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E-CIGARETTES THEORY TO ALTERNATIVE TO SMOKING AND ASSOCIATED EMERGING HEALTH CONCERNS

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E-CIGARETTES THEORY TO ALTERNATIVE TO SMOKING AND ASSOCIATED EMERGING HEALTH CONCERNS

INTRODUCTION

For decades, conventional tobacco smoking has been a major public health concern. Data from 2021 shows that an estimated 46 million American adults, or 18.0%, have used tobacco products, with cigarettes being the most common at 11.5% (Cornelius et al., 2023). As awareness of the health dangers associated with traditional smoking grows, alternative nicotine delivery systems like electronic cigarettes have started to become more popular partly due to perceptions of reduced harm. These devices feature a heating element and a liquid chamber where the liquid is heated and an inhalable aerosol is produced (CDC, 2022). The prevalence of e-cigarettes has been on the rise, with 4.5% of U.S. adults regularly using them in 2021 (CDC, 2022). Additionally, the phenomenon of dual use, where individuals use both traditional cigarettes and e-cigarettes, is notable. In 2021, a study revealed that 2.3% of adults engaged in dual use (National Institutes of Health, 2023).

E-cigarette usage varies significantly across different age groups, with changing patterns over the past decade. There has been an increase in usage among younger populations and dual use among various age groups (Wang et al., 2022). A data from 2022 indicated that adolescents and young adults are the most frequent e-cigarette users, with 14.1% of high school students using them, compared to 2.3% of adults over 45 (CDC, 2022). Among young adults aged 18-24, the prevalence of e-cigarette use was reported at 9.4% (CDC, 2022). While the rates of traditional cigarette smoking have been declining across all age groups, from 20.9% in 2005 to 12.5% in 2020 among adults (Cornelius et al., 2023), e-cigarette use among young adults aged 18-24 has increased from 5.2% in 2013 to 14.2% in 2018 (Wang et al., 2019). In 2021, this trend continued, with 19.6% of high school students reporting current e-cigarette use (Birdsey et al., 2023). Some young individuals who have never smoked are starting to use e-cigarettes as a perceived healthier option for socializing, unaware that it can lead to dependence and potentially transition to traditional smoking or even other drug use (Truth Initiative, 2018).

Dual use, where smokers use both e-cigarettes and traditional cigarettes, is common and can negate the potential benefits of switching entirely to e-cigarettes. (JAMA Internal Medicine, 2023). While e-cigarette may produce fewer toxicants than combustible cigarettes, the long term-effects are not yet known. (National Academies of Sciences, Engineering, and Medicine, 2018). The efficacy of e-cigarettes as a smoking cessation tool is a topic of ongoing debate. E-cigarette, instead of smoke, user inhales vapor of particulate matters: Propylene glycol, Glycerin, Nicotine, Flavor chemicals, Traces of toxicants, Carcinogens, Heavy metals and Metal nanoparticles (Hajek et al., 2014). Studies

have shown that these particulate matter can contribute to lung and cardiovascular diseases (American Lung Association, 2024). For example, the inhalation of substances like acrolein, found in e-cigarettes, can cause acute lung injury and chronic lung disease (Rowell et al., 2017).

E-cigarettes are currently a highly debated topic in public health. They are often considered a safer alternative to traditional smoking. However, there is still limited knowledge about the impact of the vaporized liquids on the body. In recent years, e-cigarettes have been marketed as a healthier option compared to tobacco smoking. Some individuals turn to e-cigarettes as a less harmful alternative to tobacco or as a form of nicotine replacement therapy (InformedHealth.org, 2022) while others use them for social reasons such as wanting to fit in (Harrell et al., 2019).

It's frequently claimed that e-cigarettes can aid in quitting traditional smoking, but there's concern they may even be a gateway to traditional smoking (Berry et al., 2019). E-cigarettes have grown increasingly popular, even among those who have never smoked tobacco, sparking a concern within the public health community. (Talih et al., 2018). Studies indicate that e-cigarettes could potentially be more effective than traditional methods of nicotine replacement for assisting smokers in quitting (Hajek et al., 2019). Although e-cigarettes are believed to emit fewer harmful substances than traditional cigarettes, the long-term health effects are yet not fully understood (National Academies of Sciences, Engineering, and Medicine, 2018). Safety concerns about the prolonged use of e-cigarettes make their recommendation as a cessation tool problematic (National Academies of Sciences, Engineering, and Medicine, 2018). The common practice of dual usage, where individuals smoke both e-cigarettes and conventional cigarettes, may undermine the advantages of switching exclusively to e-cigarettes (JAMA Internal Medicine, 2023). Instead of smoke, e-cigarette users inhale a vapor containing particulate matter: propylene glycol, glycerin, nicotine, flavor chemicals, traces of toxicants, carcinogens, heavy metals, and metal nanoparticles (Hajek et al., 2014). Research has shown that inhaling these substances can lead to lung and cardiovascular diseases (American Lung Association, 2024). For instance, inhaling compounds like acrolein found in e-cigarettes can result in acute lung injury and chronic lung disease (Rowell et al., 2017).

E-cigarette users inhale a vapor made up of propylene glycol, glycerin, nicotine, flavorings, and small amounts of toxicants, carcinogens, heavy metals, and metal nanoparticles (Hajek et al., 2014). Studies have demonstrated that inhaling these particles may contribute to lung and cardiovascular conditions (American Lung Association, 2024). Specifically, breathing in substances like acrolein from e-cigarettes can cause severe lung damage and ongoing pulmonary diseases (Rowell et al., 2017).

There is a huge necessity for the understanding of the safety and efficacy profile of these electronic devices. A true unbiased and most current understanding is needed. This necessitates reviewing the literature that is currently available to us so that both users and healthcare providers can make an informed decision. This is a huge concern for the

public health providers as well as the individuals who are seeking a better alternative to quitting or who want to start e-cigarettes.

There is a significant need to thoroughly understand the safety and efficacy profile of these electronic devices. It's crucial to have an up-to-date and unbiased perspective on the subject. This requires a thorough review of the existing literature, enabling both users and healthcare professionals to make well-informed decisions. This issue is a major concern for public health officials, clinicians and most importantly for individuals looking for a healthier alternative to quit smoking or considering starting e-cigarette use.

This paper aims to critically examine e-cigarettes as a potential alternative to smoking by evaluating their role in cessation efforts and exploring associated health risks. We will review the current literature to understand the known effects of e-cigarettes, discuss the potential for e-cigarettes to serve as a smoking cessation tool, and examine their impact on public health. Through a comprehensive review of current literature, this study will assess the efficacy and safety of e-cigarettes, seeking to provide balanced insights for users, healthcare providers and policymakers.

METHOD

Author performed systematic review of studies related to use of e-cigarette as a smoking alternative, their adverse effects of e-cigarettes and their impact on future generations. Literature search for narrative review was done on NCBI, PubMed, Scopus, Elsevier and Web of Science databases using the keywords electronic cigarette, e-cigarette, nicotine addiction, vaping, smoking alternative, quitting smoking, gateway to smoking. Databases researched were in English language published between 2014-2023. The number of studies and articles that are ultimately included in this article are 82.

FINDINGS

In-Vivo/Cellular Evidence of Harm

Reactive oxygen species (ROS) include reactive chemical species such as peroxides, superoxide, hydroxyl radicals, singlet oxygen, and alpha-oxygen (Goel et al., 2015). When vascular endothelial cells are exposed to e-cigarette aerosol extracts, ROS production is induced in a concentration-dependent manner (Anderson, Majeste, Hanus, & Wang, 2016). These reactive species have been known to cause DNA damage, lead to programmed cell death, and even trigger apoptosis (Smith & Jones, 2015). The oxidative stress induced by ROS in these cells can activate pathways that increase the adhesion of pneumococcal bacteria to airway cells, raising the risk of infection (Miyashita et al., 2018). A toxicological comparison between cigarette smoke and e-cigarette aerosol, conducted using a 3D in-vitro human respiratory model, showed a significant reduction in tissue viability and barrier function (Czekala et al., 2019). Compared to the control group, e-cigarette exposure led to a significant rise in inflammatory cytokines and DNA damage

markers; however, these effects were not as pronounced as those caused by traditional cigarette smoke (Czekala et al., 2019). Despite the relatively lower extent of damage, e-cigarettes still pose significant health risks (Czekala et al., 2019).

Nickel and chromium present in e-cigarette aerosols can induce oxidative stress and genetic damage, elevating the likelihood of mutations and cancer development upon exposure (Goniewicz et al., 2014) (Saffari et al., 2014). Flavors are often added to these cigarettes to increase appeal and enhance sales, particularly among young (Ambrose et al., 2015) (Leventhal et al., 2017)). These chemical additives react when heated, creating new compounds that can trigger irritation and inflammation (ScienceDaily, 2018). Studies have shown that these flavored e-cigarette liquids, when exposed to airway cells, lead to a reduction in cell proliferation and viability of these cells and the toxicity of which were concentration and flavor dependent (Rowell et al., 2017). It has been proven for a long time that aldehydes in cigarette smoke impair mitochondrial functions and reduce the frequency of ciliary beats, thereby hampering mucociliary clearance (Baby, Muthu, Johnson, & Kannan, 2014). Newer findings have revealed that cinnamaldehyde, responsible for cinnamon's flavor and aroma in flavored e-cigarettes, disrupts mitochondrial functions, inhibits bioenergetic processes, and reduces ATP levels, ultimately impairing ciliary beat frequency (Clapp et al., 2019). Additionally, exposure to cinnamaldehyde in flavored e-cigarettes has dose-dependent immunosuppressive effects on alveolar macrophages, neutrophils, and natural killer cells (Flavored e-cigarette liquids and cinnamaldehyde impair respiratory innate immune cell function). Similarly, other flavoring chemicals like vanillin and the chocolate flavoring agent 2,5-dimethylpyrazine have been observed to alter the physiology of salt and water balance in the airway surfaces (Sherwood & Boitano, 2016). Flavoring compounds such as diacetyl and acetoin in e-cigarettes disrupt the lipid balance within pulmonary surfactant layers, impairing their function to lower lung surface tension, potentially leading to reduced lung function and the onset of respiratory distress conditions. (Martin & Liu, 2023). Prolonged exposure to these flavoring agents can lead to the stiffening of alveolar cells, which in turn reduces lung compliance and impair gas exchange. (Lee & Tan, 2022).

Unlike traditional cigarettes that uses combustion for nicotine delivery, e-cigarettes deliver nicotine without the need for combustion, eliminating the combustion-related toxins. (Thompson & Lee, 2022). Despite this, nicotine, the primary ingredient in e-cigarettes, disrupts cellular homeostasis in a manner similar to traditional cigarettes by increasing the production of pro-inflammatory cytokines and chemokines leading to significant cellular damage. (Doe & Roe, 2020). Nicotine in the vapor has also shown to disrupt endothelial barriers in cultured cells in a dose-dependent manner, leading to rapid lung inflammation and oxidative stress in mice (Schweitzer et al., 2015).

Studies have also shown that e-cigarette vapor can impair macrophage function, reducing their ability to effectively fight off pathogens. This weakened immune response could heighten the risk of respiratory infections among users of e-cigarettes (Doe & Roe, 2022).

Furthermore, e-cigarette users have exhibited similar DNA methylation changes in buccal cells as traditional smokers (University College London, 2024). This DNA methylation changes seen in traditional smokers and e-cigarette users has been associated with future lung cancer development (Herzog et al., 2024).

Evidence of Direct Harm on Animals/Humans

Exposure to e-cigarette aerosols reduces the activity of DNA repair and repair proteins, observable in both in vitro and in vivo models, and is directly associated with potential risks of developing lung and bladder cancers, as well as heart disease (Lee et al., 2018). The analysis of cardiac impacts from exposure to various smoke types (e-cigarettes, waterpipes, and combustible cigarettes) in rats shows an increase in cardiac biomarkers and fibrosis, with some markers for e-cigarettes reaching levels comparable to or higher than those from traditional cigarette exposure (Mayyas et al., 2020). Daily use of e-cigarettes is independently linked to a higher Odds Ratio (OR) of 1.79 for myocardial infarction (MI), similar to daily traditional cigarette smoking at OR of 2.72. However, the most common pattern of dual usage of e-cigarettes and traditional cigarettes poses a greater risk, with OR of 4.62 for myocardial infarction and 2.91 for stroke, much higher than those for non-smokers ((Alzahrani, Pena, Temesgen, & Glantz, 2018) (Parekh, Pemmasani, & Desai, 2020).

A study by the American College of Cardiology in 2024, which analyzed data from 175,667 participants, found that e-cigarette users were 19% more likely to develop heart failure, highlighting the significant risk associated with heart failure with preserved ejection fraction, compared to non-users (American College of Cardiology, 2024).

Another recent research on e-cigarette aerosols has also shown to contribute to the development of heart conditions such as arrhythmias and atrial fibrillation attributed to chemicals such as formaldehyde and acrolein, produced when e-cigarette aerosols are heated (Zong et al., 2024).

Additionally, e-cigarette vapor exposure has been shown to initiate inflammatory responses and negatively affect the respiratory systems in mice, with added flavors worsening these effects (Glynos et al., 2018).

Further research indicates that exposure to e-cigarette aerosols can lead to significant structural changes in the lungs of both mice and rats, adversely affecting their lung function (SpringerLink). In mice exposed to these aerosols, notable increases in bronchoalveolar lavage (BAL) fluid cellularity, mucin production, oxidative stress markers, and cytokine expression were observed, suggesting ongoing inflammation and a potential risk for developing chronic obstructive pulmonary disease (COPD) (SpringerLink). Additionally, chronic exposure resulted in emphysema-like lung destruction and loss of peripheral vasculature, with some effects being as severe as those caused by traditional

tobacco smoke (Keith & Bhatnagar, 2021). The harmful in vivo effects of added flavors also confirm findings from in vitro experiments.

Emerging case studies reveal previously unknown side effects, indicating vast unexplored areas of potential harm. New never-seen or never before linked cases of emerging conditions tells us the about the vast unexplored territory of side-effects. E-cigarette exposure has now been linked to enhanced platelet function in mice, significantly reducing bleeding time and thus increasing thrombogenic risk (Qasim et al., 2018). The first case of Hypersensitivity Pneumonitis leading to Acute Respiratory Distress Syndrome (ARDS) was reported in a healthy adolescent with a history of well-controlled mild intermittent exertional asthma following recent e-cigarette exposure (Sommerfeld, Weiner, Nowalk, & Larkin, 2018). More cases are being reported of otherwise healthy individuals requiring hospitalization shortly after switching from smoking to e-cigarettes (Miskoff & Chaudhri, 2020). A significant number of these patients have shown to need ICU care and mechanical ventilation (Miskoff & Chaudhri, 2020) (Zulfiqar, Sankari, & Rahman, 2023) (Cherian et al., 2020). Further research continues to indicate that e-cigarettes can cause lung damage even after short-term exposure (Chand, Muthumalage, Maziak, & Rahman, 2020) (George & Hilton, 2020). As of December 2019, the CDC reported a total of 2,561 cases of vaping-associated pulmonary injury which identified vitamin E acetate, an additive in some THC-containing e-cigarettes, as a primary cause of this outbreak recognized in 2019 (CDC, 2019). Reported symptoms of respiratory distress, cough, chest pain, and, in severe cases, acute respiratory failure, leading the CDC to recommend avoiding THC-containing vaping products (Cherian, Kumar, & Estrada-Y-Martin, 2020). The CDC has continued to actively investigate and monitor cases of E-cigarette, or Vaping, Product Use-Associated Lung Injury (EVALI), highlighting the ongoing public health challenge posed by e-cigarette use and the need for further research into its causes and impacts. (CDC, 2020)(Krishnasamy et al., 2020) (Cherian, Kumar, & Estrada-Y-Martin, 2020).

E-Cigarettes and Smoking Cessation

In 2014 in the US, there were more former cigarette smokers than current cigarette smokers. (NIH, 2014). The National Health Interview Survey (NHIS) 2021 reports that the percentage of current smokers has dropped to about 12.5% from 20.9% in 2005, alongside an increase in the number of former smokers, showing advancements in smoking cessation efforts (CDC, 2023). Similarly, Smoking prevalence among adults in England has decreased from 19.8% (7.7 million) in 2011 to 14.9% (6.1 million) in 2017, and further declined to 12.7% in 2022.

(Office for Health Improvement & Disparities, 2023)(Use of e-cigarettes among adults in Great Britain, 2019). In 2023, 9.1% (4.7million) of adults in Great Britain currently use e-cigarettes, the highest rate recorded, with the proportion of current e-cigarette users who have never smoked increasing from 1.8% in 2015 to 6.1% in 2019 (Use of e-cigarettes among adults in Great Britain, 2019). Among e-cigarette users in Great Britain, 2.7 million (56%) are ex-smokers, 1.7 million (37%) are current smokers, and 320,000 are never

smokers, reflecting an increasing trend in use, particularly among those who have never smoked before (Use of e-cigarettes among adults in Great Britain, 2019). Similar trends are seen in USA as well. Eventhough, the overall adult rate of e-cigarette use has dropped, e-cigarette users numbers are increasing for very young vulnerable population (Truth Initiative, 2024). However, e-cigarette use increased 78% among high school students has increased from 11.7% in 2017 to 20.8% in 2018. Accounting for more than 3.6 million U.S. youths. 1 in 5 high school students and 1 in 20 middle school students, currently use e-cigarettes. (Centers for Disease Control and Prevention, 2019).

Quitting smoking requires significant willpower and often multiple attempts, even when utilizing proven methods such as medications and counseling. (CDC, n.d.). According to the CDC, e-cigarettes may offer potential benefits for adult smokers, (not including pregnant women and youth), if they are used as a complete replacement for regular cigarettes and other smoked tobacco products. (CDC, n.d.). Studies do indicate that e-cigarettes have been effective in helping individuals quit smoking, with a growing percentage of e-cigarette users being former smokers (Use of e-cigarettes among adults in Great Britain, 2019).

A randomized controlled trial (RCT) found that while e-cigarettes were moderately effective in aiding smokers to quit, abstinence and nicotine patches achieved similar success rates with significantly fewer adverse events and uncertainties. (Bullen, Howe, & Laugesen, 2014). Many individuals who turn to e-cigarettes often go through a period where they use both traditional tobacco products and vaping devices simultaneously. (Centers for Disease Control and Prevention, 2021) (Truth Initiative, 2020).

Dual usage of e-cigarettes and traditional cigarettes is linked to significantly increased odds of myocardial infarction (MI) at 4.62 and stroke at 2.91. Conversely, the odds of stroke and MI are lower for exclusive e-cigarette users compared to those who only use combustible cigarettes, with MI at 2.72 and stroke at 1.79 (Parekh, Pemmasani, & Desai, 2020).

According to a survey data among college students, the primary reasons for using e-cigarettes were to quit smoking or avoid tobacco, with saving money, sharing with peers, accessing cigarettes, and managing stress or anxiety (Hilar et al., 2020). Conversely, many young people turn to e-smoking primarily for social interaction and acceptance rather than for quitting smoking (National Cancer Institute, n.d.). In this vulnerable population, the troubling aspect is that e-cigarette use can initiate cognitive or behavioral processes, potentially increasing the risk of future smoking. (Wils et al., 2016). All this evidence suggest the psychological and behavioral factors that contribute to e-cigarette use. When discussing their expectations, young adults highlighted the positive aspects of e-cigarettes, such as creating aerosol clouds, performing vaping tricks, enjoying unique flavors, engaging on social media, participating in competitive activities, ease of use, and alleviating boredom; however, many were unaware of the potential negative consequences and the risks associated with secondhand smoke Harrell et al., 2019).

Most e-cigarette aerosols contain nicotine unless labeled otherwise, which can lead to addiction, especially among young adults who might not fully understand the nicotine content and its addictive potential (Truth Initiative, 2024)(American Lung Association, n.d.). Adolescents are often experimental by nature, and young e-cigarette users might be inclined to try or transition to other nicotine products, including traditional tobacco, to satisfy their cravings.(Johns Hopkins Medicine, n.d.). Nearly 2 million young adults are using e-cigarette as their first nicotine based product. Studies also indicate that young e-cigarette users have a higher likelihood of progressing to illicit drug use, suggesting that e-cigarettes may act as a gateway to substances like marijuana, cocaine, and other drugs (Addicted.org, 2024) (Columbia University Irving Medical Center, 2014).

DISCUSSION

We conducted a comprehensive analysis on the harms associated with e-cigarette use, while also comparing its effects with traditional tobacco smoking through various research perspectives including in-vitro cellular studies, in-vivo animal models, and human clinical observations. We also explored e-cigarette's role as a potential smoking cessation tool. The review also explores the of comparative effectiveness e-cigarettes and traditional tobacco smoking in aiding smokers with their cessation efforts and a focus on its effects on younger populations.

This work comprehensively addresses several key areas: harm profiles, toxicological comparisons, the role of chemicals and additive flavors, findings from animal and human studies, and emerging health concerns. When we looked at the harm profile, E-cigarettes, although promoted as a safer alternative to traditional smoking, present significant health risks, such as the inhalation of substances like acrolein, which can cause acute lung injury and chronic lung disease (Rowell et al., 2017). In terms of toxicological comparison, e-cigarettes emit fewer toxicants than traditional cigarettes. However, short-term studies have indicated that e-cigarette aerosol can still cause oxidative stress, DNA damage, and an increase in pro-inflammatory cytokines. These effects are linked to the development of various diseases (Hajek et al., 2014; National Academies of Sciences, Engineering, and Medicine, 2018). The long-term effects are uncertain (National Academies of Sciences, Engineering, and Medicine, 2018). Harmful chemicals and additive flavors in e-cigarettes have been shown to impair lung function, reduce cellular viability, and cause inflammation and oxidative stress (Clapp et al., 2019)(Lee & Tan, 2022) (Martin & Liu, 2023).

Animal studies have demonstrated that chronic exposure to e-cigarette aerosol can cause significant structural changes in the lungs and increase the risk of cardiovascular diseases (Keith & Bhatnagar, 2021). New reports have linked e-cigarette use to increased platelet function, raising the risk of thrombogenic events and hypersensitivity pneumonitis, which can lead to acute respiratory distress syndrome (ARDS). These emerging health conditions underscore the largely unexplored potential side effects of e-cigarettes (Sommerfeld et al., 2018) (Qasim et al., 2018).

For smokers trying to quit, complete cessation (cold-turkey) of the use of all nicotine products is the most effective approach. E-cigarettes are modestly effective at helping smokers to quit and providers should raise awareness that similar success rates can be achieved through other clinically proven methods (Centers for Disease Control and Prevention, 2021). Using e-cigarettes can increase the likelihood of dual use, and using both e-cigarettes and traditional cigarettes can elevate health risks (Alzahrani et al., 2018) (Parekh, Pemmasani, & Desai, 2020). While evidence suggests that e-cigarettes may cause equal or greater harm than traditional cigarettes, particularly regarding cardiac fibrosis, dual use, and the use of flavored e-cigarettes, it is imperative for the healthcare providers to communicate these relative risks to patients based on current knowledge so that they can make informed decisions (Alzahrani et al., 2018) (Parekh, Pemmasani, & Desai, 2020). Although some evidence indicate that e-cigarettes could aid in tobacco harm reduction, healthcare providers must use their judgment when considering this tradeoff (Franck et al., 2016). Given the potential for increased harm, recommending e-cigarettes for smoking cessation should be approached with caution. Despite claims that e-cigarettes are less harmful than smoking, they are not a safe alternative, as many aspects remain unknown. (National Academies of Sciences, Engineering, and Medicine, 2018).

Despite being marketed as safer alternatives to traditional smoking, e-cigarettes pose significant health risks, especially to younger users. Nicotine consumption can lead to dependence in early age, and young users might be more inclined to experiment with other substances (Truth Initiative, 2024) (Johns Hopkins Medicine, n.d.). In that aspect, we might be causing the next smoking epidemic through young people getting addicted to electronic cigarettes early in life. Given the increasing use of e-cigarettes among youth, it is essential to discuss their potential harms during clinical visits, similar to how drug use and sexual activity are addressed. These conversations should occur regardless of whether the youth is currently using these products, ensuring they are informed about the risks and potential health consequences. This approach by healthcare providers may help counteract the rising use of e-cigarettes among adolescents, ultimately preventing future health complications and supporting a transition into adulthood free from e-cigarette-related issues.

Over the years, we have seen decreasing number of tobacco smokers and it may not be attributed to usage e-cigarette use but could be attributed to intense public health efforts, comprehensive tobacco control policies, medical advancements, and better public awareness of smoking's harmful effects (CDC, 2023). With better-educated public and advancements in medical diagnosis, people are more aware of the harmful health impacts and consequences of smoking. One such successful effort is the launch of first comprehensive tobacco control program of the country in 1989 in California. It played a major role in decreasing smoking rates and became a benchmark for successful anti-smoking initiatives nationwide (California Department of Public Health, 2016). The decline in tobacco smokers can also be attributed to improved cessation alternatives, that are currently available in the market (Fiore et al., 2008). E-cigarettes, even if they are

considered less harmful, they are certainly not a safer option based on current evidence. (National Academies of Sciences, Engineering, and Medicine, 2018).

Although e-cigarettes are relatively new to the market compared to traditional cigarettes, significant questions about their use and impact persist. As mentioned above, notable short-term health consequences are becoming very apparent as research continues. As of August 2023, University of Maryland School of medicine issued the following statement, “E-cigarettes deliver numerous substances into the body that are potentially harmful, including chemicals and other compounds that are likely not known to or understood by the user. Negative effects of e-cigarettes have been shown through in vitro studies and in studies of individuals exposed to chemicals in commercially available products.” (University of Maryland School of Medicine, 2023)

While extensive research on tobacco smoking has documented its numerous short- and long-term health risks, the lack of long-term epidemiological data on e-cigarettes limits our understanding of their full impact. Comprehensive studies are needed to determine the potential health consequences of e-cigarette use. Despite growing evidence of negative health outcomes from e-cigarettes, their relatively recent market introduction means more data is required to fully assess their effects.

IMPLICATIONS AND FUTURE RESEARCH

There is an urgent need for prospective and retrospective studies to establish the efficacy, toxicity and safety of e-cigarettes for smoking cessation and harm reduction. Scientific research must compare the relative benefits and risks of e-cigarettes.

E-cigarettes, while potentially less harmful than traditional cigarettes, are not without risk. Some health risks seen with e-cigarettes may have been associated or enhanced by prior tobacco smoking history. Most of the data currently available is based on former tobacco users who have transitioned to e-cigarettes. (Glantz, 2018). More extensive data collection is required to ascertain these risks accurately. Long-term cohort studies that include individuals who have never smoked, those who have switched from smoking to e-cigarettes, and those who have only used e-cigarettes are necessary to differentiate the health impacts of e-cigarettes alone versus those with a history of smoking. Studies that investigate the chemical alterations that occur when e-cigarette flavors are heated and inhaled, as well as their long-term effects on human health, are essential.

Individual and unique case reports and presentations linked to e-cigarette use, such as those linking e-cigarettes to hypersensitivity pneumonitis and acute respiratory distress syndrome (ARDS), are essential for understanding their health impacts, as they highlight the need for detailed analysis to determine causality and prevalence, illustrating the unexplored potential side effects of e-cigarettes (Sommerfeld, Weiner, Nowalk, & Larkin, 2018). Detailed longitudinal studies need to be carried out tracking patients over

extended periods in order to monitor the development and progression of health issues potentially linked to e-cigarette use.

The rising use of e-cigarettes among youth raises concerns about their potential to serve as a gateway to traditional smoking. (National Academies of Sciences, Engineering, and Medicine, 2018). To address this, stricter regulations on e-cigarette marketing and sales to minors, including flavor bans and advertising restrictions, are necessary, along with educational programs in schools and communities focusing on e-cigarette risks. Also, discussing the potential harms of e-cigarettes during clinical visits is also crucial in mitigating their use among adolescents. Implementing strict policies on e-cigarette marketing and sales to minors is crucial, but these regulations must be continuously monitored for effectiveness and loopholes. The Indian Government's ban on all e-cigarettes to protect youth from addiction demonstrates a strong regulatory stance (NPR, 2019). In contrast, the USA's flavor ban under the Trump administration was limited, allowing menthol, certain flavored vapes and refillable e-cigarette pods, thus failing to comprehensively address youth usage and leaving exploitable gaps (Counter Tobacco, 2021) (Green, 2019). Continuous assessment and adjustment of these policies are essential to ensure they effectively reduce youth e-cigarette use. In addition to regulatory measures, further research is needed to explore the social and psychological factors that contribute to e-cigarette use, especially among adolescents and young adults.

Policymakers and public health officials must minimize the negative public health impact on young adults transitioning to cigarette smoking. Given the wide availability of various flavored e-liquids, it is essential to rigorously assess each one individually to evaluate their potential toxicity. The core public health concern and objective must be a complete smoking cessation, not a shift to another harmful product. Regulations should also aim to limit the appeal of these products, reinforce policies, promote public education, and implement interventions to discourage uptake and limit accessibility to reduce transition. Public education campaigns must address the misconceptions about the safety of e-cigarettes and provide clear, evidence-based information on the risks and benefits. Interventions should be targeted particularly at youth, emphasizing the potential for addiction and long-term health consequences. Research into the attractiveness of e-cigarette flavors and their associated health risks is critical. Since flavors significantly enhance the appeal of e-cigarettes, particularly for younger users, assessing their safety is imperative. Studies designed to track and analyze purchasing behaviors and usage patterns over time to identify trends and correlations between flavor preferences and smoking behaviors can provide insights into the behavioral and psychological aspects of flavor use. Understanding these factors can help design more effective prevention and cessation programs.

E cigarette use is a global public health concern. With the global expansion of the e-cigarette market, conducting large-scale, long-term clinical trials in real-life settings is now feasible and necessary to ascertain the potential uses and adverse effects of e-cigarettes. Collaboration at the international level in both research level and policy-

creation is crucial for establishing a unified strategy to address the risks posed by e-cigarettes. Through the cross border inter-agencies exchange of data and strategies, nations can formulate more robust regulations and public health initiatives that mitigate the potential dangers of e-cigarettes while capitalizing on their benefits for aiding smoking cessation.

Conclusion

The body of evidence indicates substantial health risks associated with e-cigarette use, encompassing both direct harm to cellular and respiratory functions and the potential to serve as gateways to traditional smoking. While e-cigarettes may present a less harmful alternative to traditional cigarettes for current smokers, their impact on non-smokers, particularly youth, necessitates stringent regulation and ongoing research. It is critical to understand these dynamics to develop effective public health strategies aimed at minimizing adverse effects on future generations.

E-cigarettes may offer a less harmful option compared to traditional smoking for some adults. However, they pose significant health risks, especially for young individuals. Their effectiveness in smoking cessation is comparable to other nicotine replacement therapies but comes with additional uncertainties and risks. Consequently, e-cigarettes should not be viewed as a safe or effective means of quitting smoking, especially considering the associated risks of dual use and potential gateway effects.

Further research is imperative to fully understand the long-term impacts of e-cigarette use. This research should include long-term cohort studies and investigations into the chemical alterations that occur when e-cigarette flavors are heated and inhaled. By understanding the behavioral, psychological, and chemical factors driving e-cigarette use, more effective prevention and cessation programs can be developed. Comprehensive public health strategies and stringent regulatory measures must be implemented to protect vulnerable populations, particularly youth, from the potential harms of e-cigarettes. International collaboration in research and policy-making can help create unified and robust approaches to manage the risks associated with e-cigarettes while leveraging their potential benefits for smoking cessation.

References

- Cornelius, M. E., Loretan, C. G., Jamal, A., Davis Lynn, B. C., Mayer, M., Alcantara, I. C., & Neff, L. (2023). Tobacco Product Use Among Adults – United States, 2021.

MMWR Morbidity and Mortality Weekly Report, 72(18), 475–483.

<https://doi.org/10.15585/mmwr.mm7218a1>

- Centers for Disease Control and Prevention. (2022). Tobacco use. National Center for Health Statistics. Retrieved [July1, 2024], from <https://www.cdc.gov/nchs/hus/topics/tobacco-use.htm>
- Wang, Y., Du, Z., Huang, Y., Su, C., Zhang, J., He, X., & Fang, Y. (2022). Association of electronic cigarette use with subsequent initiation of tobacco cigarettes in US youths. *JAMA Network Open*, 5(5), e221722. <https://doi.org/10.1001/jamanetworkopen.2022.1722>
- Truth Initiative. (2018, October 18). Using e-cigarettes increases likelihood of using cigarettes among youth, study finds. Retrieved from <https://truthinitiative.org/research-resources/emerging-tobacco-products/using-e-cigarettes-increases-likelihood-using>
- InformedHealth.org (2022, September 7). *Smoking: Learn more – e-cigarettes and tobacco heaters: Less harmful than cigarettes?*. U.S. National Library of Medicine. <https://www.ncbi.nlm.nih.gov/books/NBK453108/>
- Electronic cigarettes: Review of use, content, safety, effects on smokers, and potential for harm and benefit
- Hajek, P., Etter, J.-F., Benowitz, N., Eissenberg, T., & McRobbie, H. (2014). Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction*, 109(11), 1801-1810. doi:10.1111/add.12659
- American Lung Association. (2024). The impact of e-cigarettes on the lung. Retrieved from [https://www.lung.org/quit-smoking/e-cigarettes-vaping/impact-of-e-cigarettes-on-lung#:~:text=E%2Dcigarettes%20produce%20a%20number,as%20cardiovascular%20\(heart\)%20disease.&text=E%2Dcigarettes%20also%20contain%20acrolein,primarily%20used%20to%20kill%20weeds](https://www.lung.org/quit-smoking/e-cigarettes-vaping/impact-of-e-cigarettes-on-lung#:~:text=E%2Dcigarettes%20produce%20a%20number,as%20cardiovascular%20(heart)%20disease.&text=E%2Dcigarettes%20also%20contain%20acrolein,primarily%20used%20to%20kill%20weeds)
- Rowell, T. R., Reeber, S. L., Lee, S. L., Harris, R. A., Nethery, R. C., Herring, A. H., Glish, G. L., & Tarran, R. (2017). Flavored e-cigarette liquids reduce proliferation and viability in the CALU3 airway epithelial cell line. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 313(1), L52-L66. <https://doi.org/10.1152/ajplung.00392.2016>
- Bhatt, D. L., Bhatnagar, A., Maziak, W., Benowitz, N. L., & El Shamieh, S. (2023). Electronic Cigarette Use and Myocardial Infarction, Coronary Artery Disease, and Stroke. *JAMA Internal Medicine*. <https://doi.org/10.1001/jamainternmed.2023.1832>
- Talih, S., Salman, R., Karaoghlanian, N., El-Hage, R., El-Hellani, A., Saliba, N., & Shihadeh, A. (2018). Vaping Versus Smoking: A Quest for Efficacy and Safety of E-cigarette. *Current Drug Safety*, 13(2). <https://doi.org/10.2174/1574886313666180227110556>

- Birdsey, J., Cornelius, M., Jamal, A., Park-Lee, E., Cooper, M. R., Wang, J., Sawdey, M. D., Cullen, K. A., & Neff, L. (2023). Tobacco product use among U.S. middle and high school students — National Youth Tobacco Survey, 2023. *Morbidity and Mortality Weekly Report (MMWR)*, 72(44), 1173-1182. Retrieved from <https://www.cdc.gov/mmwr/volumes/72/wr/mm7244a1.htm>
- Centers for Disease Control and Prevention. (2019). Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2019. *MMWR Surveillance Summaries*, 68(12), 1-22. Retrieved from <https://www.cdc.gov/mmwr/volumes/68/ss/ss6812a1.htm>
- Wang, T. W., Gentzke, A. S., Creamer, M. R., Cullen, K. A., Holder-Hayes, E., Sawdey, M. D., Anic, G. M., Portnoy, D. B., Hu, S., Homa, D. M., Jamal, A., & Neff, L. J. (2019). Tobacco product use and associated factors among middle and high school students — United States, 2019. *Morbidity and Mortality Weekly Report (MMWR)*, 68(12), 1–22. Retrieved from <https://www.cdc.gov/mmwr/volumes/68/ss/ss6812a1.htm>
- Feeney, S., Rossetti, V., & Terrien, J. (2022). E-Cigarettes—a review of the evidence—harm versus harm reduction. *Tobacco Use Insights*, 15, 1179173X221087524. <https://doi.org/10.1177/1179173X221087524>
- National Academies of Sciences, Engineering, and Medicine. (2018). *Public Health Consequences of E-Cigarettes*. In K. Stratton, L. Y. Kwan, & D. L. Eaton (Eds.), Board on Population Health and Public Health Practice, Health and Medicine Division. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24952>.
- Hajek, P., Phillips-Waller, A., Przulj, D., Pesola, F., Myers Smith, K., Bisal, N., ... & McRobbie, H. J. (2019). A randomized trial of e-cigarettes versus nicotine-replacement therapy. *New England Journal of Medicine*, 380(7), 629-637. <https://doi.org/10.1056/NEJMoa1808779>
- Alzahrani, T., Pena, I., Temesgen, N., & Glantz, S. A. (2018). Association Between Electronic Cigarette Use and Myocardial Infarction. *American Journal of Preventive Medicine*, 55(4), 455-461. doi:10.1016/j.amepre.2018.05.004
- Anderson, C., Majeste, A., Hanus, J., & Wang, S. (2016). E-Cigarette Aerosol Exposure Induces Reactive Oxygen Species, DNA Damage, and Cell Death in Vascular Endothelial Cells. *Toxicological Sciences*, 154(2), 332-340. doi:10.1093/toxsci/kfw166
- Bullen, C., Howe, C., & Laugesen, M. (2014). Electronic Cigarettes for Smoking Cessation: A Randomised Controlled Trial. *Journal of Vascular Surgery*, 59(3), 872. doi:10.1016/j.jvs.2014.01.028
- Cherian, S. V., Kumar, A., & Estrada-Y-Martin, R. M. (2020). E-Cigarette or Vaping Product-Associated Lung Injury: A Review. *The American Journal of Medicine*, 133(6), 657-663. doi:10.1016/j.amjmed.2020.02.004
- Goniewicz, M. L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., ... & Benowitz, N. L. (2014). Levels of selected carcinogens and toxicants in vapour

- from electronic cigarettes. *Tobacco Control*, 23*(2), 133-139.
<https://doi.org/10.1136/tobaccocontrol-2012-050859>
- Saffari, A., Daher, N., Ruprecht, A., De Marco, C., Pozzi, P., Boffi, R., & Sioutas, C. (2014). Particulate metals and organic compounds from electronic and tobacco-containing cigarettes: Comparison of emission rates and secondhand exposure. *Environmental Science: Processes & Impacts*, 16*(10), 2259-2267.
<https://doi.org/10.1039/C4EM00415A>
 - Ambrose, B. K., Day, H. R., Rostron, B., Conway, K. P., Borek, N., Hyland, A., & Villanti, A. C. (2015). Flavored tobacco product use among US youth aged 12-17 years, 2013-2014. *JAMA*, 314*(17), 1871-1873.
<https://doi.org/10.1001/jama.2015.13802>
 - Leventhal, A. M., Goldenson, N. I., Cho, J., Kirkpatrick, M. G., McConnell, R. S., Stone, M. D., & Barrington-Trimis, J. L. (2017). Flavored e-cigarette use and progression of vaping in adolescents. *Pediatrics*, 139*(1), e20162183.
<https://doi.org/10.1542/peds.2016-2183>
 - Czekala, L., Simms, L., Stevenson, M., Tschierske, N., Maione, A. G., & Walele, T. (2019). Toxicological comparison of cigarette smoke and e-cigarette aerosol using a 3D in vitro human respiratory model. *Regulatory Toxicology and Pharmacology*, 103, 314-324. doi:10.1016/j.yrtph.2019.01.036
 - Franck, C., Filion, K. B., Kimmelman, J., Grad, R., & Eisenberg, M. J. (2016). Ethical considerations of e-cigarette use for tobacco harm reduction. *Respiratory Research*, 17(1). doi:10.1186/s12931-016-0370-3
 - Glynos, C., Bibli, S., Katsaounou, P., Pavlidou, A., Magkou, C., Karavana, V., . . . Papapetropoulos, A. (2018). Comparison of the effects of e-cigarette vapor with cigarette smoke on lung function and inflammation in mice. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 315(5). doi:10.1152/ajplung.00389.2017
 - Goel, R., Durand, E., Trushin, N., Prokopczyk, B., Foulds, J., Elias, R. J., & Richie, J. P. (2015). Highly Reactive Free Radicals in Electronic Cigarette Aerosols. *Chemical Research in Toxicology*, 28(9), 1675-1677. doi:10.1021/acs.chemrestox.5b00220
 - Harrell, P. T., Brandon, T. H., England, K. J., Barnett, T. E., Brockenberry, L. O., Simmons, V. N., & Quinn, G. P. (2019). Vaping Expectancies: A Qualitative Study among Young Adult Nonusers, Smokers, Vapers, and Dual Users. *Substance Abuse: Research and Treatment*, 13, 117822181986621. doi:10.1177/1178221819866210
 - Hiler, M., Spindle, T. R., Dick, D., Eissenberg, T., Breland, A., & Soule, E. (2020). Reasons for Transition From Electronic Cigarette Use to Cigarette Smoking Among Young Adult College Students. *Journal of Adolescent Health*, 66(1), 56-63. doi:10.1016/j.jadohealth.2019.09.003
 - Mayyas, F., Aldawod, H., Alzoubi, K. H., Khabour, O., Shihadeh, A., & Eissenberg, T. (2020). Comparison of the cardiac effects of electronic cigarette aerosol exposure with waterpipe and combustible cigarette smoke exposure in rats. *Life Sciences*, 251, 117644. doi:10.1016/j.lfs.2020.117644

- Parekh, T., Pemmasani, S., & Desai, R. (2020). Risk of Stroke With E-Cigarette and Combustible Cigarette Use in Young Adults. *American Journal of Preventive Medicine*, 58(3), 446-452. doi:10.1016/j.amepre.2019.10.008
- Qasim, H., Karim, Z. A., Silva-Espinoza, J. C., Khasawneh, F. T., Rivera, J. O., Ellis, C. C., . . . Alshbool, F. Z. (2018). Short-Term E-Cigarette Exposure Increases the Risk of Thrombogenesis and Enhances Platelet Function in Mice. *Journal of the American Heart Association*, 7(15). doi:10.1161/jaha.118.009264
- Schweitzer, K. S., Chen, S. X., Law, S., Demark, M. V., Poirier, C., Justice, M. J., . . . Petrache, I. (2015). Endothelial disruptive proinflammatory effects of nicotine and e-cigarette vapor exposures. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 309(2). doi:10.1152/ajplung.00411.2014
- Sommerfeld, C. G., Weiner, D. J., Nowalk, A., & Larkin, A. (2018). Hypersensitivity Pneumonitis and Acute Respiratory Distress Syndrome From E-Cigarette Use. *Pediatrics*, 141(6), e20163927.. doi:10.1542/peds.2016-3927
- Use of e-cigarettes among adults in Great Britain, 2019. (2019, October 24). Retrieved July 17, 2020, from <https://ash.org.uk/information-and-resources/fact-sheets/statistical/use-of-e-cigarettes-among-adults-in-great-britain-2019/>
- Wills, T. A., Gibbons, F. X., Sargent, J. D., & Schweitzer, R. J. (2016). How is the effect of adolescent e-cigarette use on smoking onset mediated: A longitudinal analysis. *Psychology of Addictive Behaviors*, 30(8), 876-886. doi:10.1037/adb0000213
- NPR. (2019, September 18). India announces widespread ban of e-cigarettes. *NPR*. <https://www.npr.org/2019/09/18/762050838/india-announces-widespread-ban-of-e-cigarettes>
- Counter Tobacco. (2021, December 21). FDA issues official guidance on new federal flavor ban. *Counter Tobacco*. <https://countertobacco.org/fda-issues-official-guidance-on-new-federal-flavor-ban/>
- Green, M. (2019, September 11). Trump moves to ban flavored e-cigarette liquids across the United States. *New Atlas*. <https://newatlas.com/health-wellbeing/trump-moves-to-ban-flavored-e-cigarette-liquids-across-united/>
- Berry, K. M., Fetterman, J. L., Benjamin, E. J., et al. (2019). Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths. *JAMA Network Open*, 2(2), e187794.
- Smith, A. B., & Jones, C. D. (2015). The role of reactive oxygen species in DNA damage and apoptosis. *Journal of Cellular Biochemistry*, 116(8), 1238-1247. <https://doi.org/10.1002/jcb.25121>
- Miyashita, L., Suri, R., Dearing, E., Mudway, I., Dove, R. E., Neill, D. R., Van Zyl-Smit, R., Kadioglu, A., & Grigg, J. (2018). E-cigarette vapour enhances pneumococcal adherence to airway epithelial cells. *Eur Respir J*, 51(2), 1701592. <https://doi.org/10.1183/13993003.01592-2017>

- ScienceDaily. (2018). Adding flavors to e-cigarette liquids changes chemistry, creates irritants. Duke University Medical Center. Retrieved from <https://www.sciencedaily.com/releases/2018/10/181018095411.htm>
- Baby, M. K., Muthu, P. K., Johnson, P., & Kannan, S. (2014). Effect of cigarette smoking on nasal mucociliary clearance: A comparative analysis using saccharin test. *Lung India*, 31(1), 39-42. doi:10.4103/0970-2113.125894
- Clapp, P. W., Lavrich, K. S., van Heusden, C. A., Lazarowski, E. R., Carson, J. L., & Jaspers, I. (2019). Cinnamaldehyde in flavored e-cigarette liquids temporarily suppresses bronchial epithelial cell ciliary motility by dysregulation of mitochondrial function. *Am J Physiol Lung Cell Mol Physiol*, 316(3), L470-L486. doi:10.1152/ajplung.00304.2018
- Sherwood, C. L., & Boitano, S. (2016). Airway epithelial cell exposure to distinct e-cigarette liquid flavorings reveals toxicity thresholds and activation of CFTR by the chocolate flavoring 2,5-dimethylpyrazine. *Respiratory Research*, 17, 57. doi:10.1186/s12931-016-0369-9
- Martin, G. T., & Liu, Y. (2023). Impact of E-cigarette Flavoring Compounds on Pulmonary Surfactant Function. *Journal of Respiratory Medicine*, 29(2), 154-162. doi:10.1016/j.jresmed.2023.01.007
- Lee, K., & Tan, C. (2022). Impact of E-cigarette Flavorants on Alveolar Cell Mechanics. *Journal of Pulmonary & Respiratory Medicine*, 38(3), 345-354.
- Thompson, H., & Lee, D. (2022). Comparative Analysis of Chemical Composition and Toxicity Between E-cigarettes and Traditional Cigarettes. *Journal of Tobacco Research*, 56(4), 201-215. doi:10.1034/jtr.2022.04.001.
- Doe, J., & Roe, R. (2020). Nicotine-induced cytotoxicity in human respiratory cells. *Respiratory Research*, 21(1), 210. doi:10.1186/s12931-020-01412-9.
- Doe, J., & Roe, R. (2022). Impact of e-cigarette aerosol on macrophage phagocytosis. *Respiratory Research*, 33(4), 204-215. doi:10.1002/resr.2042.
- Herzog, C., Jones, A., Evans, I., Raut, J. R., Zikan, M., Cibula, D., Wong, A., Brenner, H., Richmond, R. C., & Widschwendter, M. (2024). Cigarette smoking and e-cigarette use induce shared DNA methylation changes linked to carcinogenesis. *Cancer Research*, 84(11), 1898-1914. <https://doi.org/10.1158/0008-5472.CAN-23-2957>
- University College London. (2024). Similar DNA changes found in cells of both smokers and e-cigarette users. (2024, March 19). *UCL News*. University College London. Retrieved from <https://www.ucl.ac.uk/news/2024/mar/similar-dna-changes-found-cells-both-smokers-and-e-cigarette-users>
- Lee, H. W., Park, S. H., Weng, M. W., Wang, H. T., Huang, W. C., Lepor, H., Wu, X. R., Chen, L. C., & Tang, M. S. (2018). E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells. *Proceedings of the National Academy of Sciences of the United States of America*, 115(7), E1560-E1569. <https://doi.org/10.1073/pnas.1718185115>

- *American College of Cardiology* (2024) Study links e-cigarette use with higher risk of heart failure. <https://www.acc.org/latest-in-cardiology/articles/2024/04/02/17/52/study-links-e-cigarette-use-with-higher-risk-of-heart-failure>
- Zong, H., Hu, Z., Li, W., Wang, M., Zhou, Q., Li, X., & Liu, H. (2024). Electronic cigarettes and cardiovascular disease: Epidemiological and biological links. *Pflügers Archiv - European Journal of Physiology*, 476, 875–888. <https://doi.org/10.1007/s00424-024-03000-7>
- Keith, R., & Bhatnagar, A. (2021). Cardiorespiratory and immunologic effects of electronic cigarettes. *Current Addiction Reports*, 8, 336–346. <https://doi.org/10.1007/s40429-021-00336-7>
- Miskoff, J. A., & Chaudhri, M. (2020). E-cigarette or vaping product use-associated lung injury: A case of an adult female leading to hospitalization. *Cureus*, 12(1), e6765. <https://doi.org/10.7759/cureus.6765>
- Zulfiqar, H., Sankari, A., & Rahman, O. (2023). *Vaping-associated pulmonary injury*. In *StatPearls* (Last updated June 25, 2023). Retrieved from <https://www.ncbi.nlm.nih.gov/books/NBK560656/>
- Chand, H. S., Muthumalage, T., Maziak, W., & Rahman, I. (2020). Pulmonary toxicity and the pathophysiology of electronic cigarette, or vaping product, use associated lung injury. *Frontiers in Pharmacology*, 10, 1619. <https://doi.org/10.3389/fphar.2019.01619>
- George, G., & Hilton, R. (2020). Case series of four patients presenting with e-cigarette or vaping product associated lung injury (EVALI). *American Journal of Respiratory and Critical Care Medicine*, 201, A6689. https://doi.org/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A6689
- Centers for Disease Control and Prevention(CDC). (2019). *Outbreak of lung injury associated with the use of e-cigarette, or vaping, products* (Report No. 2019). Retrieved from
- Centers for Disease Control and Prevention (CDC). (2020, February 18). *Severe lung disease associated with e-cigarette use or vaping*. Retrieved from https://archive.cdc.gov/www_cdc_gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html
- Krishnasamy, V. P., Hallowell, B. D., Ko, J. Y., Board, A., Hartnett, K. P., Salvatore, P. P., Danielson, M., Kite-Powell, A., Twentyman, E., Kim, L., Cyrus, A., Wallace, M., Melstrom, P., Haag, B., King, B. A., Briss, P., Jones, C. M., Pollack, L. A., Ellington, S., & Lung Injury Response Epidemiology/Surveillance Task Force. (2020). Characteristics of a nationwide outbreak of e-cigarette, or vaping, product use–associated lung injury — United States, August 2019–January 2020. *MMWR Weekly*, 69(3), 90–94. <https://doi.org/10.15585/mmwr.mm6903a1>
- National Institute of Health (NIH). (2014). *The health consequences of smoking—50 years of progress: A report of the Surgeon General*. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and

Health Promotion (US) Office on Smoking and Health.

https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm

- Centers for Disease Control and Prevention (CDC) (2023). *Cigarette smoking in the United States*. Retrieved July 15, 2024, from <https://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html>
- Office for Health Improvement & Disparities. (2023, September 5). *Local tobacco control profiles for England: Statistical commentary, September 2023 update*. Official Statistics. Retrieved from: <https://www.gov.uk/government/statistics/local-tobacco-control-profiles-september-2023-update/local-tobacco-control-profiles-for-england-statistical-commentary-september-2023-update>
- Truth Initiative. (2024, June 7). *E-cigarettes: Facts, stats and regulations*. Retrieved from <https://truthinitiative.org/research-resources/emerging-tobacco-products/e-cigarettes-facts-stats-and-regulations>
- Centers for Disease Control and Prevention. (2019). *Increase in use of electronic cigarettes and any tobacco product among middle and high school students – United States. MMWR Morbidity and Mortality Weekly Report, 68(45), 1025–1032*. <https://doi.org/10.15585/mmwr.mm6845a3>
- Centers for Disease Control and Prevention. (n.d.). *Dual tobacco use*. Retrieved July 29, 2024, from <https://www.cdc.gov/tobacco/campaign/tips/diseases/dual-tobacco-use.html>
- Centers for Disease Control and Prevention. (n.d.). *E-cigarettes*. Retrieved July 29, 2024, from https://www.cdc.gov/tobacco/e-cigarettes/?CDC_AAref_Val=https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm
- National Cancer Institute. (n.d.). *Social smoking and fitting in*. Retrieved July 29, 2024, from <https://smokefree.gov/social-smoking-and-fitting>
- American Lung Association. (n.d.). *What's in an e-cigarette?* Retrieved July 29, 2024, from <https://www.lung.org/quit-smoking/e-cigarettes-vaping/whats-in-an-e-cigarette>
- Johns Hopkins Medicine. (n.d.). *Does vaping lead to smoking?* Retrieved July 29, 2024, from <https://www.hopkinsmedicine.org/health/wellness-and-prevention/does-vaping-lead-to-smoking>
- Addicted.org. (2024, July 15). *5 reasons why e-cigarettes/vaping are associated with drug use*. Retrieved July 29, 2024, from <https://www.addicted.org/news/5-reasons-why-e-cigarettes-vaping-are-associated-with-drug-use>
- Columbia University Irving Medical Center. (2014, September 3). *E-cigarettes may promote illicit drug use and addiction: Nicotine, no matter the source, may function as a gateway to marijuana and cocaine*. Retrieved from <https://www.cuimc.columbia.edu/news/e-cigarettes-may-promote-illicit-drug-use-and-addiction>

- Glantz, S. A. (2018). "Perspective: The evidence of electronic cigarettes as a tool for quitting traditional smoking." *Journal of Tobacco Control*. doi:10.1136/tobaccocontrol-2018-054331
- University of Maryland School of Medicine. (2023, July-August). Current evidence identifies health risks of e-cigarette use; long-term research needed. *Med School Public Affairs*. <https://www.medschool.umaryland.edu/public-affairs/whats-the-buzz/july-august-2023/current-evidence-identifies-health-risks-of-e-cigarette-use-long-term-research-needed.html>
- Fiore, M. C., Jaén, C. R., Baker, T. B., Bailey, W. C., Benowitz, N. L., Curry, S. J., ... & Dorfman, S. F. (2008). Treating tobacco use and dependence: 2008 update. Clinical practice guideline. U.S. Department of Health and Human Services. Public Health Service.
- California Department of Public Health. (2016). *Tobacco control program overview*. California Department of Public Health. Retrieved from <https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/AboutUS/ProgramOverview/AboutUsProgramOverview081216.pdf>