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FROM CIGARETTES TO THE FUTURE: ALTERNATIVE WAYS TO ADMINISTER NICOTINE

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ABSTRACT

Tobacco use continues to be one of the most critical public health challenges globally. The current number of active tobacco consumers hovers around 1.2 billion, with half of these individuals expected to die from tobacco-related causes. In recent years, there has been a rapid increase in alternative nicotine delivery methods, such as electronic nicotine delivery systems, heated tobacco products, and the resurgence of snus in the form of nicotine pouches. Most of these alternatives have been promoted as safer options compared to traditional smoking, aiming to encourage cessation of conventional tobacco use. Regrettably, narratives propagated by companies benefiting from these products often lead to an oversight of the health implications associated with these so-called "healthier alternatives." Nonetheless, although multiple studies have yielded diverse results, the latest data suggest that these alternatives do indeed impact health. This study aims to review accessible research, elucidate current knowledge on these products, and offer projections for future research.

KEYWORDS

Smoking, ENDS, Vaping, HTP, Snus, Health

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Introduction

According to the World Health Organization, tobacco kills half of its users, which is more than 8 million people each year. Cessation of tobacco smoking leads to a substantial positive influence on health status and quality of life with notably lower risks for disease and death (U.S. Department of Health and Human Services, 2020; World Health Organization, 2020). Smoking has been shown to relate to multiple cardiovascular, neurological and pulmonary diseases, not only in direct users but also to the health problems of non-users and it is still one of the greatest modifiable risk factors for systemic diseases and carcinogenic processes (Das, 2003; Onor et al., 2017; Parmar et al., 2023). The current prevalence of tobacco use in adults is estimated to have decreased since 2000, from around 33,1% to approximately 19.5% in 2024. Still, around 1 in 5 adults globally smoke (World Health Organization, 2025). Although the population of smokers is falling in numbers, it is worth noticing that the pattern of using tobacco has changed since 1800, and it is still changing. In the 18th century, the smokeless tobacco was the dominant form of tobacco consumption, which is associated with lower cancer and tobacco-related deaths (Onor et al., 2017). With the widespread growth of cigarette manufacturing, smoking with its deep inhalation and high concentrations of nicotine reached its peak. The effects of nicotine, the primary psychoactive component of tobacco sustain smoking addiction. Nicotine activates nicotine acetylcholine receptors in the brain which leads to activating the brain reward circuitry by increased firing of dopaminergic neurons, mainly in the Ventral Tegmental Area (VTA) and other reward-related regions in the brain (Dani & De Biasi, 2001). Smoking cessation can reduce a variety of health risk, including lung cancer and cardiovascular disease, but what is more important, even substantial smoking reduction without complete cessation can lead to health benefits (Chang et al., 2021; Hoffman & Tan, 2015). Nevertheless, according to Schane et al., a reduction in cigarette consumption could only be perceived as an intermediate stage between full cessation, and it cannot be presented as a safe long-term solution, as we have to aim for full cessation (Schane et al., 2010). Similarly to Zakiyah et al., who states that alternative nicotine products play a role in helping with smoking reduction and cessation, we also believe this is the context in which, despite not being regarded as healthy substances, they may contribute positively to the harm reduction process (Zakiyah et al., 2021). Therefore, this review aims to evaluate current research to establish whether those forms of nicotine administration could be considered appropriate from a public health perspective and what risks are linked to using them.

Electronic nicotine delivery systems

Introduction

Vaping is a process of inhaling vapor, which is created by heating special liquids by battery devices. This process leads to nicotine absorption through the respiratory epithelium of the lungs, similar to conventional smoking (National Academies of Sciences, 2018). Devices used to generate this vapor, which were primarily introduced to global market in 2007, are called ENDS (electronic nicotine device systems), e-cigarettes or vape and are extremely popular throughout the world as an alternative way for providing nicotine intake (Thurtle et al., 2016). Vapor produced by those devices mainly consists of propylene glycol, vegetable glycerin with several additives such as flavorings. Nevertheless, some studies found the existence of harmful substances like heavy metals, nitrosamines or formaldehyde in chemical compositions of electronic cigarette liquid (Glasser et al., 2016). Interesting matter about ingredients of those products is shown by a study conducted by Churchill et al. who showed that youth often add other substances to ENDS liquids for examples e-juices for extra flavors or drugs such as cocaine or cannabis (Churchill et al., 2023). Those studies should be a matter of higher concern as we cannot predict the health outcome of such actions. This year for the first time World Health Organization estimated the electronic cigarettes use prevalence and alarms that about 100 million people worldwide are current vape users (World Health Organization, 2025). As Tehrani et al. presents in metanalysis from 2022 the prevalence of use of the ENDS globally is 23% for the ever-in-lifetime users and 11% for current users of the vape with the higher prevalence in Europe and America compared to Asia and higher in man than women. (Tehrani et al., 2022). Taking into consideration the population of Poland, as Jankowski et al. report 5,9% of Poles declare daily use of e-cigarettes, with 15,2% declaring use in the past 30 days. Therefore, vaping prevalence is rising globally, and for this reason, it should be closely monitored for any possible health risks associated.

Health impact

Cardiovascular health

A 2023 meta-analysis by Rahman et al. examined the cardiovascular health of ENDS users (Rahman et al., 2023). After reviewing nearly 493 papers, 15 studies met the inclusion criteria. The participants were divided into two groups assessing independently myocardial infarction risk with over 85,000 participants in the group, and the short-term physiological effects (heart rate, blood pressure) with over 300 people in the group. E-cigarette users showed a higher risk of myocardial infarction compared to people who never smoke before using ENDS. What is more the pooled data indicated significant increases in systolic blood pressure, diastolic blood pressure, mean blood pressure, and heart rate for ENDS users versus non-users (Rahman et al., 2023). Consequently, e-cigarettes cannot be marketed as cardiovascular-safe products, given the well-established links between these outcomes and adverse cardiovascular effects (Bundy et al., 2017; Dennison Himmelfarb et al., 2025; Han et al., 2019; Pan et al., 2020). Nonetheless, the authors note that e-cigarettes remain a better alternative to traditional cigarettes. In conclusion, even though some observed outcomes did not reach statistical significance, the overall trend suggests that individuals who have never used nicotine but start vaping face higher risks of cardiac incidence than those who have never used nicotine.

Pulmonary health

Throughout the years, multiple researchers have tried to develop a consistent scientific position regarding the impact of e-cigarettes on lung function and chronic obstructive pulmonary disease (COPD) development. Former systematic reviews by Honeycutt et al., Wills et al., or Cook et al. were beneficial for this purpose, suggesting that ENDS may be less harmful than classic cigarettes (Cook et al., 2023; Honeycutt et al., 2022; Wills et al., 2024). Nevertheless, there was no unambiguous evidence confirming the thesis that ENDS directly influence the risk of COPD or are responsible for depleted respiratory parameters (forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC)) in healthy individuals. Whereas meta-analysis performed by Song et al., which included over 3,5 million participants, undisputedly showed that using ENDS in people who never smoked is not harmless. The evidence from this study points to the risk of COPD being 44% higher in the group of e-cigarette users compared to never-smokers. What is more, the risk of developing COPD was almost two times higher in dual users who were using both conventional and electronic cigarettes. Both in works by Willls et al. and Song et al. we can also find a search for the answer about the pathophysiology of adverse effects of e-smoking on the lungs. Although the results of studies in vivo and in vitro that have been analyzed by Wills et al. are not consistent, they clearly show that using ENDS is linked with increased markers of inflammation and oxidative stress, as well as epithelium injury and remodeling of airway structure (Song et al., 2025; Wills et al., 2024). Consequently, what is known is closely related to adverse health effects on human health.

Mental health

Recent studies have raised concerns about the potential link between using ENDS and mental health. Becker et al. attempted to provide a systematic review of mental health comorbidities associated with ENDS in adolescence (Becker et al., 2021). Their systematic review found that ENDS use could be related to underlying psychiatric conditions such as ADHD, depression, or anxiety. Conversely, a systematic review and meta-analysis conducted by Awad et al. found that the likelihood of suicidal ideation, suicidal planning, and suicidal attempts was, respectively 49%, 131%, and 150% higher in users compared to non-users (Awad et al., 2024). However, these odds should be interpreted with caution, as many of the included studies were cross-sectional, making it difficult to establish causality or determine the direction of the relationship between e-cigarettes and mental health disorders. Additionally, variability in how exposure and outcomes were measured can lead to significant heterogeneity in results. Nonetheless, the findings are important, suggesting that e-cigarettes could contribute to psychological vulnerability (Awad et al., 2024). These results are consistent with previous reviews such as the scoping review by Javed et al. which linked e-cigarettes with depression, suicidal ideation, and suicidal attempts (Javed et al., 2022). The studies mentioned above clearly indicate that prevention efforts regarding e-cigarette use are crucial, not only for physical health but also for mental health.

Heated tobacco products

Introduction

Another form of administering nicotine that is gaining prevalence is heated tobacco products (HTP), which in 2022 in Poland reached the prevalence of ENDS users (Miller et al., 2025). The mechanism of action of these devices is based on creating an aerosol from tobacco by heating it to around 240-350 degrees, which is significantly lower than the temperatures reached by traditional cigarettes, which can exceed 600 degrees (Jankowski et al., 2019). Tobacco sticks used for HTP devices are made mainly from pressed tobacco mixed with glycerin, guar gum, cellulose and polymer film filter with overall toxic chemicals levels lower than in classic cigarette smoke. Nevertheless, the content of over 20 toxic chemicals was found to be higher than in cigarette smoke (Upadhyay et al., 2023). The content of nicotine is around 70 to 80% of those values found in conventional cigarettes (Jankowski et al., 2019). There are various of models of those devices such as “IQOS” by Phillip Morris with a catchy abbreviation expander (“I QUIT SMOKING”), “glo” by British American Tobacco or “plum” by Japan Tobacco International, all working on very similar technology with minor differences almost unnoticeable to users (Jankowski et al., 2019).

Health impact

From the moment of mass introduction in 2014, several meta-analyses and systematic reviews undertaking the topic of harmfulness and the impact of the HTP on the human body were created. Braznell et al. tried to establish the impact of HTP on biomarkers of potential harm (BoPH) and compare those values with those observed at conventional smokers, non-smokers or e-cigarette users (Braznell et al., 2025). The results showed that despite the fact that short-term reduction of biomarkers like carbon monoxide or 1-hydroxypyrene was observed, there were no consistent improvements in BoPH values. What is even more important is that no significant improvement in clinical markers such as spirometry or cardiovascular health biomarkers was observed (Braznell et al., 2025). On the other hand, Akiyama and Sherwood et al. showed that switching from traditional cigarettes to HTP led to a reduction in several biomarkers of exposure (BoE), including carbon monoxide and acrolein metabolites, but still there was no significant or little reduction in BoPH, including markers of inflammation, oxidative stress or endothelial function. What is more, similar to Braznell et al. no improvement in clinical markers of lung or cardiovascular function was observed (Akiyama & Sherwood, 2021). Summarizing even though the exposure to some contains could be reduced by switching to HTP, we still lack the proof that this translates into measurable health benefits (Akram et al., 2025). In contrast to recently presented papers, Znyk et al. in their systematic review, tried to assess measurable health outcomes which are associated with exclusive use of HTP or in comparison to conventional cigarette smoking as well as with other nicotine delivery systems. Analyzing almost 50 reports, the authors found that some of them indeed reported substantial health improvement in the health of HTP users, compared to traditional smoking (Znyk & Kaleta, 2025). Taking into consideration respiratory health a few analyzed studies in mentioned review tried to determine the influence of HTP products on pulmonary health. One of the most notable longitudinal studies included in review by Znyk et al. conducted by Polosa et al. tried to evaluate health outcomes in COPD patients who switched for HTP from conventional cigarettes and were evaluated in a period of 3 years follow-up (Polosa et al., 2021). The results showed significant improvement in outcomes that are related to COPD, which are the number of exacerbations per year, the CAT score and the 6-minute walk test

distance. What is more, the lung function parameters FEV1, FVC stabilized in contrast to the group of patients that did not give up traditional smoking, where those parameters were progressively declined during the observational period. Although promising results presented by Polosa et al. is an exception in the literature. The general tendency in the analysis performed by Znyk et al. is that, even with improvements in self-reported respiratory symptoms or fewer COPD exacerbations, parameters such as lung function, measured by FEV1 and FVC, show no significant improvement (Polosa et al., 2021). Evaluating cardiovascular outcomes, Znyk et al, in their systematic review reported no substantial long-term health benefits with a temporary increase in blood pressure, heart rate and arterial stiffness directly after HTP use, similar to conventional cigarettes. Taking into consideration metabolic parameters, no significant differences were found between conventional cigarette users and HTP users concerning BMI, cholesterol and glucose concentration. On the other hand, HTP users reported fewer sputum production and coughing compared to conventional smokers. All this put together could lead to the conclusion that in fact, switching from conventional cigarettes could lead to potential reduced exposure to detrimental substances and improve well-being.

Summary of findings on heated tobacco products health

Taking into consideration the quoted studies, it may lead to a few conclusions. Switching from conventional cigarettes to HTP is associated with a reduction of BoE, which tell us that actual intake of harmful substances during HTP use is significantly lower than conventional cigarettes. Nevertheless, the biomarkers of potential harm despite a few favorable results of low certainty, do not support the thesis that lower exposure transfer into long-term health benefits. In clinical aspects, there is no strong evidence from long-term studies supporting any benefits for pulmonary, cardiovascular or metabolic health. Single studies which revealed those benefits are low quality, performed on small populations, although they set a direction for further development of this topic. In summary, this is an alternative to standard smoking that should be considered, but as the evidence is scarce and uncertain, caution should be exercised when recommending it to patients.

Oral nicotine products and snus

Introduction

In contrast to the forms of nicotine delivery discussed in previous paragraphs, smokeless tobacco products (SLTs) and the most recent innovations in nicotine administration, oral nicotine products (ONPs), both deliver nicotine without combustion through the oral mucosa (O'Connor et al., 2022). Regarding SLTs this paper will focus on the forms that dominate in Europe: snus, which is made from ground tobacco mixed with salt and water, and processed using a unique manufacturing method that distinguishes it from other SLTs. This special process, similar to pasteurization, is said to reduce nitrosamine levels in snus, thereby mitigating its carcinogenic risk (Rostron et al., 2018). What is worth noticing that in European Union sales of original tobacco snus is prohibited with a single exception for Swedish territory, which is strictly connected with the deep history of traditional use of this form of tobacco in this region (O'Connor et al., 2022). The ONPs are mainly cellulose nicotine pouches (NPs), which are similar to snus and contain nicotine but no tobacco itself. Instead of tobacco, the NPs contains synthetic nicotine, eventually nicotine obtained from tobacco, which is made into pre-portioned granulate powder (Travis et al., 2024). As well as snus, NPs are used in a similar way, which involves placing a product between the upper lip and gum. This allows nicotine to be absorbed through the oral mucosa, avoiding the inhalation of any gases.

Health impact - Snus

Valen et al., in their systematic analysis, attempted to determine the risk of developing cancer and the risk of death after a cancer diagnosis among Swedish snus users compared to non-tobacco users. Considering the higher rate of snus use among the male population, the studies included in the systematic review were limited to this demographic group. After analyzing 15 studies (14 cohort studies and one control study), it was found that the prevalence of esophageal, pancreatic, stomach, and rectal cancers was higher among snus users. Nevertheless, they highlight the need for further research, as the included studies were of moderate to low quality (Valen et al., 2023). Rostron et al. aimed to establish the relationship between snus use and the risk of cardiovascular disease in European and North American populations. This systematic review and meta-analysis included studies on both snus and other SLTs, such as chewing tobacco. Interestingly, these studies clearly indicated an increased risk of cardiac disease and stroke for users of chewing or dipping tobacco (Rostron et al., 2018). However, a similar correlation was not observed for Swedish snus users, where an increased risk of ischemic heart disease, myocardial infarction, and stroke was not confirmed. The authors linked these results to the previously mentioned specialized process of snus production, which reduces the presence of harmful substances. Hajat et al. also analyzed the impact of SLTs, particularly Swedish snus, on

cardiovascular disease and carcinogenic potential (Hajat et al., 2021). Consistent with Rostron et al., they found no substantial evidence of increased cardiovascular risk among Swedish snus users, supported by robust studies. Regarding carcinogenic potential, Swedish snus similarly did not appear to increase risk; however, the analyzed studies were of lower quality. Overall, we can conclude that Swedish snus does not significantly elevate carcinogenic potential, although a slight increase cannot be entirely ruled out. The result of a large meta-analysis conducted by Htay et al., analyzing 72 studies published between 2000 and 2023, merely confirms the results presented above. The study found an increased risk of developing head and neck, esophagus stomach, and pancreatic cancers among other SLTs users, again with a small or statistically nonsignificant increased risk for snus users (Htay et al., 2025). However, considering all-cause mortality and specific-cause mortality, Byhamre et al. presented a study which followed eight prospective cohorts comprising nearly 170,000 participants. The included participants had never smoked, which minimizes bias related to smoking being a strong risk factor for the evaluated outcomes. Results showed that the adjusted risk for all-cause mortality and cardiovascular mortality in exclusive snus users was significantly higher than in never tobacco users (Byhamre et al., 2021). Nevertheless, residual confounding, cohort heterogeneity, and self-reported data limit causal inferences. However, these findings suggest that snus is not harmless, warranting further longitudinal investigation.

The systematic reviews and meta-analyses cited above by Valen, Rostron, and Hajat, as well as the data provided by Clarke et al. and Lee et al., collectively indicate that the use of snus is linked to fewer adverse health effects compared to conventional smoking (Clarke et al., 2019; Hajat et al., 2021; Lee, 2013; Rostron et al., 2018; Valen et al., 2023). These findings provide strong evidence that, even if snus is not harmless, the potential for harm reduction by switching from cigarettes to snus is significant, as it substantially reduces exposure to harmful substances produced during tobacco combustion and decreases the overall disease burden.

Health impact – Nicotine pouches

Recent years have shown considerable interest in the matter of using nicotine pouches in place of other forms of alternative nicotine. Oral nicotine products, according to numerous studies, contain low levels of cancerogenic substances, especially the dangerous tobacco-specific nitrosamines (TSNAs) whose concentrations are undetectable in most commercially available nicotine pouches, providing an advantage in terms of carcinogenicity compared to other tobacco-containing products (Bundesinstitut für Risikobewertung, 2022; Mallock et al., 2024). Unfortunately, the number of available studies addressing this topic is very limited, as those need time to develop, and ONPs are products that just recently launched in the market (2016 in US and 2018 in Europe) (Mallock et al., 2024).

Zamarripa et al., in their review of the literature, suggest that the nicotine pouches are a promising alternative in terms of health for classic tobacco products – snus or conventional smoking and could help with withdrawal symptoms leading to an increased rate of cessation (Zamarripa et al., 2024). However, nicotine remains the primary active agent in those products and it is commonly known to affect cardiovascular health. Adverse effects include increased heart rate, vasoconstriction and elevated blood pressure (Benowitz & Burbank, 2016; La Rosa et al., 2023; Skotsimara et al., 2019). A cross-sectional study by Mallock et al. showed that mentioned hemodynamic effects of using NPs are dose dependent. When a higher dosage pouch (30mg) induced significant changes in hemodynamic parameters (heart rate, peripheral and central blood pressure, augmentation index and total peripheral resistance), those alterations were almost unnoticeable when using low dosage pouches (6mg). What is worth noticing is that authors also conclude that knowledge of only nicotine content of the product does not allow estimating real nicotine delivery level which warrants caution in the evaluation of nicotine consumption (Mallock-Ohnesorg et al., 2024). This data should suggest heightened caution in individuals with cardiovascular disease because nicotine can strain the cardiovascular system even in the absence of combustion products typical for conventional smoking (Dennison Himmelfarb et al., 2025).

A Study by Geijerstam et al. aims to measure the effects of nicotine pouch cessation, showing that after 12 weeks, we can expect improvement in systolic home-measured blood pressure, glycated hemoglobin levels and body weight. Those results show that with high probability, this relation can be reversed into a conclusion that chronic use of nicotine pouches may chronically raise blood pressure and affect metabolic parameters (af Geijerstam et al., 2025).

Zamaripa et al. reported a comprehensive review of data that are available concerning health-related aspects of NPs, stating that this form of nicotine intake is likely to do less harm than conventional forms of tobacco and is a good option for suppressing nicotine withdrawal syndrome, which can help in cessation. Nevertheless, authors emphasize that additional research is needed to check if those forms of nicotine

supplementation would be used long-term by tobacco users. Above that, these form of nicotine intake has a high likelihood of encouraging young people to try it because of different flavors and ease of discreet use in public, which can lead to a decrease in public health benefits (Zamarripa et al., 2024, 2025). Furthermore, many of these ingredients are classified as hazardous and are not authorized as food flavorings or even are classified as possible carcinogens (Dennison Himmelfarb et al., 2025).

The most concerning aspect of nicotine pouches use is localized exposure to nicotine and other substances in high concentrations, which is directly connected with the method of use. Rungraungrayabkul et al. tried to determine the impact of nicotine pouch use on oral health. They found that mucosal changes in NPs users are common, ranging from wrinkling to various white lesions. The severity of these changes correlated with the number of NPs consumed per day, as well as with the duration of single-pouch use (Rungraungrayabkul et al., 2024).

Summary of findings on oral nicotine products and smokeless tobacco products

Taking into consideration available data, NPs seems to pose lower health-related risks than conventional cigarettes or even smokeless tobacco. Nevertheless, as mentioned above, there are no risk-free substitutes, as we have to be aware of adverse effects on cardiovascular health, localized inflammation, or even exposure to some potentially carcinogenic compounds in limited situations. In future years, research that is unbiased by companies selling these products will be crucial for establishing strong evidence for the long-term use of these products. Similarly, snus, as shown above, could be used as a harm-reduction strategy for smokers who are unable or unwilling to quit nicotine entirely. Nonetheless, this is a highly addictive product, and monitoring long-term effects is crucial—especially concerning the risk of initiation in non-smokers. However, the pursuit of perfection can sometimes hinder progress; by opposing these forms of nicotine administration, we discourage smokers from switching from conventional cigarettes, which are undeniably more harmful.

Conclusions

With over 1,2 billion tobacco users worldwide, resulting in nearly 8 million lives lost each year, there is an urgent need to explore and research new approaches to increase rates of smoking cessation and harm reduction. Recent developments such as ENDS, HTPs, snus, and NPs have emerged as potential tools to achieve these objectives. Data indicates that using these nicotine delivery methods as alternatives to conventional smoking can significantly reduce individual risk, though they are not completely harmless. ENDS and heated tobacco products can decrease exposure to many combustion-related compounds. Snus and NPS are lower-risk options that do not involve inhaling gases, thereby reducing respiratory and cardiovascular risks among users. These potential benefits are promising; however, uncertainties remain regarding long-term health effects, patterns of dual use, and their impact on non-smokers, especially youth and adolescents, which could increase initiation rates. Therefore, thorough research is essential to clarify safety profiles, optimize harm reduction strategies, and guide evidence-based nicotine harm reduction policies.

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