THE TURKISH JOURNAL ON ADDICTIONS
www.addicta.com.tr

INVITED REVIEW

Other Highlights and New Products on the Agenda: E-Cigarettes/Electronic Nicotine Delivery Systems, Electronic Non-Nicotine Delivery Systems, and Heated Tobacco Products

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Abstract

E-cigarettes have emerged as a prominent product primarily driven by the tobacco industry. Serving as a strategic lifeline for a tobacco industry facing constrained opportunities, e-cigarettes present a concerning landscape, especially in relation to youth and public health. These devices, often marketed with an age restriction on cigarette sales, inadvertently facilitate the development of nicotine addiction in children and young individuals. They provide a means for perpetuating nicotine dependency among smokers, given the limitations on smoking in public spaces. E-cigarettes are capable of delivering potent nicotine concentrations, contributing to youth addiction and the subsequent adoption of conventional cigarettes and other addictive substances. While some research suggests that transitioning from smoking to e-cigarettes may reduce harm, additional studies are required to establish this conclusively. Notably, the co-use of e-cigarettes and traditional cigarettes poses greater health risks than using either product in isolation. The therapeutic potential of e-cigarettes in smoking cessation is evident when utilized within a structured intervention but not as consumer commodities. It is crucial to acknowledge that e-cigarette technology is continually evolving, making it challenging to assess their long-term health implications accurately. The allure of flavored tobacco products, particularly to the youth, remains a major concern within this landscape.
Keywords: E-cigarettes, ENDS, ENNDS, HTPs, vaping

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Received: December 10, 2023
Accepted: December 14, 2023
Publication Date: March 15, 2025

Definitions

e-cigarettes/electronic nicotine delivery systems (ENDS)/electronic non-nicotine delivery systems (ENNDS): These are electronic devices with batteries that release inhalable vapor used for consuming substances such as nicotine, tetrahydrocannabinol (THC), cannabidiol (CBD), and butane mixed oils (dabs). E-cigarettes typically consist of a battery, liquid cartridge, heating element (atomizer), and mouthpiece, which convert the liquid into an aerosol.

Heated tobacco products (HTPs)/T-vapor: These electronic devices heat tobacco at lower temperatures (up to 350°C) compared to traditional cigarettes, turning nicotine and other chemicals into vapor. Some e-cigarettes also contain tobacco.

Vaping: The act of inhaling aerosol or vapor produced by ENDS, ENNDS, or HTPs.

Introduction

Electronic nicotine delivery systems (ENDS)/heated tobacco products (HTPs)/e-cigarettes can deliver nicotine levels ranging from 0 to 35 μg in each puff, depending on the type. On average, consuming about 30 puffs from these devices can deliver nicotine equivalent to that obtained from smoking a cigarette. Certain e-cigarettes may provide even higher nicotine concentrations. The amount of nicotine intake depends not only on the nicotine cartridge's content but also on device features and user behavior. E-cigarettes can lead users to consume more nicotine compared to traditional cigarettes (Ramôa et al., 2016). The lethal dose of nicotine

Cite this article as: Özlü, T. (2025). Other highlights and new products on the agenda: E-cigarettes, ENDS, ENNDS and HTPs. *Addicta: The Turkish Journal on Addictions*, 12(1), 10-19.

DOI: 10.5152/ADDICTA.2025.23128

ranges from 10 to 60 mg, and some e-cigarettes contain nicotine concentrations of up to 100 mg/mL. Salivary cotinine levels in e-cigarette users can be as high as 322 ng/mL, whereas it is 113 ng/mL in smokers and only 2.4 ng/mL in non-smokers (Etter & Bullen, 2011; Etter et al., 2000; Cameron et al., 2014).

ENDS contain various bioactive chemicals apart from nicotine and can even be nicotine free. Even without additives, ENDS/electronic non-nicotine delivery systems (ENNDS) produce aerosols containing glycols, aldehydes, volatile organic compounds, polycyclic aromatic hydrocarbons, tobacco-specific nitrosamines, metals, silicate particles, and other elements. Toxic substances such as dicarbonyls (glyoxal, methylglyoxal, diacetyl) and hydroxycarbonyls (acetol) contribute to significant health issues. While the levels of these toxins are lower than in cigarette smoke, they can vary widely between brands and sometimes exceed tobacco smoke levels (WHO, 2016; Visser et al., 2015). Metals like lead, chromium, nickel, and formaldehyde have been found in ENDS aerosols in concentrations equal to or higher than in conventional cigarettes (Visser et al., 2015. Goniewicz et al., 2013).

The liquid inside these products' cartridges, besides nicotine, contains propylene glycol, ethanol, water, tobacco flower, and various essences and chemicals depending on the type. They can include thousands of different flavors and fragrances, such as mint, fruit flavors, chocolate, solvents, volatiles, and similar chemicals. Some products may even contain cannabis, marijuana, or hemp extracts. The appeal of flavors, especially fruit and toffee-like ones, can attract children and teenagers and influence their preferences (Ambrose et al., 2015; Vasiljevic et al., 2016). Nearly 8000 different flavors have been reported in e-cigarette liquids.

e-Cigarette, Electronic Nicotine Delivery System, Electronic Non-nicotine Delivery System, Heated Tobacco Product Market

Initially, ENDS/ENNDS were marketed by companies independent of traditional multinational tobacco companies. Today, products like ENDS/ENNDS and HTPs are primarily marketed by tobacco companies (Etter et al. 2000). Regulatory approvals in the United States and the European Union are expected to increase the dominance of multinational tobacco companies in the market by raising the cost of bringing new devices to market. This situation poses a significant threat to tobacco control efforts. There are concerns that the entry of multinational tobacco companies into the ENDS/ENNDS market serves strategic objectives (WHO, 2016): Minimizing the threat to tobacco sales by promoting ENDS as a complement to tobacco or by controlling technological innovations to enhance its effectiveness as a smoking cessation aid. Encouraging adults to continue smoking and enticing children to initiate smoking through ENDS/ENNDS advertising. Advocating for ENDS/ENNDS to engage and influence policymakers, scientists, and tobacco control advocates by highlighting potential smoking cessation benefits, gaining credibility through corporate social responsibility initiatives, and undermining the WHO Framework Convention on Tobacco Control.

It is claimed in marketing that e-cigarettes do not contain harmful substances generated during tobacco combustion and provide a safe alternative to cigarettes without causing tobacco-related diseases. The tobacco industry's history of false health claims, such as asserting in the 1960s that cigarettes were not harmful to health (Grana et al., 2014), raises skepticism about these claims. For example, in a 1954 full-page newspaper advertisement known as the "Frank Statement," 14 tobacco companies stated, "We believe the products we make are not injurious to health ... We always have and always will cooperate closely with those whose task it is to safeguard the public health" (https://www.tobaccofreekids.org/research/factsheets/pdf/0268.pdf). James Bowling, the vice president of Philip Morris, said in 1972, "if our product is harmful, we'll stop making it" (http://www.sourcewatch.org/index.php/James_Chandler_Bowling). Such statements were made even though the same industry later admitted that cigarettes were harmful. Reflecting on this history, one might think, "How many times have we heard this tale before?" It is suggested that the industry is repeating the same tactics while expecting different outcomes (Braillon, 2016). In reality, e-cigarettes serve as a strategic tool for the industry to perpetuate nicotine addiction (Crotty et al., 2015). Furthermore, they can act as a gateway for young individuals who cannot purchase cigarettes to develop nicotine addiction early in life (McCarthy, 2015; Klein, 2015; Fillon, 2016). By normalizing smoking in society, e-cigarettes serve as a barrier against anti-smoking efforts (Auf et al., 2016). Susan Cameron, CEO of Reynolds American, even stated that "e-cigarettes and other non-combustible products will make the tobacco industry more socially acceptable" (http://fortune.com/2014/08/08/reynolds-american-ceo-talks-tobaccos-future/).

Over the past decade, cigarette sales have declined in developed countries. New products like ENDS/ENNDS and HTPs exemplify the tobacco industry's search for alternative products to cigarettes as it faces increasing constraints due to tobacco control measures worldwide. The demand for these products is rapidly rising. In a market research study from 2014, 466 brands and 7764 different products were identified (Zhu et al., 2014). The global ENDS/ENNDS market reached $10 billion in 2015 and is expected to reach $27 billion by 2022 (WHO, 2016). According to Euromonitor's 2017 data, total HTP sales in 2016 amounted to $2.1 billion and were projected to reach $17.9 billion by 2021 (Euromonitor International, 2017; 2018).

The marketing messages surrounding e-cigarettes often emphasize their potential benefits, such as helping users quit smoking, reducing harm, enabling use in social settings, and offering a wide array of appealing flavors. These messages are designed to attract consumers with promises of a safer alternative to traditional cigarettes and a customized vaping experience (Lyu et al., 2022).

E-cigarette Use Among Youth

The prevalence of e-cigarette use among high school students in the United States has undergone a significant surge. Between 2011 and 2015, there was a tenfold increase in e-cigarette usage among this demographic. E-cigarette adoption is particularly pronounced among young individuals, encompassing both those who already smoke and those who have never engaged in smoking before (Singh et al., 2016; Bunnell et al., 2015; Bostean et al., 2015; Wills et al., 2015).

According to data from the National Youth Tobacco Survey in the United States, the rate of high school students using e-cigarettes, which stood at 20.8% in 2018, escalated to 27.5% in 2019. Notably, a staggering 97% of young users opt for flavored e-cigarette products. A comprehensive review by the World Health Organization (WHO) examining ENDS/ENNDS use among individuals aged 20 and under reveals intriguing trends. Among non-smokers, the prevalence of ENDS/ENNDS use hovers around 2%, but this figure dramatically rises to 13% and 19% in countries such as the United States (specifically, Florida) and Poland, respectively. Meanwhile, current usage rates among smokers reach approximately 17%. The use of ENDS/ENNDS is notably more pronounced in Florida (44.8% for ages 11 – 14 and 51.7% for ages 15 – 18) and Poland (57.4%). Worryingly, in the span of just 3 years, both Florida and Poland witnessed a staggering five- and eight-fold increase, respectively, in ENDS/ENNDS use among young non-smokers (WHO, 2016).

The initial costs associated with refillable ENNDS devices and disposable ENDS/ENNDS products are typically higher than traditional cigarettes. There exists a notable inverse correlation between ENDS/ENNDS sales and cigarette prices. When cigarette prices are elevated, it often leads to an upsurge in ENDS/ENNDS sales (Huang et al., 2014). High cigarette prices seem to drive an increased inclination toward adopting e-cigarettes and similar products.

Emerging Concerns and Criticisms

Recent scientific literature has raised several noteworthy concerns and criticisms regarding products like ENDS/ENNDS and HTPs. In essence, these are novel products that both foster nicotine addiction and perpetuate existing nicotine dependencies. They represent a means of cultivating nicotine addiction while sidestepping restrictions on tobacco sales to minors. Furthermore, they can act as a transitional step towards tobacco usage and even other addictive substances, such as cannabis. Despite smoking bans in social settings, they sustain addiction by satisfying the need for nicotine, thereby undermining anti-tobacco efforts within society (Schraufnagel, 2015; Leventhal et al., 2015; Giroud et al., 2015).

A substantial debate surrounds the question of whether the increasing use of ENDS/ENNDS among non-smokers serves as a precursor to smoking. Longitudinal studies currently available indicate that the utilization of ENDS/ENNDS by young individuals who have never smoked before at least doubles the likelihood of them initiating smoking (WHO, 2016; Gornall, 2015; Forrester, 2015; Ordonez et al., 2015; Chatham-Stephens et al., 2014; Primack et al., 2015; Leventhal et al., 2015).

A meta-analysis, for instance, reveals that individuals aged 14 to 30 who use e-cigarettes are more prone to initiate smoking compared to their non-e-cigarette using counterparts (Soneji et al., 2017). Additionally, multiple studies corroborate this finding (East et al., 2018; O'Brien, 2021).

E-cigarette use has also been linked to heightened consumption of marijuana, stimulants, and poly-substances (Bentivegna et al., 2019). In a cohort study involving 9,828 adolescents, the rate of e-cigarette use in the first year following initiation was associated with a twofold increase in cannabis initiation (Sun et al., 2022). Another study involving 20,675 students found that e-cigarette users were three times more likely to use cannabis compared to their peers (Trivers et al., 2018). In a separate study, this ratio was nearly four times higher (Fadus et al., 2019).

Health Implications

The long-term safety of these products remains shrouded in uncertainty, with questions lingering about the extent and nature of user exposure. Although the levels of carcinogenic and toxic substances in these products are lower than in traditional cigarettes (Grana, R., 2014), their consumption varies widely among individuals and product types. Furthermore, concurrent use with conventional cigarettes can amplify the risks associated with nicotine. Similar to smoking, passive effects from these products are conceivable, and in some instances, tobacco can be added to certain products (Gornall, 2015).

E-cigarettes are by no means benign and have been associated with an escalating number of poisoning cases in tandem with their market growth (Forrester, 2015; Ordonez et al., 2015). The Centers for Disease Control and Prevention (CDC) reported a noteworthy shift in poisoning cases, with incidents related to e-cigarettes surging from 0.3% to 41% of total cases between 2010 and 2014. It is noteworthy that while 94.9% of tobacco-related poisonings involve children aged 0 – 5, only 51.1% of e-cigarette poisonings fall within this age group, with 42% affecting individuals over 20 years old. The occurrence of adverse events related to e-cigarettes significantly outpaced those associated with traditional cigarettes (57.8% vs. 36%; $P < 0.001$) (Chatham-Stephens et al., 2014). Notably, some e-cigarettes contain nicotine concentrations as high as 100 mg/mL, while the lethal dose of nicotine is estimated to be 10 – 60 mg. Salivary cotinine levels in e-cigarette users were measured at 322 ng/mL, significantly exceeding the levels in smokers (113 ng/mL) and non-smokers (2.4 ng/mL) (Etter & Bullen, 2011). Data from the CDC reveals that among 238 cases of acute harm related to e-cigarettes, 53% were attributed to traumatic incidents, such as e-cigarette explosions or burns, while 24% were respiratory events, and 12% involved poisoning (Tzortzi et al., 2020).

Aside from their acute toxicity and potent addictive qualities, nicotine may exert adverse effects on cardiovascular health, particularly when used during pregnancy. Although not inherently carcinogenic, nicotine can act as a "tumor promoter" and appears to play a role in neurodegeneration. Exposure to nicotine during fetal development and adolescence can lead to long-term consequences for brain development, potentially resulting in learning disabilities and anxiety disorders. Sufficient evidence warrants warnings against the use of ENDS and nicotine by children, adolescents, pregnant women, and women of reproductive age (WHO 2016, Kutlu & Gould, 2015; Yuan et al., 2015; Hall et al., 2015).

Propylene glycol, used as a base in e-liquids, can irritate the lungs and other organs. E-cigarettes produce significantly finer particles compared to traditional cigarettes, potentially leading to higher lung deposition (WHO 2016).

The health impacts of flavorings used in e-liquids remain inadequately researched. Heated and inhaled flavors like popcorn and cinnamon are particularly concerning, as flavorings can act as irritants, potentially causing airway inflammation and cytotoxic

effects (WHO 2016, Kreiss et al., 2022; Behar et al., 2014; Tierney et al., 2015; Lerner et al., 2015; Cervellati et al., 2014).

Literature reviews have linked e-cigarette use to harmful immunological effects, including the formation of pro-inflammatory cytokines and oxidative stress, which may raise the risk of immunological and infectious lung diseases, such as asthma and chronic obstructive pulmonary disease (COPD) (Seok GH, et al. 2023).

E-cigarette use has been correlated with an elevated risk of respiratory diseases, such as COPD, emphysema, chronic bronchitis, and asthma, independent of smoking (Xie et al., 2020). In fact, e-cigarette users were found to have a 2.1-fold higher likelihood of obstructive pulmonary dysfunction (Joshi et al., 2021). CT studies have provided evidence of impaired lung gas exchange associated with e-cigarette use (Javelle, 2020). In one study, e-cigarette users were associated with higher rates of coronary heart disease, arrhythmias, chest pain, and cardiovascular symptoms (Espinoza-Derout, J., et.al, 2022)

Among adolescents, e-cigarette use has been associated with depression, suicidal ideation, and suicide attempts, with significantly higher rates of suicide attempts among e-cigarette users compared to non-users (Espinoza-Derout et al., 2022).

In summary, ENDS/ENNDS are far from harmless, and their long-term use is anticipated to heighten the risk of chronic obstructive pulmonary disease, lung cancer, and potentially cardiovascular disease, along with several other conditions typically linked to smoking (WHO 2016; Britton et al., 2016).

Immediate Physiological Impact

E-cigarettes induce acute physiological responses in users. Following use, they elicit a rise in diastolic blood pressure, an increase in heart rate, and a reduction in exhaled nitric oxide. Furthermore, studies have demonstrated that e-cigarette usage leads to elevated respiratory impedance, which reflects peripheral airway resistance and contributes to increased overall airway resistance (Orellana-Barrios et al., 2015).

Extensive research has probed the effects of e-cigarettes on lung function. Findings indicate that these devices exhibit cytotoxicity towards respiratory tract epithelial cells, resulting in decreased cell viability and heightened airway inflammation. Additionally, e-cigarette use has been associated with an increased susceptibility to respiratory infections and an exacerbation of the virulence of *Staphylococcus aureus*. Furthermore, cytotoxicity has been observed in airway fibroblasts, causing alterations in their morphology. In response to e-cigarette use, the airways exhibit elevated inflammatory cell counts, greater cytokine release, and increased susceptibility to infections. Moreover, endothelial cells experience diminished viability and electrical resistance (Rowell & Tarran, 2015).

Research has shown that within just 5 min of e-cigarette use by healthy smokers, airway resistance, impedance, and oxidative stress all surge (Tarran et al., 2012).

Studies conducted on rat cardiac myoblast cell cultures have revealed that various sweeteners found in the refill solutions of five different e-cigarette manufacturers exhibit cytotoxic properties (Farsalinos et al., 2013). Furthermore, clinical trials have confirmed that e-cigarette use results in increased systolic and diastolic blood pressure, as well as a heightened heart rate (Yan & D'Ruiz, 2015).

Experimental models have demonstrated that e-cigarettes have detrimental effects on cell viability, leading to decreased clonogenic survival and increased rates of apoptosis and necrosis (Yu et al. 2016).

It is also well-documented that e-cigarette batteries pose risks, as they have been known to explode, causing severe burns, chemical exposure, and physical trauma (https://onedio.com/haber/elektronik-sigara-patladi-boynu-kirildi-629697).

EVALI (E-cigarette, or Vaping, Product Use-Associated Lung Injury) (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html)

EVALI is a respiratory illness that manifests acutely or subacutely in individuals using e-cigarettes, sometimes progressing to respiratory failure.

According to the report from the Centers for Disease Control and Prevention (CDC), the first case in the USA was identified on March 31, 2019. By February 18, 2020, a total of 2807 cases of hospitalized individuals with e-cigarette or vaping product use-related lung injury (EVALI) or associated fatalities had been reported across all 50 states, the District of Columbia, and two US territories. Tragically, there were 68 confirmed deaths. The median age of affected patients was 24 years, with an age range spanning from 13 to 85 years. Among the patients who succumbed to the illness, the mean age was 49.5 years, with ages ranging from 15 to 75, and 66% of them were male. Among the 2022 hospitalized patients with available data on substance use, 82% reported using products containing THC, while 33% reported exclusive use of products containing tetrahydrocannabinol (THC). Additionally, 57% of the patients reported using products containing nicotine, with 14% solely using nicotine-containing products.

The available data strongly suggest that products containing THC play a significant role in this epidemic. However, the specific chemical or chemicals responsible for causing EVALI have not yet been definitively identified, and the possibility that products containing nicotine may contribute to this condition has not been ruled out.

The clinical presentation of EVALI typically begins with respiratory symptoms, including cough, chest pain, and shortness of breath, which was experienced by 95% of patients (323/339). Gastrointestinal symptoms often accompany these respiratory issues, with 77% of patients (262/339) reporting abdominal pain, nausea, vomiting, and diarrhea. Interestingly, in some cases, gastrointestinal symptoms precede respiratory symptoms. Moreover, 85% of patients presented with general symptoms such as fever, chills, and weight loss.

Upon examination, tachycardia was observed in 55% of patients (169/310), tachypnea in 45% (77/172), and desaturation (oxygen saturation <95%) in 57% (143/253). Auscultation of the chest usually yielded normal findings.

Radiological assessments, including chest x-rays, often reveal pulmonary infiltrates. Thoracic CT scans frequently exhibit bilateral ground glass opacities, although radiography can be positive even in cases where no symptoms are evident. However, it is important to note that chest x-ray and CT findings may not always correlate with clinical symptoms. Severe or deteriorating disease can be accompanied by complications such as pneumothorax or pneumomediastinum, as well as conditions like pneumonia or pulmonary embolism.

Thoracic CT scans have reported a range of findings, including consolidation, diffuse ground glass opacities, confluent ground glass opacities, mosaic attenuation, bronchial dilatation, traction bronchiectasis, septal thickenings and fibrosis, peripheral reticulation, and pleural effusion.

Pathologically, EVALI is characterized by airway-focused acute lung injury. Severe bronchiolitis is commonly observed, with marked mucosal edema, alterations in bronchiolar epithelium, and peribronchiolar organization. Accumulation of foamy or vacuum macrophages in the peribronchiolar air spaces, along with pneumocyte vacuolization, is evident. In severe cases, extensive alveolar damage and hyaline membranes are observed (Krishnasamy et al. 2020).

Confirmed cases of EVALI are defined as those involving e-cigarette (vaping) use within 90 days before symptom onset, infiltrates on chest x-ray/CT, an absence of signs of infection (determined through various tests including respiratory viral panels, influenza polymerase chain reaction (PCR), *Streptococcus* pneumonia, urine antigen tests for *Legionella*, sputum, bronchoalveolar lavage, blood culture, and human immunodeficiency virus testing), and no medical records indicating alternative diagnoses such as cardiac, rheumatological, or neoplastic diseases.

Possible cases of EVALI involve e-cigarette (vaping) use within 90 days before symptom onset, infiltrates on chest x-ray/CT, evidence of infection detected by culture or PCR, although the clinician believes that infection is not the sole cause of the respiratory illness or infection testing has not been performed. Similar to confirmed cases, possible cases have no medical records suggesting alternative diagnoses like cardiac, rheumatological, or neoplastic diseases.

Patients presenting with respiratory distress, reduced pulmonary reserve, oxygen saturation below 95%, or comorbidities should be hospitalized. Patients with milder suspected lung injury may receive outpatient care but should be scheduled for follow-up within 24 – 48 h, ensuring normal oxygen saturation, and provided with adequate care and social support. Corticosteroids can be considered as part of the treatment regimen. Early antibiotic therapy to cover potential causes of advanced pneumonia in the community is strongly recommended, and antiviral treatment should be considered in cases of suspected influenza.

Impact on Smoking Cessation

The influence of e-cigarettes on smoking cessation is a topic that has generated both supporting and opposing research findings.

Numerous studies examining the effect of e-cigarettes on smoking cessation have primarily focused on short-term follow-ups, lacking data on sustained long-term quit rates (Yasmeen et al., 2019). Some smoking cessation trials involving e-cigarettes have suggested that these devices do not surpass the effectiveness of nicotine replacement therapy (NRT), and in fact, e-cigarette use is often associated with lower rates of smoking cessation (Grana et al., 2014 Orr et al., 2014). Interestingly, it is worth noting that studies reporting positive outcomes regarding smoking cessation and e-cigarettes are frequently linked, either directly or indirectly, to the support of tobacco companies (Bullen et al., 2013; Kosmider & Anastasi, 2016). This association with commercial and other vested interests in the tobacco and ENDS/ENNDS industry raises concerns. In an analysis of 105 studies examining fluid and emission compositions, it was discovered that 30% of these studies had authors who received funding from the tobacco or ENDS/ENNDS industry (WHO, 2016).

A meta-analysis revealed that e-cigarette use was associated with reduced rates of smoking cessation (28%; odds ratio: 0.72, 95% CI 0.57 – 0.91) in both longitudinal and cross-sectional studies (Xie et al., 2018). Another meta-analysis, with a particular focus on e-cigarettes containing nicotine, suggested that these products were more effective than NRT in facilitating smoking cessation and reduction (Vanderkam et al., 2022).

A Cochrane systematic review encompassing 16,000 smokers found that nicotine-containing e-cigarettes were linked to higher quit rates compared to NRT and non-nicotine e-cigarettes (Hanewinkel, R., et el. 2021). However, it is crucial to note that the use of e-cigarettes did not result in a decrease in nicotine addiction, often leading to dual use. Another systematic review supported the idea that e-cigarettes were more effective for smoking cessation than nicotine replacement therapy and behavior modification treatments (Hanewinkel et al., 2022). Nevertheless, it should be emphasized that the efficacy of e-cigarettes in smoking cessation is contingent on a structured therapeutic protocol and professional counseling (Jeremy et al., 2023; Hajek et al., 2019; Hartmann-Boyce et al., 2021; Wang et al., 2021).

Contrastingly, one meta-analysis did not find a significant increase in smoking cessation among e-cigarette users in observational studies (Wang, R. J., et al. 2021).

Smoking cessation therapy targets nicotine addiction. E-cigarettes do not eliminate nicotine addiction; rather, they perpetuate it. E-cigarettes are intrinsically addictive products and should not be considered therapeutic drugs.

Psychological dependence plays a substantial role in smoking addiction. Behavioral treatment methods are integral to smoking cessation, requiring individuals to change behaviors associated with smoking, which can include disposing of items such as lighters and ashtrays and modifying habits like consuming tea and coffee. However, e-cigarettes perpetuate smoking behavior, reinforcing nicotine addiction.

The scientific evidence on the effectiveness of ENDS/ENNDS in smoking cessation is limited. While some studies suggest that ENDS use may hinder smoking cessation efforts, the quality of evidence is often very low, and the participant pool is frequently limited (McRobbie et al., 2014; GRADE Working Group, 2004; Biener & Hargraves, 2014; Brose et al., 2014).

Nicotine replacement therapy (NRT) is a recognized method for quitting smoking. However, NRT is intended for short-term use, carefully dosed, and administered under medical supervision. It is distinct from smoking and thus helps eliminate behavioral addiction. In contrast, the nicotine content and usage patterns of e-cigarettes are uncertain, and some do not contain nicotine at all. Furthermore, e-cigarettes contain numerous potentially harmful substances. Their use is typically long-term rather than temporary, and their side effects and contraindications are not well defined. E-cigarettes are not medical products designed to aid smoking cessation, and they are not supervised by medical professionals. Resembling cigarettes, e-cigarettes sustain behavioral addiction associated with smoking. Importantly, there is a lack of long-term data demonstrating that the transition from cigarettes to e-cigarettes yields the same benefits as quitting smoking altogether.

It is essential to highlight that e-cigarettes are not among the seven FDA-approved products for tobacco use treatment. The US Preventive Services Task Force has cited insufficient evidence regarding the benefits and risks of e-cigarettes in smoking cessation. The American Thoracic Society (ATS) recommends varenicline, rather than e-cigarettes, as the preferred option for smoking cessation (Kathuria, 2022).

Finally, it is crucial to differentiate between the controlled use of e-cigarettes in experimental studies to support smoking cessation and their real-world use by consumers. Relying on the results of controlled studies to promote widespread use is deceptive.

In conclusion, findings related to the impact of e-cigarettes on smoking cessation are not universally applicable. The diverse array of e-cigarette types, ingredients, doses, and mixtures available on the market precludes the generalization of results obtained from specific e-cigarette brands used in research studies.

Moreover, switching from cigarettes to e-cigarettes did not lead to improvements in lung function among individuals with pre-existing lung conditions (Polosa et al., 2016; Bowler et al., 2017). Longer-term investigations are necessary to determine whether such a transition can yield improvements in lung function, as spirometry changes can typically only be reliably detected after several years of smoking cessation (Woodruff et al., 2016).

Dual Use

As concerns arose regarding the efficacy of e-cigarettes in helping individuals quit smoking, proponents of these products began advocating for dual usethe simultaneous use of both e-cigarettes and traditional cigarettes – as a strategy to reduce the harm associated with smoking (Polosa et al., 2011). From a business perspective, this notion is understandable, as it allows companies to profit from both products when customers use them concurrently.

A population-based study revealed that the association between e-cigarette use and respiratory symptoms, such as chronic cough, sputum production, or wheezing, was notably stronger among dual users (Hedman et al., 2018). The risk of developing respiratory conditions was found to be higher in individuals using both e-cigarettes and traditional cigarettes compared to those using either product alone (Bhatta & Glantz, 2020). Additionally, dual users were shown to have greater exposure to toxic substances, including nitrosamines, polycyclic aromatic hydrocarbons, and volatile organic compounds, than exclusive smokers (Glantz et al., 2018). Although some contradictory findings exist (Hartmann-Boyce et al., 2023), current research generally indicates that dual use is as harmful as, or possibly even more harmful than, smoking alone (Pisinger & Rasmussen, 2022).

Furthermore, a study by Leventhal et al. demonstrated that dual use, often recommended to mitigate smoking-related harm, particularly among individuals with psychiatric conditions, is associated with an increase in psychiatric comorbidity (Leventhal et al., 2016).

Passive Influence

Compared to homes without smokers, households using e-cigarettes have significantly higher airborne nicotine levels. Moreover, cotinine levels in non-smoking individuals residing in these households increase significantly due to passive exposure to e-cigarette aerosols (Leventhal et al., 2016). In homes where e-cigarettes are used, airborne nicotine levels are approximately 5.7 times higher than in homes with traditional cigarette smoking. However, biomarker levels (urine and salivary cotinine) in non-smoker volunteers exposed to e-cigarettes are similar to those exposed to traditional cigarettes. This passive exposure results in non-smokers absorbing nicotine (Ballbè et al., 2014).

Passive exposure to e-cigarettes is not limited to nicotine alone. Studies have detected the presence of toxins such as formaldehyde, acetaldehyde, isoprene, acetic acid, 2-butanodione, acetone, propanol, propylene glycol, diacetin (from flavorings), nicotine, and traces of apple oil (3-methylbutyl-3-methylbutanoate) in e-cigarette smoking rooms, albeit at lower levels compared to traditional smoking rooms (Flouris et al., 2013). Another study conducted in a cafe where three people used e-cigarettes observed elevated levels of carcinogens, including 1,2-propanediol, glycerin, aluminum, and seven polycyclic aromatic hydrocarbons, in the ambient air (Schripp et al., 2013).

Although there is limited research on this subject, passive aerosol (secondhand) exposure from ENDS/ENNDS users is believed to carry the potential for adverse effects (WHO 2016; Schober et al., 2014; Hess et al., 2016). Environmental aerosol is recognized as a source of air pollution due to fine and ultrafine particles, particulate matter containing 1,2-propanediol, various volatile organic compounds, heavy metals, and nicotine. The CDC warns that exposure to e-cigarettes may lead young people to initiate smoking (source: CDC).

Public Health Measures

The CDC (U.S. Department of Health and Human Services / Centers for Disease Control and Prevention) asserts that these products are not benign, that young people's initiation of e-cigarettes may lead to future smoking, and that e-cigarette use among young individuals is on the rise.

The World Health Organization (WHO) recommends specific measures to safeguard public health, including preventing non-smokers and youth from initiating ENDS/ENNDS use, particularly focusing on vulnerable populations. These measures also involve minimizing potential health risks for ENDS/ENNDS

Table 1.
Recommendations to Protect Society from the Harmful Effects of e-cigarettes (Grana et al., 2014)

1. **Age Restrictions Consistent with Cigarette Sales:** The sale of e-cigarettes should be restricted to individuals who are legally allowed to purchase cigarettes. Furthermore, e-cigarette sales should be prohibited in locations where traditional cigarette sales are banned.
2. **Uniform Advertising Restrictions:** Apply advertising restrictions on e-cigarettes at a level equivalent to those imposed on traditional cigarettes. This approach prevents the potential glamorization and normalization of e-cigarette use.
3. **Prevent Dual Use Promotion:** Prohibit marketing and branding practices that encourage simultaneous use of both e-cigarettes and traditional cigarettes. This discourages the practice of dual use, which may exacerbate health risks.
4. **Sugar and Alcohol Flavoring Prohibition:** Ban the use of sugar and alcoholic sweeteners and flavorings in e-cigarette products. Such additives may make these products more appealing, especially to young users.
5. **Evidence-Based Smoking Cessation Claims:** Restrict claims that suggest e-cigarettes are effective tools for smoking cessation, particularly when insufficient scientific evidence supports these assertions. This helps prevent misleading information.
6. **Establish Robust Product Regulations:** Implement comprehensive standards for the regulation and promotion of e-cigarette products. This includes rigorous testing, quality control, and transparent labeling to ensure consumer safety and awareness.

users and protecting non-users from exposure to emissions. Additionally, WHO recommends countering unsubstantiated health claims associated with ENDS/ENNDS and ensuring that tobacco control efforts guard against all commercial and other interests related to ENDS/ENNDS, including those of the tobacco industry (WHO, 2016).

The challenges in controlling the tobacco pandemic necessitate a vigilant and sensitive approach to e-cigarettes from the outset. In this context, Grana et al. (Grana et al., 2014) have outlined measures to protect society from the risks associated with e-cigarettes (Table 1).

In our country, electronic cigarettes are categorized as "tobacco products under the framework of Law No. 4207 on the Prevention and Control of Harmful Effects of Tobacco Products, irrespective of their content. Notably, no electronic cigarettes have received official licensing in our country, rendering their importation illegal.

Conclusion

E-cigarettes have emerged as a prominent product primarily driven by the tobacco industry. Serving as a strategic lifeline for a tobacco industry facing constrained opportunities, e-cigarettes present a concerning landscape, especially in relation to youth and public health.

These devices, often marketed with an age restriction on cigarette sales, inadvertently facilitate the development of nicotine addiction in children and young individuals. They provide a means for perpetuating nicotine dependency among smokers, given the limitations on smoking in public spaces. Furthermore, e-cigarettes function as barriers to anti-smoking efforts within society.

The tobacco industry's promotion of e-cigarettes as smoking cessation tools redirects control efforts toward its own interests. E-cigarettes are capable of delivering potent nicotine concentrations, contributing to youth addiction and the subsequent adoption of conventional cigarettes and other addictive substances. While some research suggests that transitioning from smoking to e-cigarettes may reduce harm, additional studies are required to establish this conclusively.

Notably, the co-use of e-cigarettes and traditional cigarettes poses greater health risks than using either product in isolation. The therapeutic potential of e-cigarettes in smoking cessation is evident when utilized within a structured intervention but not as consumer commodities.

It is crucial to acknowledge that e-cigarette technology is continually evolving, making it challenging to assess their long-term health implications accurately. The allure of flavored tobacco products, particularly to the youth, remains a major concern within this landscape.

The evidence remains resolute: young individuals and those who have never smoked should refrain from initiating e-cigarette use. In the face of these complex dynamics, policymakers and public health authorities must remain vigilant and proactive in their efforts to protect the well-being of society, especially our youth, from the potential risks associated with e-cigarettes.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author has no conflict of interest to declare.

Funding: The author declared that this study has received no financial support.

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