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The impact of e-cigarette smoking on the body and sport activity - a review of articles

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ABSTRACT

Introduction and Purpose: The aim of this article is to provide a comprehensive summary of the existing data on the impact of e-cigarette smoking on the human body and sport activity, taking into account collected clinical studies.

Research Objective: This review article presents a thorough analysis of the available data regarding the effects of e-cigarette use on human health. The authors provide the current state of knowledge based on numerous clinical, laboratory, and observational studies. Special attention is given to the mechanisms of action of e-cigarettes and the chemical composition of the aerosol they generate, which - despite the absence of combustion - contains a number of potentially toxic compounds. The article discusses the effects of vaping on various body systems, including cardiovascular, respiratory, nervous systems, and the oral cavity. Additionally, the topic of the impact of physical activity is discussed.

Materials and Methods: The article is based on an analysis of research available on PubMed. A literature review was conducted using the following keywords: “e-cigarettes,” “vaping,” “EVALI,” “sport activity “ and “impact on the body”.

Conclusions: Although e-cigarettes are often perceived as a less harmful alternative to traditional cigarettes, they are not without health risks—their use may lead to changes in the cardiovascular, respiratory, and nervous systems, as well as the oral cavity. Of particular concern are the effects of use during pregnancy and the risk of addiction among youth. Despite their potential role in harm reduction among smokers, their long-term safety and effectiveness in smoking cessation require further research.

Keywords: e-cigarettes, nicotine, cardiovascular system, oral health, blood-brain barrier, sport , activity

1.Introduction

At the very beginning, it is worth mentioning that the originator who initiated the idea related to e-cigarettes is Hon Lik - a Chinese pharmacist who created them exactly 22 years ago. [1] Since that breakthrough moment, the technology has spread on a global scale, both across European countries and the USA. Estimating the prevalence of e-cigarette use in Poland remains challenging due to limited and inconsistent data. According to the Institute for Economic Forecasts and Analysis, sales of e-cigarettes in Poland reached approximately 100 million units in 2023. Data from the report “Reduction of Cigarette Smoking and E-Cigarette Use, Particularly Among the Younger Generation of Poles” published by the Public Health Committee of the Polish Academy of Sciences indicate that 4.8% of Poles use e-cigarettes, while 4% use heated tobacco products. [2] The trend of increasingly frequent use of e-cigarettes is noticeable among adults (who previously smoked traditional cigarettes) as well as among the younger population in society - especially youth, who eagerly reach for e-cigarettes as something new. There is a widely accepted opinion that e-cigarettes are a safer form and an alternative to traditional tobacco products.

It is important to note that during the aerosol production process, there is no direct combustion involved. Primarily, their operation is based on heating special liquids. Nevertheless, it should be remembered that electronic cigarettes are not completely free of harmful chemical

compounds. It turns out that they may have a direct effect on the cardiovascular and respiratory systems, disrupt endothelial function, and influence cellular processes. This mainly concerns their impact on increasing the risk of oxidative stress and inflammation. This translates into the fact that e-tobacco products have become the subject of increasingly intense scientific debates and research involving them.

Some experts predict that in the coming years, e-cigarette sales may surpass those of traditional cigarettes. Such rapid market growth of these devices represents a significant turning point in efforts to reduce tobacco use. However, there is still a lack of sufficiently precise analyses that would unequivocally confirm their exact effects. [3]

2. General Characteristics of E-cigarettes

The term “e-cigarettes” actually refers to a wide range of devices, encompassing hundreds of products designed to deliver nicotine in an inhaled form, mimicking traditional smoking. In most cases, they take the form of portable, battery-powered devices. They are characterized by a discreet appearance, often resembling a pen or USB flash drive. It is also worth mentioning the chemical composition of e-cigarettes. It differs significantly from that found in tobacco smoke, with nicotine being one of the few common components in both sources. They often contain additional flavorings aimed at increasing their taste appeal. Important ingredients also include moisture-retaining agents such as propylene glycol (PG) and vegetable glycerin (glycerol).

Although the U.S. Food and Drug Administration (FDA) recognizes most of these flavoring and moisturizing substances as safe for consumption as food additives (classifying them as GRAS – Generally Recognized As Safe), there is still a lack of clear data regarding the risks of their long-term inhalation. [4] While aerosols from e-cigarettes generally contain lower amounts of toxins than smoke from traditional cigarettes, they are not completely harmless. Harmful substances such as heavy metals, volatile organic compounds, and carcinogens have been found in them.

Similarly, heated tobacco products (HTPs) generate an aerosol with lower concentrations of many toxic substances, including carbon monoxide, formaldehyde, acetaldehyde, and polycyclic aromatic hydrocarbons, which are well known for their negative health effects. Heated tobacco devices (HTPs) deliver approximately 70-80% of the nicotine compared to traditional cigarettes. This means that although their nicotine content is lower, they still carry a risk of addiction. [5] Increasingly, serious health problems related to e-cigarettes are being observed. Although our knowledge about the short-term effects of e-cigarettes is growing, the long-term health consequences, measured over many years, remain unclear and are the subject of ongoing research. [6]

3. Factors Associated with an Increased Risk of Side Effects Related to E-cigarette Use

Due to the fact that the use of e-cigarettes has gained increasing popularity worldwide, in-depth studies have been conducted on the adverse effects associated with them. An interesting conclusion is that a correlation has been observed between certain risk factors and more frequently reported health complaints related to addiction. These factors include: younger age (especially within the 18–24 age group), male gender, short duration of use (<6 months), concurrent smoking of traditional cigarettes, use of disposable devices, use of liquids containing nicotine, and menthol/mint flavors (compared to sweet flavors). Unfortunately, the conducted study was cross-sectional in nature, and it was emphasized that the descriptive data obtained could be subject to possible errors in symptom attribution. The adverse effects were mainly mild. Among those reporting symptoms, 35.1% sought medical help. This most often concerned cases of oral irritation (46.8% of people with this symptom) and loss of taste (45.2%). [7]

How an e-cigarette affects health depends on several factors - including the type of device used, how its heating element operates, the temperature it reaches, and the materials it is made of. Equally important is the quality of the liquid and the flavor additives. Since devices can differ significantly, the amount of harmful substances released during use can also vary widely. [8]

4. The impact of smoking e-cigarettes on the body

4.1. Cardiovascular System

Studies comparing different groups of e-cigarette users indicate that bodily responses may vary depending on prior experience with nicotine and tobacco smoking. Individuals who have never smoked traditional cigarettes may be more sensitive to the effects of nicotine contained in e-cigarettes. In their case, reactions such as increased blood pressure are more frequently observed, which can be significant from the perspective of cardiovascular health. Conversely, people who previously smoked cigarettes and then completely switched to exclusive e-cigarette use may experience some beneficial changes. This group has shown a reduction in the negative impact on the heart and blood vessels compared to traditional smoking. Although this does not always translate into improvements in parameters such as heart rate or cardiac function, there is a noticeable reduced burden on the circulatory system, especially regarding blood pressure.

However, attention should be paid to individuals who use both e-cigarettes and conventional tobacco products simultaneously - so-called dual users. In their case, there is no clear evidence that such an approach reduces the risk of heart disease. On the contrary, some studies suggest that the negative effects may accumulate, potentially increasing the risk of cardiovascular problems. Considering the current state of scientific knowledge, it can be said that although e-cigarettes may be less harmful than traditional cigarettes, they are not completely harmless to cardiovascular health. Their use is associated with certain changes in bodily functions that, in some individuals - especially those with pre-existing conditions - may have significant health implications.

Available scientific evidence indicates that e-cigarette use induces significant physiological changes even over a short period of use. The most commonly observed effects include increased heart rate (HR) [9], heart rate variability (HRV), and elevated blood pressure. Other observed bodily responses include changes in blood oxygen saturation, increased inflammatory markers, heightened arterial stiffness, signs of endothelial dysfunction, increased oxidative stress, as well as structural and functional changes in the heart. [10] E-cigarette use exerts a noticeable impact on the cardiovascular system, particularly concerning vascular elasticity. Even after a single use of these devices, an increase in arterial stiffness is observed, as confirmed by measurements such as pulse wave velocity and augmentation index. These changes may indicate an elevated risk of heart and circulatory diseases. [11] Additionally, inhalation of e-cigarette aerosol contributes to increased levels of substances indicative of oxidative stress, such as malondialdehyde in the blood. Elevated levels of this marker suggest that e-cigarette use may lead to cellular damage resulting from an imbalance between free radicals and the body's defense mechanisms.

4.2. Respiratory system

E-cigarettes operate using battery power, which activates a heating element. This element heats a special liquid (e-liquid) to a temperature of approximately 200–300°C, producing an aerosol that is then inhaled into the lungs. [12] Chemical analyses of e-cigarette aerosol have revealed the presence of numerous potentially harmful substances, such as aldehydes (e.g., formaldehyde and acetaldehyde), volatile organic compounds (VOCs), heavy metals, and ultrafine particles capable of penetrating deeper into the lungs. Although these compounds are present, their

concentrations are generally much lower than those found in cigarette smoke. Nevertheless, it is important to consider that exposure to e-cigarette aerosol is comparable to that experienced during tobacco smoking.

A range of changes in the respiratory tract is observed, including increased airway resistance, decreased bronchial conductance, and increased impedance and overall resistance. These phenomena are similar to those seen in traditional cigarette smokers. Many analyses indicate an immediate decrease in exhaled nitric oxide levels, which is also characteristic of tobacco smoking. However, findings regarding levels of inflammatory signaling molecules are inconsistent, with studies showing both increases and decreases following exposure. [13]

It is worth noting that e-cigarette use is also associated with the development of acute bronchitis and increased airway hypersensitivity to allergens. However, no direct evidence has been found that e-cigarette use has a clear impact on asthma symptoms - such as wheezing. McConnell et al. emphasize the urgent need for further toxicological analyses and studies, particularly focusing on the long-term effects of e-cigarette use. [14]

Clinical studies conducted on both smokers and non-smokers have shown that the use of IQOS® leads to an immediate and significant decline in lung function. These changes were measured by reductions in parameters such as peak expiratory flow and forced expiratory flow at 25% and 50% of vital capacity. Additionally, an increase in airway resistance was observed. Furthermore, laboratory (in vitro) studies using IQOS® aerosols confirmed their toxic effects on human cells, including bronchial epithelial cells and other respiratory system cells. [15]

EVALI - E-cigarette or Vaping product Use-Associated Lung Injury

With the growing popularity of vaping, especially among younger users, the medical world faced a serious new health challenge in the summer of 2019. At that time, a mysterious lung disease was identified, which quickly raised concerns in the medical community and was officially named EVALI - an acronym for “E-cigarette, or Vaping, product Use-Associated Lung Injury.” This disease manifests in a very sudden and alarming manner. One of its most severe symptoms is a significant drop in oxygen saturation levels in the blood, which in many cases required immediate treatment involving oxygen therapy. At the same time, patients exhibited a strong systemic inflammatory response. This defensive reaction of the body was reflected, among other things, by an increased white blood cell count, a typical indicator of ongoing inflammation. The most common complaints reported by patients included respiratory symptoms such as cough, shortness of breath, and chest pain. Importantly, over 80% of patients also reported gastrointestinal disturbances - including nausea, vomiting, and abdominal pain. Additionally, many experienced general symptoms characteristic of infection or inflammation, such as fever, extreme fatigue, chills, and overall weakness. Many patients required hospitalization and advanced medical care. Depending on the severity of symptoms and the extent of lung damage, various forms of respiratory support were used. In milder cases, oxygen administration was sufficient, but in more advanced cases, non-invasive ventilation or even mechanical ventilation was necessary. In the most severe cases, when traditional methods failed, patients underwent life-saving specialized procedures such as extracorporeal membrane oxygenation (ECMO), used when the lungs cease to function adequately on their own. [16]

4.3. Nervous System

Studies on human brain endothelial cells have shown that exposure to e-cigarette aerosol can lead to mitochondrial dysfunction, increased intracellular calcium levels, and intensified stress in the endoplasmic reticulum. Such cellular responses are important because mitochondrial dysfunction has been linked to increased permeability of the blood-brain barrier. Notably, negative changes were observed even with exposure to nicotine-free e-cigarettes. Further research into the effects of substances found in tobacco smoke and e-cigarette aerosol has

revealed concerning cellular and molecular alterations, particularly regarding their impact on the nervous system. Both traditional cigarette smoking and inhaling vapor from electronic vaping devices can lead to increased oxidative stress - a condition where an excess of free radicals accumulates, damaging cells and disrupting their normal function.

One of the most worrying phenomena observed is the adverse effect on the blood-brain barrier. Researchers noted increased activity of pro-inflammatory molecules such as TNF- α and PECAM-1, signaling on going inflammation in the body. Simultaneously, reduced levels of certain proteins responsible for tight junctions between endothelial cells, such as ZO-1, were observed. These proteins are crucial as they maintain the integrity of the blood-brain barrier. Their weakening leads to loosening of these junctions, which in turn results in increased permeability of blood vessels - especially to larger molecules that normally should not pass into the brain. [17]

4.4. Oral cavity

One area that particularly deserved attention is the potential impact of e-cigarettes on oral health. Unfortunately, despite the growing number of users, knowledge about the long-term consequences of vaping on the mouth and teeth remains fragmentary and incomplete. Based on a meta-analysis conducted by Muhammed Szabil and his colleagues, we can refer here to the impact of smoking on periodontitis. This is actually a disease with a complex etiology. Its primary cause is bacterial biofilms adhering to the surface of the teeth. However, its development and severity are significantly modified by a range of other risk factors. Among them, key roles are played by genetic predispositions, the general health status of the body, as well as lifestyle choices (including cigarette smoking). According to data from the Global Burden of Disease Study, severe periodontitis is the sixth most common disease worldwide. This high prevalence, combined with its impact on tooth loss and its association with systemic health problems such as cardiovascular diseases and diabetes, makes periodontitis a serious global public health challenge.

The analysis showed that traditional cigarette smokers had significantly higher levels of dental plaque, deeper periodontal pockets, attachment loss, marginal bone loss and elevated concentrations of pro-inflammatory mediators compared to e-cigarette users and non-smokers. However, the authors did not provide a sufficiently detailed comparative assessment between e-cigarette users and never-smokers. [18] It is also worth noting that an increased risk of dental caries development has been observed in association with e-cigarette use. This relationship is driven by the interaction of substances contained in the aerosol that directly affect tooth enamel. This is mainly explained by an increased predisposition for microorganisms to adhere directly to the tooth surface due to the action of glycerin and flavoring agents. This causes biofilm to develop faster, leading to progressive demineralization. [19]

Some studies have analyzed how smoking affects the effectiveness of periodontal disease treatment. One study showed that traditional cigarette smokers had a weaker therapeutic response in sites with pocket depths > 4 mm after six months of treatment compared to e-cigarette users.

Another study found, however, that compared to non-smokers, e-cigarette users responded worse to treatment after plaque removal - more frequently requiring surgical intervention. Nevertheless, their treatment response did not differ statistically significantly from that observed in traditional smokers. [20]

Microbiological analyses have shown that e-cigarette users have a different composition of oral microbiota compared to non-users. There are also suspicions that this altered microbiome may be more harmful. Although clinical research results regarding the impact of e-cigarettes on oral health are still insufficient, epidemiological observations indicate more frequent occurrences of dry mouth, irritation and gum problems among users. [21]

5. E-cigarettes and Their Potentially Carcinogenic Components

Studies clearly indicate the presence of toxic chemical compounds in the vapor exhaled from e-cigarettes, raising serious health concerns. Formaldehyde, classified as a human carcinogen, and acetaldehyde, a potential carcinogen, have been detected in this vapor. Additionally, acrolein is present, known for its irritating effects on the respiratory tract and its potential contribution to cardiovascular diseases, similar to those seen in traditional cigarette smokers. Exposure to these carbonyl compounds often leads to irritation of the mouth and throat, which are among the most commonly reported side effects among e-cigarette users. Moreover, research shows that simultaneous exposure to formaldehyde, acetaldehyde, and acrolein can cause stronger irritation than each compound individually. Further studies are needed to assess the full range of short- and long-term health risks both for e-cigarette users themselves and for those exposed to secondhand vapor.

Toxic metals such as cadmium, nickel, and lead have also been identified in the vapor of analyzed e-cigarettes. However, since these same elements were also detected in trace amounts in Nicorette® inhalers and control samples, it is impossible to definitively state whether e-cigarettes themselves are a significant source of exposure to these substances. This uncertainty calls for further research to exclude other sources of contamination. [22] Currently, there is no dedicated screening program targeted exclusively at e-cigarette users for early detection of lung cancer. This group has not yet been included in separate diagnostic recommendations due to a lack of clear and sufficiently strong scientific evidence supporting the need for such action. Nevertheless, as research on the long-term effects of vaping progresses, it is possible that in the future - if more convincing data emerge - the scope of screening programs may be expanded. This could apply not only to e-cigarette users but also to individuals exposed to other significant environmental hazards that may increase the risk of developing respiratory system cancers. [23] In turn, detailed molecular analyses have shown that e-cigarette vapor is harmful to DNA, causing strand breaks. Additionally, toxic effects on cells have been observed, manifested by cell damage and reduced survival capacity. [24]

6. Electronic cigarettes as a tool for quitting traditional smoking

Tobacco smoking is a global public health problem that imposes enormous economic and social burdens. Its impact on health is catastrophic, as nicotine contained in cigarettes is recognized as a key risk factor for many serious diseases. These include primarily lung cancer, cardiovascular diseases, strokes, and chronic lung diseases. [25] Tobacco smoking remains the leading preventable cause of premature death worldwide. According to the recommendations of the World Health Organization (WHO), an effective strategy to combat the negative effects of smoking should focus on supporting smokers to completely quit the addiction. [26]

In light of these considerations, there has been growing interest in whether e-cigarettes could be a better alternative in achieving this goal. Consequently, analyses have been conducted suggesting that e-cigarettes may be helpful in reducing the habit of smoking and in the process of quitting altogether. However, their effectiveness appears to be moderate. This means that while they offer some support to individuals wishing to break the addiction, their role in this process is neither decisively conclusive nor comprehensive. Potentially, e-cigarettes may serve as a transitional or harm-reduction tool but not necessarily as a universal solution for every smoker. A cautious approach is recommended regarding the “promotion” of e-cigarettes, especially among young adults and people with low levels of nicotine dependence. [27] Although e-cigarettes contain fewer toxic substances than tobacco smoke, their long-term safety is not yet fully understood. Nevertheless, in the context of the harmfulness of traditional cigarette smoking, e-cigarettes may represent a less harmful alternative, particularly for those who have not succeeded with other cessation methods. [28] The increased concentration of

nicotine found in e-cigarettes may provide certain benefits to adults who have previously smoked traditional cigarettes and are currently seeking effective methods to break nicotine addiction. For them, a higher nicotine dose may help reduce nicotine cravings and alleviate withdrawal symptoms, potentially increasing the chances of completely quitting conventional smoking. However, this same feature - a high nicotine content - poses a serious risk to adolescents and young adults who have no prior exposure to nicotine. [29] In their case, rapid development of addiction may occur, raising significant health and social concerns, especially since the nervous system of young individuals is more vulnerable to the effects of psychoactive substances. Although many people view e-cigarettes as a tool supporting smoking cessation, their effectiveness in this role has not yet been conclusively confirmed. Further well-designed, long-term scientific studies are necessary to assess whether they can truly be an effective aid in nicotine addiction therapy. [30]

7. E-cigarette use during pregnancy and the puerperium

The belief that e-cigarettes represent a safer alternative to traditional tobacco products may lead pregnant women to switch from conventional cigarettes to electronic nicotine delivery systems. From their perspective, such a transition may seem to reduce the exposure—both for themselves and their developing fetus—to harmful tar substances and numerous carcinogenic compounds present in tobacco smoke. As a result, while they may quit smoking conventional cigarettes, many continue to maintain their nicotine intake, albeit in a different form.

However, it is essential to emphasize that many of the adverse health outcomes associated with smoking during pregnancy are not solely attributable to other constituents of tobacco smoke but are largely a consequence of nicotine exposure itself. Nicotine exerts toxic effects on the developing fetal nervous system, can impair placental blood flow, and may negatively influence fetal growth and development during the prenatal period. In light of this, the use of e-cigarettes during pregnancy cannot be considered a neutral or safe alternative. Moreover, due to the false sense of safety often associated with these devices, some women may increase the frequency of vaping compared to their previous use of combustible cigarettes. This can lead to even greater nicotine exposure, posing significant health risks to both the mother and the developing child. Therefore, e-cigarettes do not eliminate the risks associated with nicotine use during pregnancy; on the contrary, they may amplify them, particularly if they result in more frequent or prolonged exposure to nicotine. [31]

This topic is further explored in the research conducted by Mills et al., who examined the use of e-cigarettes by women in the postpartum period, also referred to as the "fourth trimester of pregnancy." Their publication focuses on the health consequences of e-cigarette use during this critical phase, with particular emphasis on cardiovascular function and overall maternal health. The postpartum period, encompassing the first twelve weeks after childbirth, involves a series of physiological recovery and adaptation processes in the maternal body.

The aim of their study was to fill the existing knowledge gap regarding the health effects of exposure to e-cigarette aerosol during pregnancy. Such insights are particularly important, as e-cigarettes are often mistakenly viewed as significantly less harmful than traditional tobacco products—an assumption that, despite lacking conclusive scientific evidence, is frequently extended to the context of pregnancy.

Furthermore, experimental studies using animal models have demonstrated serious risks associated with prenatal exposure to nicotine-containing aerosol. Animals exposed to substances found in e-cigarettes during pregnancy exhibited higher rates of miscarriage, and their offspring showed lower survival rates until weaning. [32] These findings suggest that e-cigarette use during pregnancy may disrupt normal fetal development and reduce fetal viability, raising substantial health concerns. Given the potential and according to some data, actual risks related to nicotine presence in the pregnant body, the most recommended and safest approach

remains complete cessation of all nicotine-containing products. The use of nicotine-based therapies, such as nicotine replacement therapy (NRT) or e-cigarettes, should only be considered in cases where the only alternative is continued use of traditional combustible tobacco. [33] In other words, nicotine substitutes may be considered as a harm reduction strategy, but not as a first-line treatment for pregnant women.

8. The impact of e-cigarette smoking on the sport activity.

Heated tobacco products, including IQOS®, have been promoted as alternatives that may reduce exposure to certain toxic substances in comparison with conventional cigarettes. Nevertheless, their use cannot be considered free of health risks. The perception of IQOS® as a safer option—largely shaped by marketing strategies and public messaging—has contributed to its increasing popularity, particularly among adolescents and young adults. [34] Studies conducted among adolescents indicate a relationship between the use of e-cigarettes and lower levels of physical activity compared with non-smokers. These findings suggest that the use of such nicotine products may be associated with reduced engagement in physical activity. Similar conclusions were obtained in a study involving a cohort of young men in which selected indicators of physical fitness were assessed. Individuals who reported using e-cigarettes achieved significantly poorer results in fitness tests than non-smokers. Even more unfavorable results were observed among so-called dual users, defined as individuals who use both e-cigarettes and traditional cigarettes. [35]

9. Conclusions

Despite the growing popularity of e-cigarettes as a supposedly “safer” alternative to traditional tobacco products, a growing body of research demonstrates that their use is not free from serious health risks. The aerosols produced by e-cigarettes contain numerous harmful substances, including heavy metals, aldehydes, carcinogens, and ultrafine particles, all of which can adversely affect the respiratory, cardiovascular, and nervous systems. Even short-term use of e-cigarettes has been shown to increase blood pressure, elevate heart rate, impair endothelial function, and intensify oxidative stress. In the respiratory system, e-cigarette use has been linked to increased airway resistance, reduced bronchial conductance, symptoms of acute bronchitis, and associations with EVALI (e-cigarette or vaping product use-associated lung injury). Additionally, e-cigarette aerosols negatively impact the blood–brain barrier by increasing its permeability and triggering inflammatory responses. Oral health is also compromised with users experiencing a higher risk of dental caries, periodontal disease, dry mouth, and alterations in the oral microbiome. While e-cigarettes generally contain fewer toxic substances than conventional cigarettes, their long-term health effects remain insufficiently understood. Particularly concerning is the use of e-cigarettes during pregnancy, as women - misled by the perception of reduced harm - may continue delivering nicotine to their bodies in this form. Studies indicate that nicotine itself, regardless of the method of administration, may disrupt fetal development, increase the risk of miscarriage, and reduce offspring survival. Consequently, e-cigarettes not only fail to eliminate the risks associated with smoking during pregnancy but may in fact exacerbate them. In the context of smoking cessation, e-cigarettes may serve as a harm reduction tool for adult smokers who have not succeeded with other methods. Nevertheless, their effectiveness in supporting complete cessation remains limited. Moreover, their promotion among young adults and non-smokers poses a significant risk of initiating nicotine dependence. This calls for cautious evaluation of e-cigarettes and underscores the need for further long-term research.

Disclosures

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