute risk profile	The potential health risks posed to a user compared to not having smoked. While expected to be low, it dictates the net harm if adopted by never-smokers
Smoking cessation effectiveness	The ability of the product to substitute combustible cigarettes. This depends on: Pharmacokinetics: Can it deliver nicotine fast enough (T_{max}) and in sufficient quantity (C_{max}) to relieve cravings? Sensory experience: Mouthfeel and flavor satisfaction. User acceptability: Ease of use and social acceptability
Uptake by non-smokers	The prevalence of use among those who have never smoked or would not have initiated nicotine use otherwise (never-smokers and youth). High uptake in this group reduces the net public health benefit
Gateway vs. Diversion	Gateway Effect: The risk that pouch use leads to nicotine addiction and subsequent transition to combustible smoking. Diversion Effect: The potential for pouches to steer youth or curious non-users away from combustible cigarettes, acting as a "firewall" against smoking initiation
Dual use	The pattern of using both pouches and cigarettes. No benefit: If used only to cope with temporary smoking bans (bridging) without reducing overall smoke intake. Beneficial: If used as a transitional phase leading to reduced smoking intensity and eventual complete cessation

products results in a net gain or loss for public health, one can apply the following formula [20]:

$Public\ health\ impact_{NP} = (hazard_{SM-NP} \times smoking\ cessation) - (hazard_{NP} \times use\ among\ non-smokers) - (hazard_{SM} \times smoking\ initiation)$.

Where: *NP* Nicotine Pouch, *SM* Smoking, $hazard_{SM-NP}$ The difference in hazard between smoking and using nicotine pouches.

The first component of the equation ($hazard_{SM-NP} \times smoking\ cessation$) represents the potential public health gain. Perhaps the most critical variable for any smoking substitute is the relative toxicity and risk profile. It is well-established that the combustion of tobacco generates thousands of chemicals, with over 70 distinct carcinogens identified in cigarette smoke [21]. This process is the primary driver of smoking-related morbidity, including cardiovascular disease, chronic obstructive pulmonary disease (COPD), and various malignancies [22–26]. Consequently, complete smoking cessation, by removing exposure to these toxins, significantly reduces mortality risk, even as a secondary preventive measure [27–33]. Therefore, the relative risk of nicotine pouches compared to smoking is a crucial aspect in estimating their public health effects.

Another important factor, incorporated in the first component of the equation, is the smoking cessation effectiveness of nicotine pouches. If the product is not an effective substitute, or if it merely supplements smoking without leading to cessation (dual use) or substantial smoking reduction, the positive value of this factor diminishes. While quitting smoking has strong benefits, there is extensive evidence that a substantial proportion of smokers who develop smoking-related disease fail to quit after their diagnosis, or subsequently relapse [30, 34–38] While reduction in smoking consumption (cutting down) may offer some individual benefit, it is difficult to quantify at the population level and is therefore omitted from this simplified formula for clarity, focusing instead on complete cessation.

The second component ($hazard_{NP} \times use\ among\ non-smokers$) represents the primary subtractive factor: the direct risk to new users. Nicotine pouch use is an oral habit that can create dependence. If these products are adopted by individuals who never smoked and never would have smoked, any health risk associated with the pouches—however small—represents a net increase in public health harm compared to previous total abstinence. Therefore, monitoring the prevalence of use among never-smokers is critical in determining this variable. This applies particularly to youth. However, this parameter involves another aspect: whether some never smokers who start using nicotine pouches would have smoked had pouches not been available. Such a possibility exists mainly for young people, and is difficult to directly quantify.

The third component ($hazard_{SM} \times smoking\ initiation$) accounts for the "gateway" hypothesis. This variable considers the possibility that nicotine pouches might serve as an entry point to nicotine dependence for non-users, who subsequently transition to combustible tobacco use. If pouches would act as a catalyst for smoking initiation for a substantial proportion of users, particularly among youth, the high hazard associated with smoking ($hazard_{SM}$) would heavily weight the equation toward a negative public health outcome. Importantly, this component is valid if there is a direct, causal link between pouch initiation and subsequent smoking, which is the core definition of the "gateway" theory. Conversely, if pouches act as a "diversion", steering

curious adolescents away from combustible cigarettes, this term would be negligible or potentially inverted [39].

Consequently, the total public health impact is not determined solely by the product's chemical profile but is equally dependent on behavioral patterns: whether the product is successfully targeted at current smokers or if it inadvertently recruits non-smokers into the landscape of nicotine, and/or causes subsequent tobacco cigarette use. A review of all the factors that need to be examined when assessing the public health impact of nicotine pouches is shown in Table 1.

Safety/risk profile of nicotine pouches

Nicotine pouch composition

To accurately assess the health impact of nicotine pouches, their safety profile must be evaluated in comparison to combustible cigarettes (relative risk) and in isolation (absolute risk). Currently available evidence focuses mainly on the chemistry, toxicology, and acute physiological effects of these products, due to their recent introduction to the market.

Nicotine pouches are fundamentally tobacco-free products consisting of a fiber pouch containing a nicotine-infused matrix. The base materials vary somewhat across products but consistently include cellulose-derived components. Other compounds include water, humectants, sweeteners, pH adjusters such as carbonates and bicarbonates, and, of course, nicotine [40, 41]. The inclusion of alkaline agents is important, as higher pH levels facilitate the deprotonation of nicotine, thereby increasing its bioavailability and absorption rate through the oral mucosa [42]. Unlike traditional smokeless tobacco, the nicotine used in these pouches is pharmaceutical-grade, usually derived from tobacco (although it can also be synthesized in a laboratory), and is free from tobacco leaf and its associated impurities. Nicotine content varies significantly between products. A study by the United States CDC examined 37 products from six manufacturers and found the total nicotine content ranging from 1.29 to 6.11 mg/pouch, with free-base nicotine constituting 7.7−99.2% of the total content [42]. Another study examining 46 nicotine pouches (including two nicotine-free pouches) from the German market measured up to 47.5 mg nicotine per pouch, with the median value being 9.48 mg/pouch and the median proportion of free-base nicotine being 86% [43]. Moisture measurements also show dramatic variation between products, with ranges from 1.12 to 47.2% reported in one study and up to 50% in another [40, 42]. There seems to be dry and moist variants of nicotine pouches, with moisture content in products of the same brand ranging from 3 to 37% [41].

Chemical analyses have consistently demonstrated that nicotine pouches occupy the lowest end of the tobacco/nicotine product risk continuum [40]. Comprehensive studies characterizing the chemical composition of these products have found that they contain no detectable levels of most harmful and potentially harmful constituents (HPHCs) found in cigarette smoke. While some analyses have detected trace amounts of substances, such as formaldehyde, and metals such as chromium, the levels are generally comparable to or lower than those found in medically licensed NRTs and significantly lower than in Swedish snus [40, 41]. Crucially, levels of tobacco-specific nitrosamines (TSNAs)—potent carcinogens abundant in cured tobacco—are either undetectable or present at negligible amounts in nicotine pouches [40, 43]. A German study identified TSNAs in 26 of the 44 nicotine-containing pouches tested [43]. However, the levels were either below or close to the quantification limits. The highest measured concentrations of NNN and NNK were 13 ng and 5.4 ng/pouch, respectively, which were lower compared with tobacco cigarettes and snus [44, 45]. Even compared to Scandinavian snus products that follow the GothiaTek standard in the manufacturing process, a standard which particularly focused on reducing TSNA levels [46], nicotine pouches contained lower levels [41]. Such levels were similar to nicotine gums and e-cigarettes [47–50], suggesting that the use of pharmaceutical grade nicotine is a major step in removing these harmful compounds, and should be the standard for all nicotine pouches.

In vitro studies

Across multiple in-vitro toxicological assessments, nicotine pouches consistently show far lower biological activity than cigarette smoke. Miller-Holt et al. and Keyser et al. [51, 52] found that nicotine pouch extracts produced minimal to no cytotoxicity, mutagenicity, or genotoxicity compared with cigarette smoke condensate. Bishop et al. examined the effects of a nicotine pouch product compared with a reference snus and a reference tobacco cigarette on viability, cell health markers, oxidative stress and genotoxicity using human oral fibroblasts (HGF) and human lung epithelial cells (H292) [53]. They found minimal effects of the nicotine pouch compared to the other products. In a broader pre-clinical assessment, Yu et al. [54] demonstrated that nicotine pouches generated substantially lower toxicity than both combustible cigarette smoke and traditional smokeless tobacco. Unlike a reference snus product, nicotine pouches were not found to induce oxidative stress, cell stress, protein and DNA damage, while limited signaling or inflammatory markers were induced [55]. One study reported some variability among products, with a cytotoxic response in two of the five nicotine pouches tested, and upregulation of interleukin 6 and heme oxygenase 1 gene expression in human gingival fibroblasts by one and three products, respectively [56]. Interestingly, toxicity was not directly dependent on

nicotine concentration or osmolarity, with flavorings being the likely culprit. Collectively, these studies support the conclusion that nicotine pouches present a significantly reduced in-vitro toxicological profile compared to tobacco cigarettes and, in many cases, snus.

Biomarkers of exposure

Obviously, clinical data are more important, considering the problems in translating in vitro findings into real world human effects. Biomarkers of exposure studies are essential because they give objective, human-relevant measures of the internal dose of HPHCs from different nicotine products, allow the comparison of exposures across product types much faster than waiting for disease outcomes, reveal which specific toxicants are (or aren't) reduced when smokers switch to alternative products, and provide actionable evidence for regulators and harm-reduction policy [57]. Such studies have demonstrated substantially reduced exposure to tobacco-related toxicants among nicotine pouch users compared to cigarette smokers. Exclusive nicotine pouch users showed 91% lower total NNAL levels, a key biomarker of tobacco-specific nitrosamine exposure linked to cancer risk, with levels being similar to former smokers not using any nicotine product [58]. Biomarkers of exposure to acrolein (3-HPMA), benzene (S-PMA), and 1, 3-butadiene (MHBMA) were also substantially reduced, by 78.8%, 97.2%, and 93.5% respectively. A study analyzing data from 4527 participants in the Population Assessment of Tobacco and Health (PATH) study wave 7, found that minor tobacco alkaloids anabasine and anatabine were 94 and 97% lower in exclusive nicotine pouch users than smokers, and lead exposure was significantly lower compared to both cigarette smokers and e-cigarette users [59]. They also had no significant differences in levels of metals or minor tobacco alkaloids compared to non-tobacco users. A randomized controlled trial of adults switching from cigarettes to nicotine pouches found that creatinine-adjusted total urinary NNAL and 18 of 19 other biomarkers of exposure (with the exception of nicotine equivalents) were significantly lower after 7 days of nicotine pouch use compared to continued smoking [60]. Geometric least-square means were reduced by approximately 42–96% across biomarkers compared to the smoking group, with reductions comparable to complete tobacco cessation. Biomarkers of potential harm also showed favorable profiles in nicotine pouch users compared to smokers [58]. Carboxyhemoglobin was, as expected, 46% lower in nicotine pouch users. White blood cell count, an inflammatory marker, was 19% lower. Fractional exhaled nitric oxide, which is typically suppressed in smokers due to subclinical airway damage, was 107% higher in nicotine pouch users. Other biomarkers of potential harm, mainly for the cardiovascular system such as sICAM-1 and 8-Epi-PGF2α, showed a trend toward lower levels compared to smokers, but did not reach statistical significance.

Oral health effects

Several studies have evaluated the effects of nicotine pouches on oral health. A randomized, open-label, parallel-group study, assigned adult smoking participants to ad libitum use of 2, 4, or 8 mg nicotine pouches or continuous smoking for 24 weeks [61]. The study documented a 20–28% reduction in gingival inflammation and a 23–30% reduction in gingival bleeding in pouch users compared to continuous smokers, as well as a 60% reduction in an index measuring the intensity and area of extrinsic tooth stains. Compared to snus use, which causes characteristic oral mucosal lesions known as snuff dipper's lesions [62], nicotine pouch use was associated with reduction in pre-existing lesions during a 6-week period [63]. Another study tested a novel nicotine pouch, with an impermeable barrier for protecting the gum to minimize direct gingival irritation, for 5 weeks in snus and regular nicotine pouch users [64]. They found reduced prevalence and severity of snus-related lesions, while gingival irritation was reduced by 90% and all three cases of self-reported gingivitis at baseline were eliminated after 5 weeks. A case series of four nicotine pouch users (two of whom were past smokeless tobacco users) and one smokeless tobacco user reported the presence of white lesions at the placement sites, and histopathological changes, mainly parakeratosis with acanthotic epithelium, intraepithelial and connective tissue edema and inflammatory infiltration [65]. Another study collected saliva from nicotine pouch users and found the presence of some periodontopathogenic bacteria [66]. Mallock-Ohnesorg et al. [67] tested the acute effects of using nicotine pouches for 20 min, with a nicotine content from 0 to 30 mg per pouch, in 15 cigarette smokers. They reported moderate mouth irritation with pouches containing 0 mg, 6 mg and 20 mg of nicotine, and strong irritation with the 30 mg sample. Finally, Dowd et al. surveyed 118 adult pouch users who self-reported adverse effects such as mouth lesions, upset stomach, sore mouth, sore throat, and nausea [68]. However, most participants were also smoking tobacco cigarettes, and more than half were using e-cigarettes. Thus, it is unclear whether these effects could be attributed exclusively to pouch use.

In general, currently available evidence indicates improvement in oral health parameters from using nicotine pouches compared to smoking and snus use, but also the possibility for pouches to cause acute and longer-term mucosal irritation when compared to non-use of any oral nicotine or tobacco product.

Epidemiological evidence

Epidemiological studies are necessary to examine whether the preferable toxicological profile and the reduced exposure to tobacco toxins are related to reduced risk for smoking-related disease. While such evidence is currently unavailable due to the recent marketing and availability of nicotine pouches, public health assessments can rely on a "bridging" rationale. This approach utilizes the extensive epidemiological data available on Swedish snus—a pasteurized, oral tobacco product—as a worst-case scenario proxy. The scientific justification for this comparison lies in the similarities in product design, pharmacokinetics, and usage patterns. Both products are placed between the lip and gum, deliver nicotine through the oral mucosa, and are used for prolonged periods. However, a crucial distinction exists: snus contains cured tobacco, which, despite rigorous processing standards (GothiaTek), still contains plant-based impurities, heavy metals, and low levels of TSNAs [46]. Nicotine pouches eliminate the agricultural residues and plant-specific toxins found in snus. Therefore, if the extensive data on snus demonstrates a low-risk profile compared to smoking, it is scientifically plausible to infer that nicotine pouches—which are chemically simpler and cleaner—would carry in a worst case scenario an equivalent, or, more likely, a lower risk.

Evidence regarding snus use and severe health outcomes is reassuring and provides a strong proof of concept for oral harm reduction. Concerning respiratory health, large-scale observational studies have consistently shown that snus use is not associated with an increased risk of lung cancer or chronic obstructive pulmonary disease, particularly for studies performed in Nordic countries, reflecting the lack of toxin inhalation from snus use [69–72]. Regarding cardiovascular disease, the data is more nuanced but generally favorable compared to smoking. While nicotine is a sympathomimetic agent that transiently increases heart rate and blood pressure, epidemiological data suggests that this does not translate into the same cardiovascular risk profile as smoking. Studies from Sweden have failed to identify any association between snus use and acute myocardial infarction [73, 74], with the authors concluding that toxic components other than nicotine appear implicated in the pathophysiology of smoking related ischemic heart disease. This conclusion was based on evidence that snus users obtain similar or even higher levels of nicotine compared to smokers, as shown by measurements of cotinine levels [75, 76]. In fact, one of the studies found a protective effect for fatal and nonfatal acute myocardial infarction among daily snus users, but a trend towards higher risk for fatal acute myocardial infarction, The higher case-fatality rate in users who do suffer a cardiovascular event, was also shown in another study [77], and this was also confirmed in a systematic review and meta-analysis [71]. A pooled analysis of eight Swedish prospective cohort studies including 130 485 men who never smoked found that the use of snus was not associated with an elevated risk of stroke, while no risk was found even among heavy users (using more than seven cans per week) or long-term users (more than 20 years of use), although case fatality was found to be higher [78]. Since nicotine pouches contain pure nicotine and no tobacco, the cardiovascular risk is expected to be no higher than that of snus. While the acute effects of snus use on blood pressure and heart rate appear to be similar to smoking and are attributed to nicotine, eight of the nine cross-sectional studies in Sweden comparing blood pressure in oral smokeless tobacco users and non-users did not find elevated blood pressure among snus users [76]. Concerning cancer, historically the main concern for oral products, partly relevant to the type and location of exposure, is oropharyngeal, esophageal and pancreatic cancer. However, modern Swedish snus, which has reduced TSNA levels, has demonstrated a radically different risk profile compared to traditional chewing tobacco or combustible cigarettes. A systematic literature review found that, compared to never tobacco users, snus use was not associated with elevated risk for most cancer sites after adjustment for smoking, including oropharyngeal cancer (RR 0.97, 95% CI 0.68–1.37) and esophageal cancer (RR 1.10, 95% CI 0.92–1.33) [79]. A pooled analysis of nine prospective cohort studies also did not identify an elevated risk for oropharyngeal cancer among snus users compared to non-users [80]. It should be noted that this contrasts with the effects of other oral tobacco products; for example, products available mainly in Southeast Asia such as gutkha and pan tobacco are associated with seven to nine-fold higher risk for oral cancer [81]. The evidence on oral cancer is reassuring considering that snus appears to induce more oral mucosal lesions than nicotine pouches, as mentioned above. Pancreatic cancer has historically been a concern with smokeless tobacco use. While earlier studies suggested a statistically significant association [82], more recent pooled analyses controlling for smoking history and alcohol consumption have found no significant link between snus use and pancreatic cancer, and concluded that tobacco smoke constituents other than nicotine or its metabolites may account for the relationship between smoking and pancreatic cancer [83]. While no link between snus use and colorectal cancer was observed, an increased risk specifically for rectal cancer has been reported [84]. Importantly, no risk for overall cancer has been observed among snus users [79, 85]. Another issue of concern is diabetes and metabolic syndrome. Smoking is a well-established risk factor for these conditions, and the risk may persist for up to 15 years after quitting [86]. There appears to be a dose–response relationship, with higher consumption or pack-years associated with higher risk [87]. Moderate snus consumption does not appear to be associated with an elevated risk for type 2 diabetes [86, 88, 89],

although high consumption may elevate the risk [90]. There is some evidence that snus use might be associated with increased body mass index and perhaps other measures of adiposity among young women and heavy-using young men, but no link was found with glycemic status or elevated blood pressure [91]. Furthermore snus use was associated with higher HDL levels compared to non-users of any tobacco product, but also with higher triglyceride levels [92]. Still, the latter were lower compared to smokers, and there was no indication that higher intensity of snus use led to a worse lipid profile or that discontinuation of snus use led to a better lipid profile. In fact, continued users had lower triglyceride concentrations than discontinued users [92].

Safety/risk profile summary

In summary, the cumulative evidence from chemical characterization, toxicological assessments, and biomarker studies places nicotine pouches at the lowest end of the tobacco harm reduction continuum, likely adjacent to pharmaceutical nicotine replacement therapies. By decoupling nicotine delivery from combustion, or any extend of thermal degradation, and the tobacco leaf itself, these products eliminate the vast majority of carcinogens and respiratory toxins associated with smoking, while also avoiding the agricultural impurities found in Swedish snus. Although they are not necessarily risk-free, the magnitude of any potential risks is substantially lower than that of combustible tobacco. Consequently, the potential public health benefit of nicotine pouches hinges not on their toxicity, which is minimal, but rather on their ability to be adopted by smokers as a viable substitute for cigarettes.

Smoking cessation and reduction vs. nicotine use and gateway to smoking

A major determinant of the public health effects of nicotine pouches depends on their ability to successfully compete with combustible cigarettes. For a product to serve as a viable smoking substitute, it must not only be less harmful but also sufficiently satisfying to displace the urge to smoke. Randomized controlled trials (RCTs) specifically assessing nicotine pouches for smoking cessation are currently limited compared to those for e-cigarettes. A recent systematic review identified seven trials with a total of 269 adult participants, indicating that all were small scale studies [93]. One of the studies examined nicotine pouches compared to nicotine gum for only 2 weeks with a purpose of reducing, rather than quitting, smoking [94], and another pilot study compared nicotine pouches, containing 4 mg of nicotine, with e-cigarettes and no intervention (control) for 8 weeks among 45 individuals of low socioeconomic status [95]. These studies did not find any statistically significant effect on smoking cessation, but the latter found a significant reduction in cigarette consumption. All other studies involved short-term use (from a few hours up to eight days) and assessment of urges to smoke, satisfaction and plasma nicotine levels, rather than the effects on smoking substitution [96–100]. RCTs are expected to have similar challenges as in the case of e-cigarettes, considering the availability of different flavors, nicotine strengths and product type (dry and moist variants). Still, they are necessary to establish a causal link between nicotine pouches and smoking cessation, but they should be performed in a more realistic setting, with freedom of product choice and frequency of use based on self-preference. Until appropriate RCTs become available, indirect evidence regarding the potential efficacy of nicotine pouches on smoking cessation or reduction can be drawn from pharmacokinetic profiles, consumer surveys, and the historical precedent of Swedish snus.

The primary limitation of traditional NRTs, such as gums and patches, is their inability to replicate the speed and magnitude of nicotine delivery (pharmacokinetics) of a cigarette. Smoking delivers a high amount of nicotine to the brain within seconds, providing immediate relief from craving. In contrast, NRTs typically provide a slower, lower peak of nicotine, which contributes to their modest real-world efficacy [101, 102]. Nicotine pouches have been designed to bridge this gap. Pharmacokinetic studies demonstrate that while the time to maximum concentration (*Tmax*) for pouches is slower than smoking, the maximum plasma concentration (*Cmax*) can match or exceed that of cigarettes, and is significantly higher and faster than that of a nicotine gum [98, 103]. Their nicotine delivery profile appears similar to snus [97, 103]. The delay in peak plasma nicotine concentration means that nicotine pouches lack the immediate satisfaction associated with smoking, which may limit their initial appeal to heavily dependent smokers seeking rapid relief. However, despite the slower absorption, studies indicate that pouches are more efficient and satisfactory than most traditional NRTs, but less satisfactory than smoking among smokers [97, 99, 104].

While data from long-term clinical trials are emerging, real-world population data can provide important information about the interaction between product availability and smoking on a population level. Such data on nicotine pouch use are still lacking, but the most robust evidence comes from the Swedish experience with snus. Echoing the concerns historically associated with snus, the growing availability of oral nicotine products raises public health issues such as a potential increase in the total prevalence of nicotine use, serving as a "gateway" leading non-users to subsequent combustible tobacco use, or hampering smoking cessation by fostering permanent dual use (using pouches in smoke-free environments while continuing to smoke elsewhere) rather than complete abstinence [105]. However, long-term

population data from Sweden strongly contradict these fears. In an analysis of over 60,000 participants, Ramström et al. found that the "gateway" hypothesis was effectively refuted [105]. Those who began daily tobacco use using snus were much less likely to subsequently take up smoking than those who had not, both among males (17.6% vs. 45.9%), and females (8.2% vs. 40.2%). This was confirmed in another study from Sweden [106]. Furthermore, rather than hindering cessation, the uptake of snus among established smokers was associated with significantly higher success rates in quitting smoking compared to those who did not use snus [105]. Finally, the data indicated that prolonged daily dual use is uncommon; instead, dual use appears to be a transient state that serves as a stepping-stone toward complete smoking cessation. Another analysis of seven Norwegian cross-sectional studies also found that dual use is often a transitional phase that leads to smoking reduction and eventually complete cessation [107]. This individual-level data is reinforced by macro-level trends: despite the high and stable prevalence of snus use, daily smoking rates in Sweden have continuously plummeted to record lows, a trajectory that is incompatible with a gateway effect. Therefore, if nicotine pouches mimic the behavioral trajectory of snus, they are likely to function as an "exit" from smoking rather than an entryway. In fact, a recent study on US adult smokers found that those who used pouches were significantly more likely to attempt to quit smoking and were successful in reducing their cigarette consumption [18].

In conclusion, while long-term clinical trial data are still maturing, the convergence of pharmacokinetic efficacy and extensive epidemiological evidence from similar products suggests a positive public health potential. Nicotine pouches appear to possess the necessary nicotine delivery profile to satisfy adult smokers, although the speed of delivery is lacking. Population-level data, particularly from Scandinavia, strongly indicate that such oral nicotine products function as an "exit" from combustible tobacco rather than a "gateway" to it. Consequently, current evidence supports the view that nicotine pouches could serve as a viable and effective tool for smoking cessation and reduction, potentially accelerating the decline of smoking prevalence without increasing the aggregate burden of tobacco-related disease. However, specific studies on nicotine pouches, as well as continuous monitoring of their use patterns, are needed in order to fully characterize their interaction with smoking.

Nicotine pouch use by population subgroups

Since nicotine pouches are intended to function as smoking substitutes, their public health impact is dependent on who uses them. Ideally, use should be concentrated among current and former smokers seeking harm reduction. Conversely, high prevalence among never-smokers—particularly adolescents—could adversely affect public health due to the creation of new nicotine dependence, although the main effect for public health is coming from harm rather than dependence per se.

The global nicotine pouch market was estimated at approximately USD 5.4 billion in 2024, with projections to reach USD 25.4 billion by 2030 [108]. The US appears to be the largest market, accounting for more than 70% of the global market, followed by Europe [108]. A 183.7% increase in the nicotine pouch sales from September 2022 to September 2024 was reported in the US, with a respective increase of 207% from January 2023 to April 2025 [109, 110]. The monthly sales were estimated to be more than 1 billion units in May 2024, more than triple the corresponding sales in July 2021 [111].

While market data provide a more updated image of use trends, population surveys show that nicotine pouch use among adults remain relatively low. In the US, a large nationally representative study analyzing data from 2022 found that the prevalence of current nicotine pouch use among adults was only 0.4%, with 2.9% reporting ever use [112]. Daily use was estimated at 0.18%, with higher prevalence among males and non-Hispanic White participants [113]. Use was almost exclusively confined among people with a tobacco use history, but current and daily use of nicotine pouches was highest among adults who recently quit another tobacco product, particularly smokeless tobacco products and tobacco cigarettes [113]. Those reporting a past-year quit attempt were threefold more likely to be current nicotine pouch users compared to those who did not [113]. It should be mentioned that, the first market authorization for nicotine pouch products in the US by the FDA was granted in January 2025 [114]. In Poland in 2024, past 30-day use was reported at 4.3% [115]. Current smoking and ever use of e-cigarettes or heated tobacco products was associated with ever use of nicotine pouches, but no data was provided about factors associated with current use. In the UK, nicotine pouch current use was reported by 0.26% in 2021 but rose to 1% in 2024 and 2025 [116–118].

Nicotine pouch use among youth and young adults appears to be low. In the US, age group 18–24 years had the second highest use prevalence in 2023, according to one study, but current use was confined to 0.6% of participants [113]. The CDC reported that 1.8% of US youth reported current nicotine pouch use in 2024, with no change compared to 2023 [119]. Less than 30% of users reported frequent use (use for 20–30 of the past 30 days). Other studies in the US reported that the majority of youth and young adults using nicotine pouches also reported smoking tobacco cigarettes, but the surveys were performed in 2022 [120, 121]. More recent data come from the TEENS + study in the US, with the survey being performed between February

and June 2025 [122]. Current use was reported by 3.5% of participants aged 13–20 years and 5.8% of those aged 21–27 years. The vast majority (approximately 80% in both age groups) reported using at least one additional tobacco or nicotine product besides nicotine pouches [122]. In the UK, use rose from 0.7% in 2022 to 4.0% in 2025 in age group 16–24 years [117]. Another study from the UK specifically looking at age group 11–18 years reported a 1.2% current use rate in 2024 [118].

In conclusion, current epidemiological data indicates that nicotine pouches are primarily being adopted by the intended target population of adult smokers and recent quitters, supporting their potential role in harm reduction. However, the explosive growth of the market, coupled with emerging signals of increasing uptake among youth and young adults, necessitates caution and continuous monitoring. While prevalence among adolescents currently remains lower than that of e-cigarettes, and use is often linked to poly-tobacco and nicotine product consumption, the rapid upward trend in sales and the evolving product landscape require rigorous surveillance and preemptive regulatory intervention, including the strict implementation of sales bans to youth, as an essential measure. Such regulatory actions, as well as continuous monitoring of population use patterns and characteristics of users, are fundamental prerequisites for preventing youth initiation and preserving the harm reduction potential for adults..

Discussion

The present analysis highlights that nicotine pouches represent a significant evolution in the landscape of tobacco harm reduction, offering a potential substitute for combustible cigarettes that is likely far less hazardous. The synthesis of available evidence regarding their safety profile, efficacy in smoking cessation, and patterns of use among different population subgroups suggests a positive public health potential, provided that uptake remains mainly concentrated among current and former smokers. However, this potential is accompanied by some limitations, such as the speed of nicotine delivery, and distinct challenges, particularly regarding product standardization, labeling inconsistencies, and regulatory oversight. To fully understand the position of nicotine pouches in the harm reduction continuum, it is necessary to examine the specific findings regarding their chemical and toxicological profile, followed by an assessment of the regulatory measures required to mitigate potential emerging risks. An overview of these scientific findings, alongside the emerging regulatory challenges discussed below, is provided in Table 2.

The cumulative evidence presented in this analysis suggests that these products occupy the lowest end of the risk

Table 2 Overview of main findings and challenges in nicotine pouch research

Domain	Key findings & evidence	Challenges and regulatory needs
Chemical composition	Tobacco-Free: Composed of pharmaceutical-grade nicotine, fillers (cellulose), pH adjusters, and flavorings. Reduced Impurities: Most harmful and potentially harmful constituents (HPHCs) found in smoke are undetectable. TSNAs: Tobacco-specific nitrosamines are negligible or significantly lower than in Swedish snus	Inconsistent Labeling: Nicotine content is often vaguely characterized. Studies show arbitrary descriptors do not correlate with actual strength. Standardization: Need for harmonized labeling requiring the exact amount of nicotine per pouch to be stated on packaging
Toxicology & ingredients	Cytotoxicity: In vitro studies show minimal to no cytotoxicity or genotoxicity compared to cigarette smoke. Biomarkers: Users show significantly reduced levels of biomarkers for acrolein, benzene, and NNAL compared to smokers	Flavoring Safety: Some flavorings exceed EFSA Acceptable Daily Intake limits. Unauthorized food flavorings and impurities (e.g., myosmine) have been detected. Nicotine levels: Products with very high levels of nicotine, raising the possibility for acute intoxication
Clinical & epidemiological	Bridging Data: Long-term data from Swedish snus (a "worst-case proxy") shows no link to lung cancer or respiratory disease and minimal (if any) cardiovascular risk. Gateway Refutation: Scandinavian data suggests oral nicotine products act as an exit from smoking rather than a gateway to it	Lack of Direct Long-term Data: Epidemiological studies specific to nicotine pouches (distinct from snus) are currently unavailable due to their recent market entry. Surveillance: Continuous monitoring is needed to confirm if pouches mimic the safe track record of snus
Usage patterns	Nicotine Delivery: Modern pouches with alkaline pH can match the C_{max} of cigarettes, providing better craving relief than traditional NRT gums. Target Population: Current use is concentrated among current or former smokers, supporting the harm reduction utility	Multiple Pouch Use: Unlike vaping or heated tobacco products, users can physically use multiple pouches simultaneously, risking acute nicotine intoxication. Monitor population use: The fast-growing market means that monitoring use should be continuously and systematically recorded

continuum for nicotine delivery systems, likely comparable to pharmaceutical NRTs. By decoupling nicotine from the combustion of tobacco, the primary driver of smoking-related morbidity and mortality, nicotine pouches demonstrate a toxicological profile that is drastically reduced compared to cigarettes. Chemical characterization studies consistently show that HPHCs, including TSNAs, are either undetectable or present at levels significantly lower than those found in Swedish snus.

This reduction in toxicity is corroborated by human biomarker data, which indicate that smokers who switch to nicotine pouches experience reductions in exposure to specific toxicants (such as NNAL, acrolein, and benzene) comparable to those observed after complete smoking cessation. Furthermore, while long-term epidemiological data on nicotine pouches are currently unavailable, the "bridging" principle utilizing the extensive history of Swedish snus provides a compelling proof of concept. Given that snus, which contains cured tobacco and agricultural impurities, has not been linked to significant increases in lung disease, oral cancer, or cardiovascular morbidity, it is scientifically plausible that the cleaner, tobacco-free matrix of nicotine pouches poses an even lower risk. Consequently, the public health equation heavily favors the use of pouches as a substitute for combustible cigarettes. However, it is essential to generate product-specific epidemiological evidence. Healthcare professionals should record the use of nicotine pouches in detail, preferably with information about use duration, frequency and consumption, similar to what has been established for smoking, so that future analyses will establish meaningful epidemiological data on clinical endpoints.

Oral health is an issue that needs particular attention with nicotine pouches. Current evidence verifies their harm reduction potential compared to smoking but also snus use. However, more randomized controlled studies are needed, with longer follow-up periods and appropriate comparator groups, including groups of former smokers who have quit without the use of any alternative product. Studies should stratify participants by nicotine dose, usage frequency, and duration, to clarify any potential dose–response relationships. Histopathological monitoring should include serial biopsies, to assess whether lesions progress, stabilize, or regress with continued use or cessation, while microbiome studies should include quantitative assessment, to determine whether bacterial changes represent colonization with pathogenic potential or transient detection. The epidemiological evidence on the lack of an association between snus use and oral cancer appears reassuring, considering that snus causes more mucosal lesions than nicotine pouches which, however, do not appear to be linked with long-term risk for malignancy [123].

Despite the promising safety profile, the rapid expansion of the nicotine pouch market has highlighted significant regulatory gaps and quality control issues that must be addressed to maximize public health benefits. A primary concern is the lack of standardization in product characterization and labeling. Current marketing practices regarding nicotine strength are often inconsistent and potentially misleading. Research indicates that nicotine content is often characterized vaguely, with some products lacking any descriptors regarding strength. A recent analysis of the German market found that 29 of 44 tested products had inadequate nicotine content labeling, often using arbitrary descriptors (e.g., "strong", "extra strong") that did not correlate with the actual nicotine content [43]. This inconsistency prevents consumers from making informed decisions, creates confusion when switching from one brand to another, and complicates the titration process for smokers attempting to switch. To address this, regulatory frameworks should enforce the harmonization of labeling. While consumer-friendly categories (e.g., low, medium, high) may remain for marketing purposes, it is important that the exact amount of nicotine per pouch is clearly stated on the packaging.

Beyond labeling, the absolute nicotine content in some commercially available pouches raises significant safety concerns. Market surveillance by the German Federal Institute for Risk Assessment (BfR) identified products containing up to 47.5 mg of nicotine per pouch [43]. Pharmacokinetic data indicate that such high-dose products result in plasma nicotine levels significantly higher than those obtained from smoking, potentially causing adverse acute hemodynamic effects and maintaining or deepening dependence severity. To mitigate these risks while ensuring the product remains satisfying for smokers, regulators should establish a maximum nicotine limit per pouch. The German Federal Institute for Risk Assessment (BfR) suggests that a limit of 16.6 mg per pouch is appropriate [124]. This threshold is derived from pharmacokinetic modeling indicating that such a nicotine content yields a blood plasma concentration of approximately 16.2 ng/mL, which is roughly equivalent to the systemic absorption following the consumption of a standard cigarette. Capping nicotine content at this level would ensure the product is sufficient to relieve cravings for adult smokers without exposing users to excessive toxicity or unnecessary physiological stress. Obviously some heavy smokers with higher nicotine needs, who can obtain more nicotine from a cigarette by adjusting their puffing behavior, may not be satisfied with such levels; however, nicotine pouches offer the possibility of more frequent or even simultaneous use of two nicotine pouches (of the same or different nicotine content) in order to account for higher nicotine needs.

While the absence of tobacco eliminates many toxins, the complex chemical matrix of flavorings in nicotine pouches introduces new challenges. A comprehensive screening of flavorings and ingredients raised some quality concerns [125]. The study found that certain flavorings resulted in

exposure levels exceeding the Acceptable Daily Intake limits set by the European Food Safety Authority (EFSA) when assuming moderate pouch consumption. Furthermore, the analysis identified 13 substances not authorized as food flavorings by the EFSA, including impurities such as myosmine and ledol [125]. Of particular concern was the detection of three substances classified as possibly carcinogenic to humans (Group 2B), including methyleugenol and estragole. However, both are naturally occurring compound and the latter is still Generally Recognized As Safe (GRAS) and used as a food additive. While these findings do not equate the risk of pouches to that of combustible cigarettes, they underscore the necessity for implementing ingredient standards. Manufacturers must ensure that pharmaceutical-grade nicotine is not contaminated with tobacco-derived impurities and that flavorings meet safety standards for oral mucosal absorption, rather than just ingestion. The use of flavoring additives is also a characteristic that differentiates nicotine pouches from snus. Thus, while the bridging principle is scientifically plausible and can generate reasonable estimates about the clinical effects of nicotine pouch use, these differences in product composition necessitate the validation of potential effects through product-specific epidemiological surveillance.

Finally, a unique behavioral aspect of nicotine pouches warrants specific regulatory attention. Unlike vaping devices or heated tobacco products, which have physical limitations on concurrent use, and similar to nicotine gums or other pharmaceutical oral nicotine products, the discrete nature of pouches allows for the simultaneous use of multiple units or repetitive dosing at short time intervals. This practice raises the potential for acute nicotine intoxication, particularly among nicotine-naïve users. While some heavily dependent smokers may require higher nicotine doses to alleviate cravings, the unsupervised simultaneous use of multiple high-strength pouches poses an avoidable risk. There is already a case report of acute nicotine intoxication from repetitive dosing, which was however resolved within 24 h without any adverse long-term health consequences [126]. Therefore, regulators should consider mandating a warning label explicitly advising that “only one pouch should be used at a time”. This serves as a necessary precautionary measure to prevent adverse events while maintaining the product’s accessibility for adult smokers.

The evidence summarized in this review offers actionable guidance for internists and general practitioners encountering patients who smoke. For adult smokers who are unwilling or unable to quit using approved pharmaceutical interventions, healthcare professionals may consider framing nicotine pouches as a pragmatic harm reduction tool. In clinical practice, particularly in high-risk patients such as those with diabetes and cardiovascular disease, the priority is the elimination of combustible tobacco; while nicotine pouches are not risk-free, the transition to a tobacco-free oral product could lower the burden of oxidative stress and inflammation associated with disease development and progression. Nicotine pouches probably represent the lowest risk harm reduction product currently available, with a profile close to pharmaceutical NRTs but with better nicotine delivery which could more effectively address nicotine cravings in smokers. Practical counseling should emphasize the importance of complete substitution as the ultimate goal, given the lower risk potential compared to dual use and to avoid potential relapse to exclusive smoking, and should explain the uncertainty concerning long-term absolute risks. Furthermore, given the availability of high-strength products, healthcare providers should advise patients against "stacking" (simultaneous use of multiple pouches) to prevent acute nicotine toxicity and should screen for pouch use when patients present with symptoms of sympathetic overstimulation.

In conclusion, nicotine pouches have the potential to act as a powerful tool for smoking cessation, offering a viable “exit” from combustible tobacco that is acceptable to consumers and substantially less hazardous to health. However, their net public health impact depends on a balanced regulatory approach. This approach must ensure product availability for adult smokers while enforcing strict quality control standards regarding ingredients (including use of GRAS flavors and establishing nicotine limits), reducing labeling inconsistencies and inaccuracies, and monitoring usage patterns to prevent acute toxicity and youth initiation. If these challenges are successfully met with appropriate, evidence-based regulatory interventions and surveillance studies to monitor use by different population subgroups, nicotine pouches could play a pivotal role in accelerating the obsolescence of cigarette smoking.

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Declarations

Conflict of interest KF is an external research associate at the University of West Attica and the University of Patras in Greece. He has published more than 110 studies on smoking and tobacco harm reduction. He has no conflict of interest to report for e-cigarettes and heated tobacco products. Very recently, he has contributed to the development of research protocols for nicotine pouches for a manufacturer.

Ethical statement No ethics committee approval was sought for this study since it does not involve human subjects or experimental procedures on animals.

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