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Electronic Cigarettes for Tobacco Use Cessation: Its Efficacy and Hazards

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A B S T R A C T

The utilization of electronic cigarettes (e-cigarettes) as a tool for quitting smoking presents a scenario marked by a blend of benefits and possible drawbacks. Since their introduction in 2007, the surge in e-cigarette usage emphasizes their widespread acceptance among smokers, yet research indicates a possible rise in individuals dependent on nicotine and those using traditional combustible cigarettes. By switching to e-cigarettes, traditional smokers may no longer use tobacco cigarettes; instead, they will use e-cigarettes as a smoking assist. Despite claims of being a safer alternative, studies suggest an overall detriment to the general population. Proposed strategies to address the complexities of tobacco use involve implementing tobacco-free environments and increasing public awareness. The efficacy of e-cigarettes is subject to conflicting research findings; while certain studies advocate for their superiority over traditional methods, others raise doubts about their safety. This ongoing discourse centers on the specific constituents of e-cigarettes, including nicotine and flavorings. Issues regarding respiratory and cardiovascular consequences, fluctuations in mood, and effects on fertility and oral health are emphasized, underscoring the necessity for a comprehensive and equitable evaluation of the potential advantages and drawbacks linked to their usage. This review examines information sourced from various databases, assessing systematic reviews and clinical trials related to the utilization of e-cigarettes for smoking cessation. Despite the acknowledged health advantages of quitting tobacco, debates persist regarding the effectiveness of e-cigarettes in facilitating cessation.

Keywords: e-cigarettes, traditional smokers, nicotine, smoking cessation

I. Introduction

In accordance with the World Health Organization (2023) report, the alarming threat of the tobacco epidemic to public health claimed the lives of 8 million individuals annually [1]. Approximately 7 million of these fatalities are associated with the use of tobacco, with an additional 1.3 million resulting from the exposure of nonsmokers to secondhand smoke [1]. This predicament stands as a significant contributor to premature mortality and disability [2].

Nicotine, a constituent of tobacco, is recognized as an addictive agent [3]. Its primary action involves interaction with specific nicotinic acetylcholine receptors in the brain, increasing acetylcholine release and metabolism [4]. Simultaneously, nicotine stimulates the dopaminergic system, causing an increase in dopamine at the nucleus accumbens [4]. The adverse influence of tobacco on both overall and oral well-being is noteworthy, ultimately playing a role in the onset of non-communicable conditions like oral cancer and chronic heart disease [5]. Despite a thorough understanding of its adverse impacts on the human body, it persists as a significant issue within public health [6].

Ceasing tobacco smoking positively impacts health improvement and significantly diminishes the likelihood of diseases and mortality [7]. The discussion surrounding tobacco cessation includes the utilization of electronic cigarettes. These battery-operated devices distribute nicotine and additional additives to the respiratory tract through vapor instead of conventional smoke (10). The aerosol generated by e-cigarettes generally contains fewer harmful substances compared to the injurious mixture of thousands of chemicals present in regular cigarette smoke (11). Advocates of e-cigarettes often present them as a reliable option, emphasizing the significant difference arising from the lack of tobacco combustion (10).

There is a strong likelihood that the utilization of nicotine replacement therapy starting from the quit day enhances smoking cessation rates [8]. Additional approaches targeting the challenges posed by tobacco consumption include creating smoke-free environments, increasing public awareness of the risks linked to tobacco addiction, and implementing higher taxes on tobacco products. These elements constitute essential components of a comprehensive strategy designed to address the complexities associated with tobacco use [9].

2. Methods

In conducting this article review, diverse databases, such as the National Library of Medicine, Oxford Academic, JAMA Network, ScienceDirect, AHA Journals, ResearchGate, and Google Scholar, were employed to access systematic reviews and clinical trials on the subject of electronic cigarettes for tobacco cessation. The abstracts of the identified articles were scrutinized using search algorithms to determine their alignment with the inclusion criteria of this article. The review was executed meticulously to offer a comprehensive evaluation encompassing both the effectiveness and potential harm associated with the utilization of electronic cigarettes in tobacco cessation.

3. E-Cigarettes: Does it help in Tobacco Cessation?

After being initially brought to the American market in 2007, electronic cigarettes, or "e-cigarettes," gained popularity among American smokers as a tool for quitting between 2014 and 2016. In the US, e-cigarette sales almost quadrupled between 2013 and 2017. a surge among young individuals linked to quick adoption. The number of people who successfully quit smoking should rise in response to a comparable rise when using e-cigarettes (either in addition to or instead of nicotine), provided that their efficacy is verified [12].

E-cigarette usage was reported by a considerable percentage of ex-smokers who gave up smoking (7.6%), with the highest incidence of daily e-cigarette use among ex-smokers. Certainly, it makes sense that the general rise of traditional combustible cigarette smokers and nicotine-dependent users is being aided by the accessibility of e-cigarettes. In the United States, simulation models reveal that, despite the somewhat implausible and unsupported assumption that e-cigarettes are 95% safer than traditional smoking, the net population-level harm causes a loss of 1.5 million years of lifespan. According to some, e-cigarettes can assist long-term smokers in giving up traditional cigarettes and possibly other tobacco products. This is another argument in favor of e-cigarette use [12].

According to the 2014 Eurobarometer survey, which included 28 European nations, using e-cigarettes is more likely to impede than to aid in quitting smoking. Similarly, using e-cigarettes was shown to be much less probable than trying to quit without using e-cigarettes in a study of 1,357 adult smokers who were hospitalized and wanted to quit and got hospital counseling. It was demonstrated that there was a low smoking cessation rate after six months. E-cigarette proponents contend that extensive e-cigarette usage may aid in quitting smoking and lessen the health risks connected to smoking combustible cigarettes [13].

4. Clinical Findings on the Effectiveness of E-Cigarettes for Tobacco Cessation

4.1 The Effectiveness of E-Cigarettes for Smoking Cessation: A Comparison With Nicotine Replacement Therapy and No Use of Evidence-Based Cessation Aids in the German Population (Kotz, D. et. al, 2022) [14]

In an extensive survey conducted in households across Germany, individuals striving to cease smoking with the aid of electronic cigarettes exhibited a twofold likelihood of achieving smoking abstinence, in contrast to individuals trying to stop without any scientifically grounded assistance. Specifically, consumers of electronic cigarettes containing nicotine were beyond as likely to report sobriety. Conversely, the effectiveness comparison between electronic cigarettes without nicotine and unaided attempts yielded inconclusive results, with no statistically significant effect estimate.

The findings strongly suggest that electronic cigarettes exhibit greater efficacy when used with nicotine, as the nicotine in ECs acts as a substitute for that in cigarettes, alleviating withdrawal symptoms. Additionally, a Cochrane review corroborates this, indicating that electronic cigarettes with nicotine surpass NRT in effectiveness. Notably, the research findings indicated that 65% of individuals who successfully maintained long-term abstinence ($\geqslant$ six months) through the use of electronic cigarettes were still using the device throughout the survey. Nevertheless, the potential influence of prolonged electronic cigarette usage on long-term relapse to smoking remains insufficiently investigated. Although the prolonged use of electronic cigarettes is deemed safer than traditional smoking, it is not devoid of potential health risks.

Consequently, this research adds to the expanding mass of knowledge indicating that incorporating electronic cigarettes into efforts to quit smoking, especially those containing nicotine, is linked to higher rates of success compared to unassisted attempts. There is a pressing demand for research studies to scrutinize the effectiveness of electronic cigarettes in a German setting, examining the masses and specific situations such as patient care, especially for individuals with chronic tobacco-related illnesses.

4.2 Efficacy and Safety of E-Cigarette Use for Smoking Cessation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (Levett, JY. et. al, 2023) [15]

This study sought to analyze how effective and safe electronic cigarettes are in facilitating smoking cessation, relative to traditional methods. Despite a growing interest among smokers in having another option or replacement through the use of e-cigarette, the effectiveness and safety of this approach are still a topic of debate. The study involved a systematic review in combination with meta-analysis of randomized controlled trials (RCTs) that includes a follow-up duration with a minimum duration of six months, focusing on biochemically validated abstinence. The comparison was between e-cigarettes that contain nicotine and any other aids in the application of smoking cessation therapy.

The analysis of data from five RCTs, involving 3253 participants, revealed that abstinence rates witnessed a notable decrease with traditional smoking cessation methods, in stark contrast to the notable increase observed with nicotine e-cigarettes. This was established through the rigorous standard of biochemically confirmed abstinence during the extended follow-up period. Moreover, nicotine e-cigarettes demonstrated greater efficacy in encouraging refraining from smoking when contrasted with non-nicotine e-cigarettes. Notably, during the maximum observational period or follow-up session, the reported occurrence of severe complications such as critical adverse events was minimal in the trials conducted which suggests a positive safety profile for employing e-cigarettes in initiatives to quit smoking.

In conclusion, individuals striving to quit smoking may discover that conventional methods are less effective than nicotine e-cigarettes in promoting cessation like the standard behavioral smoking cessation therapies or application of nicotine replacement. The findings hint at a potential benefit of using e-cigarettes in reducing health risks linked to smoking. However, due to the continued dispute surrounding the utilization of e-cigarettes in replacement of traditional cigarettes, continued scrutiny to further research is essential to thoroughly examine the extended effects and potential risks connected with this method.

4.3 A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy (Hajek, P., et. al, 2019) [16]

In a clinical trial contrasting the benefits of e-cigarettes and nicotine replacement therapy for smoking cessation, e-cigarettes emerged as more effective. This is particularly noteworthy since nicotine replacement therapy was administered under expert supervision, participants had access to a broad range of nicotine replacement medications, and 88.1% employed combination therapies. Significantly, e-cigarettes had a more pronounced impact in this study compared to previous research, attributed to factors like smokers actively seeking assistance to quit, receiving face-to-face support, and using refillable e-cigarettes with a varied selection of e-liquids. On the contrary, earlier studies generally lacked face-to-face support and utilized first-generation cartridge technologies, which are less proficient in delivering nicotine.

The research clarified the factors contributing to the superior effectiveness of e-cigarettes compared to nicotine replacement therapies. E-cigarettes demonstrated greater efficacy in alleviating tobacco withdrawal symptoms, surpassing the benefits of nicotine replacement therapy. Moreover, the utilization of refillable devices allowed for better customization of nicotine doses according to individual requirements. However, concerns have been raised regarding the relatively high prevalence of persistent e-cigarette usage, potentially harboring undisclosed health risks. On a positive note, prolonged use of e-cigarettes might assist in mitigating withdrawal symptoms and providing some of the enjoyable subjective experiences associated with smoking.

The investigators found that both e-cigarettes and nicotine replacement therapy exhibited modest side effects, with e-cigarettes leading to more throat or oral irritation, while nicotine replacement induced a higher incidence of nausea. There were varied results regarding the impact of e-cigarettes on the respiratory system. Although more e-cigarette users reported severe respiratory adverse effects, the difference was not statistically significant, and some afflicted users did not vape at all. Positive effects on respiratory outcomes have also been recorded, with antibacterial properties of propylene glycol and glycerin proposed as possible causes.

The study acknowledged some limitations, such as the challenge of blinding product allocations and potential biases resulting from participant expectations. The results may not apply to smokers who are less addicted or to those who are using less efficient first-generation e-cigarettes, but they are probably relevant to addicted smokers who are looking for treatment. More studies are needed to verify these findings outside of the UK. services, as well as to compare various degrees of assistance in e-cigarette research. In conclusion, refillable e-cigarettes outperformed nicotine replacement treatment in this large-scale experiment, providing important insights into smoking cessation tactics.

4.4 UK Clinical Trial Compares E-cigarettes, Nicotine-Replacement Products for Smoking Cessation (National Cancer Institute, 2019) [17]

A recent investigation revealed that individuals using electronic cigarettes exhibit a greater likelihood of quitting smoking compared to those opting for tobacco cessation aids. In the United Kingdom, the study disclosed an 18% success rate in smoking cessation within one year for electronic cigarette users, contrasting with a 9.9% success rate for NRT users. Study participants were randomly assigned to either the electronic cigarette or NRT group, and underwent four weeks of counseling with a local clinician. Despite both groups rating their assigned product as less satisfying than cigarettes, those in the electronic cigarette group reported higher satisfaction and found electronic cigarettes more beneficial in abstaining from smoking than those in the NRT group. The study authors acknowledged the unspecified prolonged health effects of electronic cigarette use but underscored the importance of weighing the benefits of electronic cigarettes for smoking cessation against potential risks.

The randomized controlled trials (RCTs) within the study indicated that electronic cigarettes surpassed tobacco cessation aid in achieving continuous abstinence for $\geqslant$6 months and 7-day point abstinence rates. However, conclusive evidence supporting the superiority of electronic cigarettes over NRT for achieving <6 months of continuous abstinence and 7-day point abstinence rates was not established. The trial also observed that electronic cigarettes containing nicotine yielded higher quit rates compared to both NRT and nicotine-free electronic cigarettes. Concerning safety, adverse events were comparable between electronic cigarettes and NRT, but the electronic cigarette group experienced a lower incidence of low birth weight. While the trial suggests that electronic cigarettes could serve as a viable option for smoking cessation, further research is imperative to validate their effectiveness and safety.

4.5 Associations Between E-cigarette Use and E-Cigarette Flavors with Cigarette Smoking Quit and Quit Success: Evidence From a U.S. Large, Nationally Representative 2018-2019 Survey (Mok, Y. et. al, 2019) [18]

Multiple studies examined the relationship between electronic cigarettes (e-cigarettes) to smoking cessation, however, e-cigarettes flavors on smoking cessation have often been overlooked. The paper shows that people who use e-cigarettes that are non-tobacco flavored were more probable to stop smoking, when compared to those who use alternative tobacco-flavored or unflavored e-cigarettes. Of the different flavors, peppermint or menthol e-cigarettes are the most likely to motivate you to quit smoking and succeed. Users of flavored e-cigarettes for more than 20 days is linked to an even higher chance of quitting and success in quitting smoking.

Studies indicate that individuals who regularly utilize e-cigarettes, particularly those opting for flavored varieties, make attempts to quit smoking and achieve success. Specifically, those presently using menthol or peppermint-flavored e-cigarettes showed greater odds of quitting smoking successfully, when compared to users who used other non-tobacco flavors, however, when further examined these variances showed to be statistically insignificant. These findings align with prior research on the efficacy as an aid of smoking cessation of e-cigarettes, underscoring their capacity to assist individuals in quitting smoking. Despite the absence of a significant distinction between flavors such as non-tobacco, menthol, and mint-flavored e-cigarettes research indicates that maintaining availability of menthol or mint-flavored alternatives can contribute to preserving their potential role in smoking cessation efforts.

Consequently, the utilization of electronic cigarettes is linked to an increased chance of smoking cessation. Individuals opting for flavored electronic cigarettes have a greater chance of achieving successful smoking cessation. Notably, there is no statistically significant distinction in the efficacy between non-tobacco-flavored products and menthol or mint flavored e-cigarettes. This implies that there is a potential of electronic cigarettes to assist current smokers in quitting could be upheld if menthol or peppermint-flavored alternatives remain accessible.

4.6 Comparative clinical effectiveness and safety of tobacco cessation pharmacotherapies and electronic cigarettes: a systematic review and network meta-analysis of randomized controlled trials (Thomas, K., et. al, 2022) [19]

The use of tobacco contributes significantly to disease and early mortality worldwide and has a large financial cost. The Institute of Health and Healthcare Excellence (NICE) in the UK has approved varenicline, bupropion, and nicotine replacement therapy (NRT) as three medication therapies for smoking cessation. Electronic cigarettes, or e-cigarettes, are safe for smokers who are unable to quit using other medications, even though they are not regarded as a smoking cessation medication in the US. The safety of smoking cessation drugs, particularly varenicline, bupropion, and e-cigarettes, has come under scrutiny.

To compare any two medicines, network meta-analysis combines implicit and explicit evidence from randomized controlled trials (RCTs). This study has limitations even though it is the most thorough analysis of smoking cessation drugs to date. The literature search was conducted over two years ago, which may have excluded more recent findings, particularly those pertaining to e-cigarettes. A sizable fraction of the research lacked safety information from industry-sponsored trials conducted by pharmaceutical firms in implementing products, showed high risk or unexplained bias, and had trouble identifying bias. Another drawback is the presumption that counseling and medication are complementary when used together.

This study supports the use of varenicline and NRT monotherapy as first-line treatment for smoking cessation, in accordance with NICE guidelines. It has been shown that the combination of counseling and pharmaceutical treatment can boost the rate of smoking cessation. Nevertheless, additional investigation is required to confirm the efficacy of these treatments.

4.7 Effectiveness of e-Cigarettes as Aids for Smoking Cessation: Evidence from the PATH Study Cohort, 2017-2019 (Chen, R., et. al, 2022) [20]

A nationally representative cohort study conducted in the US is called PATH. A stratified sample of homes based on address was obtained through the use of a screening survey; the sample comprised people of African heritage, young adults between the ages of 18 and 24, and tobacco smokers. The study employed questions on current usage of various products, such as e-cigarettes, cigarillos, and cigars, to identify foregoing smokers who had substituted for alternate sources of nicotine. Filtered chicken, smokeless items, hookah, pipes, and snus. When questioned about their typical nicotine content, e-cigarette users were given eight response options, ranging from 0% to 4+, in addition to the option to "don't know."

The PATH study's findings demonstrated that, in comparison to non-smokers using alternative medications, e-cigarette users that utilize a smoking cessation aid had a lower chance of effectively quitting, abstaining, or using e-cigarettes. Less than 7 out of every 100 attempts to quit smoking are successful when using e-cigarettes, and changing to e-cigarettes does not lower the chance of relapsing when compared to people who recently quit using other ways. Because of JUUL Labs' successful launch and promotion of high-nicotine e-cigarettes, there was a notable increase in e-cigarette product sales and usage from 2013 to 2018. As a result, from 17.4% to 12.4% of people, e-cigarette users were able to quit smoking. percentage of current 2019 quit attempts. The usefulness of high-nicotine e-cigarettes in reducing relapse has to be further investigated in the PATH cohort. This study contains limitations as well as strengths, such as a sizable cohort that is typical of the US population and a wide range of potential confounders.

There was static data on the usage of e-cigarettes to help people quit smoking in 2017, despite a period of tremendous growth in e-cigarette sales and rising nicotine content. High-nicotine e-cigarettes like JUUL, which are widely seen to closely match the sensation of smoking, have not been quickly adopted by smokers wanting to stop or switch to other nicotine delivery methods. The study found no benefits to giving up e-cigarettes as a support

system for stopping smoking or as a replacement for smoking. For all that, there is proof that smokers started using high-nicotine e-cigarettes in 2019. As a result, the PATH study needs to be followed up on in order to ascertain whether or not these modifications will have a positive impact on future health.

5. Ingredients of E-Cigarettes

Electronic cigarettes, battery-powered devices, operate by heating a liquid called e-liquid, producing an aerosol that users inhale [21]. Despite their frequent promotion as smoking cessation tools, there is ongoing debate about the effectiveness and safety of e-cigarettes, mainly due to a lack of comprehensive research on their long-term health effects [22]. Generally, e-cigarettes contain the following:

5.1 Nicotine

The main ingredient in e-cigarettes that contributes to their potential effectiveness for smoking cessation is nicotine [23]. The presence of this addictive substance in e-cigarettes aids in alleviating cravings and withdrawal symptoms linked to the cessation of smoking [24]. Nicotine functions as the predominant addictive element in both tobacco and electronic cigarettes, exerting its impact on the brain's reward system, thereby eliciting pleasurable sensations and fortifying persistent use [25, 26]. Research findings indicate the potential efficacy of e-cigarettes in facilitating smoking cessation, and there is some empirical support suggesting their potential superiority to nicotine replacement therapy (NRT) within specific demographic subsets. These observations underscore the multifaceted nature of nicotine addiction and the nuanced effectiveness of various cessation methods [27].

5.2 Prevalent Additives

Certain components identified in e-cigarettes, such as Propylene Glycol (PG) and Glycerol, commonly serve as additives in electronic cigarettes, acting as solvents for flavorings and nicotine [28]. Propylene Glycol (PG) and Vegetable Glycerin (VG) constitute the primary ingredients in e-cigarette liquids, playing a key role in vapor production when heated [29]. While they are both generally considered safe for inhalation, they have different properties and effects on the vaping experience [30]. The efficacy of both is to deliver a stronger "throat hit," similar to the feeling of smoking a traditional cigarette [31]. They carry flavors more effectively, resulting in a more intense flavor experience [32]. It creates a thinner vapor, making it easier to inhale and draw more frequently [33] E-cigarettes often contain various flavorings, including fruit, candy, and dessert flavors. These flavors can make e-cigarettes appealing, particularly to young people, and may contribute to addiction [34].

5.3 Humectants

Electronic cigarettes employ humectants as solvent carriers within e-liquids to generate aerosols simulating the smoke produced by combustible tobacco cigarettes. A humectant is a substance with the capacity to attract and retain moisture [35]. In the context of electronic cigarettes, humectants, like PG and VG, play a vital role in preventing the drying out of e-liquid and improving the overall vaping experience [36]. Additionally, less commonly employed humectants in e-cigarettes encompass ethyl alcohol, utilized to reduce e-liquid viscosity, albeit associated with irritant properties and addictive potential [37]. Another alternative is Polyethylene Glycol (PEG), a group of synthetic polymers serving as both a thickening agent and humectant in e-liquids [38]. While generally considered safe, there exists apprehension regarding the potential breakdown of PEG into harmful substances under elevated temperatures [39]. The composition of PG and VG in the e-liquid is pivotal, influencing both flavor and vapor production [40]. A higher PG concentration imparts a more pronounced throat hit and yields thinner vapor, whereas an increased VG ratio results in a sweeter taste and denser vapor [41].

In addition to these humectants, water is a prevalent constituent of e-liquids [42]. Water is used in various ways to improve the smoking quality of cigarettes and electronic cigarettes (e-cigarettes), in one study, ionized water was used as a solvent or diluent in cigarette flavors to reduce cigarette stimulus and enhance moistening feeling and softness taste without affecting odor characteristics [43].

Humectants and water are commonly used in e-cigarettes to improve the smoking experience and reduce toxicant exposure [44]. These humectants have been shown to improve the satisfaction, liking, and enjoyment of waterpipe tobacco (WT) smoking, increasing the likelihood of continued use [45]. Additionally, the use of humectants in cigarettes has been found to effectively improve the dry sensation of smoke, making the smoking experience more enjoyable [46].

6. The Hazards of E-Cigarettes

The e-cigarette, frequently viewed as a less harmful alternative to conventional cigarettes, has led to a significant shift in the tobacco market and industry in recent decades (Marques et al., 2021). The sudden escalation of e-cigarette usage among the youth can be associated with the widespread belief that e-cigarettes are less detrimental given their absence of tobacco smoke and minimal nicotine content [47]. Although these tools are regarded as a safer alternative than conventional cigarettes, it should be emphasized that this does not signify that e-cigarettes are completely risk-free. [48]. The mist produced by electronic cigarettes commonly comprises a lower concentration of harmful chemicals compared to the complex blend of chemicals found in the smoke from traditional cigarettes [49]. These chemicals include acetaldehyde, acrolein, and formaldehyde, which have the potential to induce respiratory conditions and cardiovascular disorders [50].

6.1 Respiratory System

As of 2022, electronic cigarettes in the United States have not undergone a comprehensive evaluation and approval by the FDA as a means for quitting smoking [51]. While the extended health effects of these products remain unclear, there is notable apprehension voiced by the American Lung Association (2020) about emerging evidence concerning the influence of e-cigarettes on respiratory health [52].

Michele Hart (2022), a pulmonary nurse clinician at Baystate Pulmonary Rehabilitation, highlights that vaping not only covers the lungs with vapor but also exposes them to harmful chemicals [53]. Typically, e-liquid formulations consist of taste additives, aromatic supplements, and either nicotine or tetrahydrocannabinol (THC) liquefied in a slick liquid substrate [54]. Broderick (2021) suggests that specific oil components may penetrate the lungs, triggering an inflammatory response [55]. The vapors containing glycol and glycerol induce irritation in the higher respiratory tract. Additionally, the nicotine intake through inhalation can result in symptoms such as nausea and vomiting, as indicated by Sapru et al. (2020) [23].

Ghosh et al. (2018) reported that healthy electronic cigarette customers showed inflamed and sensitive respiratory mucosa [56]. Gotts (2012) also highlighted the vulnerability of the lungs, emphasizing that even mild inflammation can have detrimental effects [57]. Researchers conducted a 5-year longitudinal survey analysis with around 10,00 subjects to explore the potential extended repercussions of using electronic cigarettes on the development of COPD. Among individuals currently smoking conventional cigarettes afflicted with or susceptible to COPD, using e-cigarettes was linked to worsened health outcomes related to the lungs, according to Bowler et al. (2017) [58]. Additionally, Wang et al. (2022) discovered that cytokine expression is activated by nicotine present in electronic cigarettes [59]. The substance also intensifies bronchial hypersensitivity, and causes destruction of pulmonary parenchyma. In the investigation undertaken by Callahan-Lyon et al. (2014), an evaluation of aerosol particles from both electronic cigarettes and traditional cigarettes was undertaken [60]. The results suggested that while the emissions from electronic cigarettes somewhat exceeded the atmospheric health standards set by the WHO, they were notably lower, being a couple times lower than the mist produced by conventional cigarettes.

6.2 Cardiovascular System

As tobacco is increasingly being replaced by e-cigarettes, which have distinct chemical compositions, manufacturers assert that the utilization of electronic cigarettes will not lead to lung or cardiovascular disorders commonly associated with traditional cigarette consumption [61]. Nonetheless, recent research has demonstrated that prolonged utilization of electronic cigarettes, commonly known as vaping products, can significantly alter the regular functioning of the arterial network, thereby elevating the susceptibility to diseases linked with cardiopathy [62]. Research suggests a correlation between the usage of electronic cigarettes and a heightened chance of having a myocardial infarction, with the probability of such occurrences escalating in tandem with the frequency of daily e-cigarette use [63]. According to a cross-sectional case-control study, it was determined that frequent use of electronic cigarettes was correlated with a change in the equilibrium of cardiac autonomic function, leading to an increase in sympathetic activity and heightened oxidative stress, both known factors correlated with an escalated risk of cardiovascular issues [64]. E-cigarettes generate heightened reactive oxygen species (ROS) in both laboratory (in-vitro) and living organisms (in vivo), particularly in endothelial cells. This results in lipid peroxidation, as well as mutations and worse, DNA damage all of which signifies oxidative stress and cellular harm mediated by ROS. [65]. Additionally, a study on prolonged contact of mice to electronic cigarette vapor has demonstrated notable impairment of aortic endothelial function, potentially resulting in compromised cardiac function and underscores the clinical implication that prolonged use of e-cigarettes, even at relatively low exposure levels, can lead to cardiovascular dysfunction [66]. Prolonged use and exposure of e-cigarettes can lead to cardiovascular disease comparable to traditional cigarette smoking, as well as the intensity of this harmful effect rises with the duration of exposure and the nicotine content [67].

The cardiovascular effects observed in humans due to electronic cigarettes are in line with the recognized effects of nicotine as of date [68]. Notedly, e-cigarettes operate by generating an aerosol of ultrafine particle mist that delivers chemicals through the respiratory system. The mist or particularly these particles that are inhaled deeply into the lungs, similar in size to or smaller than those in traditional cigarettes, exhibit biological activity, triggering inflammation, and are directly linked to the development of heart-related conditions such as acute cardiovascular events. [69, 70]. A study involving 70 current smokers attending a smoking cessation unit randomly assigned them to use nicotine-free or nicotine-containing e-cigarettes during an acute-phase protocol, followed by a month of replacing traditional cigarettes with nicotine-containing e-cigarettes in a chronic phase. The findings indicated that both conventional methods of smoking tobacco and the proposed alternative e-cigarettes elevated arterial stiffness or known as the increased rigidity of arteries, and oxidative stress which occurs when there is an uneven ratio from antioxidants to free radicals in the body, leading to cellular damage. Differences were observed between nicotine-free and nicotine-containing e-cigarettes, implying that the rise in these indicators is more significant after using nicotine-containing e-cigarette compared to those that contain without, as compared to the baseline [71]. In a randomized crossover study involving 25 tobacco smokers, the impact of using a vape that contains nicotine in contrast to the ones that are nicotine-free, as well as sham vaping which is defined as simulated or imitation vaping without actual inhalation of substances, was assessed on cardiovascular parameters and oxidative stress. The results revealed that sham vaping or nicotine-free vaping did not cause changes in the parameters mentioned. The utilization of nicotine-containing vape on the other hand has resulted in increased arterial stiffness with impaired vasodilation, incidence of hypertension, accelerated cardiac rate, and raised plasma myeloperoxidase which indicates that these effects are mainly associated with main ingredient which is nicotine. [72].

6.3 Nervous System

Electronic cigarettes (e-cigarettes) house nicotine, a material that induces mood irregularities and enduring impairment of impulse regulation. The presence of nicotine alters the synaptic formation process, posing a threat to the brain regions responsible for attention and learning [112]. Given that the

brain undergoes growth until approximately the age of 25, the establishment of stronger connections or synapses between brain cells occurs with each instance of memory creation or skill acquisition [108]. Young individuals are more prone to developing addiction in contrast to adults, given that addiction essentially involves a form of learning [109]. The inclusion of nicotine in e-cigarettes and various tobacco items can additionally predispose the adolescent brain to a heightened susceptibility to other substance dependencies. Being exposed to e-cigarette aerosols and liquids might play a role in causing delays in development, alterations in neurobehavior, and disruptions in cognitive function, suggesting potential neurotoxic consequences [110].

According to research, using e-cigarettes has adverse effects on anxiety, sadness, focus, and learning, especially in adolescents whose brains are still developing. E-cigarette usage has the potential to cause brain dysregulation, leading to illnesses such as stroke and seizure, a process linked to oxidative stress. E-cigarette aerosol is not harmless and may contain compounds that are both dangerous and possibly hazardous, such as nicotine, ultrafine particles capable of reaching the deep recesses of the lungs, and flavoring ingredients. According to recent research, the metals found in e-cigarette aerosol, often known as vape clouds, have the potential to disrupt the central nervous system [110]. The utilization of e-cigarettes has been associated with the emergence of neurological conditions like seizures, syncope, and tremors. Additionally, it undermines the integrity of the blood-brain barrier, elevating the likelihood of experiencing neurodegenerative disorders [111].

6.4 Immune System

According to research findings, the emissions from e-cigarettes possess the potential to directly compromise and impede the functionality of immune cells crucial to pulmonary well-being, particularly macrophages and alveolar epithelial cells [73]. These cells play a fundamental role in shielding the lungs against inflammation and infectious agents [74]. Recent investigations propose that e-cigarettes may impede the body's defenses against infection by disrupting neutrophils, a subtype of white blood cell [75]. Constituents within e-cigarette vapor, such as propylene glycol, vegetable glycerin, and flavorings, are identified as potential triggers for airway inflammation, compromising immunity and heightening susceptibility to respiratory infections [76]. The act of vaping electronic cigarettes is hypothesized to modify the body's inherent immunological response, thereby increasing the risk of illness [76]. Notably, users of fourth-generation e-cigarettes display the most pronounced alterations in immune markers, indicating a deviation from immune homeostasis [77].

Electronic cigarettes have been shown to elicit injurious effects on the immune system. Exposure to e-cigarette aerosol can trigger antigenic responses and enhance the production of modulatory immune system proteins [78]. Prolonged exposure to e-cigarettes leads to the disrupted immune gene control and the initiation of subclinical inflammation [79]. E-cigarette exposure negatively impacts specific cell types within the innate immune system, including the airway epithelium and neutrophils [80]. Moreover, it disrupts the innate immunity of the lungs by inducing irregular mucus makeup, undermining epithelial protective function, hindering phagocytic activity, and heightening systemic inflammatory signals [81]. The utilization of e-cigarettes disrupts pulmonary homeostasis, reduces lung function, increases airway inflammation and oxidative stress, suppresses immunity, and heightens susceptibility to respiratory infections [82]. Exposure to e-cigarette aerosol upregulates genes associated with reactive oxygen species, lipid peroxidation, and carcinogen metabolism, while simultaneously downregulating key genes in the innate immune system, underscoring the potential harm of e-cigarettes on the immune system and respiratory health [83].

6.5 Reproductive System

E-cigarettes are seen as a better alternative for individuals looking to quit cigarette smoking. However, e-cigarettes still have nicotine as its constituents, although at lower amounts compared to conventional cigarettes, it still generates toxic vapors, and can potentially cause adverse effects on the fertility of male and females [84]. Nevertheless, comprehensive exploration on e-cigarettes' effects on the reproductive system is limited, as research focuses on the use of animal models. Despite this, the information derived from them remains pertinent in understanding e-cigarettes' effects on the human reproductive system [85].

Male reproductive function is affected by the use of e-cigarettes by inducing abnormalities in sperm morphology by promoting vascularization of the seminiferous epithelium, resulting in reduced production and heightened sperm death [86]. Findings from the studies expressed that exposure to e-cigarettes caused an increased DNA damage in the testis and sperm of males. These outcomes suggest a potential for e-cigarettes to induce mutagenic effects on sperm [87]. Regarding female reproduction, impaired ovarian function is caused due to exposure to e-cigarettes. This is attributed to e-liquids in e-cigarettes, which hinder the development of ovarian follicles and lead to a reduction in estrogen release [88]. Delayed implantation in the embryo is also associated with exposure to e-cigarettes, indicating that these devices may hinder initiation of pregnancy and compromise fetal health [89]. Although these studies were not directly conducted on test human subjects, the outcomes of these studies should be considered as information that might possibly affect the reproductive system of an individual [84].

6.6 Oral Health

An increasing number of research studies have been carried out recently to investigate their effects on oral health. According to microbiological research, e-cigarette users have unique microbiomes, and there is some suggestion that this could make them more susceptible to disease than non-users. The benefits of stopping smoking for smokers who use e-cigarettes may exceed the drawbacks of using them, particularly in the short term, in terms of dental health [90]. It is possible to mitigate the detrimental effects of smoking on oral health to some degree by adopting healthy oral hygiene practices, quitting smoking, and abstaining from drugs. The best method for ensuring long-term dental health is with e-foils. Many e-cigarette users reported better physiological functions, including respiration, mood, taste, physical state, and memory, as compared to tobacco users and non-smokers [91].

According to a different cross-sectional study done in the US, utilizing e-cigarettes on a regular basis raised the chance of tooth loss from gum disease or decay [92]. They established that cells exposed to e-cigarettes had substantially reduced rates of cellular vitality and colony-forming potential as well as increased rates of cell death and tissue decay, regardless of the amount of nicotine in the vapor.

According to research by Wisniewski and colleagues, oral dysplastic keratinocytes exposed to liquid nicotine exhibit a migratory phenotype as a result of the nicotine's activation of EGFR signaling, which leads to an increase in EGFR expression and mouth cancer [93]. The cytotoxicity of vaped or inhaled e-liquids, with or without nicotine, was investigated in HGF to assess the safety of these novel electronic devices in the oral cavity [94]. According to a test-tube study, there may be a higher chance of tooth decay if specific compounds that taste sweet are combined with e-liquid viscosity. Since separate research employed different brands of e-cigarettes, which can have significantly different chemicals, the findings that are now available should be evaluated very cautiously [95].

7. Untoward Health Impact of E-Cigarettes to the Surrounding People

E-cigarettes pose risks for youth, young adults, pregnant individuals, and non-tobacco-using adults. While e-cigarettes may have benefits for some individuals and drawbacks for others, there is still a lot that scientists need to uncover about their efficacy in helping adults quit smoking, particularly in terms of their impact on those in close proximity [48]. Much like exposure to tobacco smoke, individuals near to e-cigarette use can breathe in secondhand emissions that consist of chemical-containing tiny droplets combined with gaseous mixtures. Aerosols from e-cigarettes are reported to contribute to particulate matter pollution (PM), consist of fine particles (PM2.5) with a diameter less than 2.5 mm that can penetrate deeply into the lung's areas involved in gas exchange, posing a potential risk of lung damage and entry into the bloodstream to adversely affect other organs, contributing to the global mortality risk and being linked to respiratory and cardiovascular events [96, 97] Several studies have identified the presence of nicotine in the secondhand aerosols that was emitted from electronic cigarettes, and a review in 2018 by the National Academies of Sciences, Engineering, and Medicine definitively established that the utilization of these devices significantly increases levels of airborne particles of nicotine in indoor settings compared to the normal outdoor concentrations [98]. Biomarker investigations indicate that individuals exposed to passive inhalation of e-cigarette vapors can take in chemicals, including nicotine, as shown by a study using cotinine—a biomarker indicating exposure to the chemical—that revealed heightened levels of this substance in the urine, serum and in the blood of non-smokers following exposure to involuntary passive e-cigarette intake. [99, 100]

According to a cross-sectional study, secondhand aerosols (SHA) and its consistent exposure to them within household vicinity was independently linked to increased rates of asthma symptoms, indicating an adverse effect on respiratory health in adolescents [101]. Another prospective study carried out on a cohort of young adults (n=2097) from 2014 to 2019 in Southern California found that exposure to secondhand nicotine-containing e-cigarette was also linked with a greater frequency of records of bronchitis symptoms [102]. It has been reported that significant proportion of young adults develop a nicotine addiction by using e-cigarette nicotine delivery systems, which may increase vulnerability of the influence on the population to addiction with other nicotine products, thereby contributing to the emergence of vaping-related pulmonary injury outbreaks, compounded by a growing body of evidence highlighting potential adverse effects regarding the usage of vape [103, 104].

The threat does not end there, as there is a potential of thirdhand exposure as well through chemical remnants that remain on surfaces and fabrics of clothing after e-cigarette smoking sessions that may serve as a source of indirect contact or exposure when unsuspecting individuals come into contact with or inhale the off-gassing from these contaminated areas, a facet often overlooked by many [105]. Findings from a study utilizing a mouse model indicate that the vapor from third-hand exposure to e-cigarette nicotine delivery systems resulted in decreased lung inflammatory responses, suppressed macrophage infiltration into airways, reduced airway resistance, and alterations in the weights of the spleen and brain. Consequently, acute exposure to third-hand e-cigarette emissions led to modifications in both immune responses and organ development [106].

Considering the rise of evidence suggesting potential hazards and adverse effects associated with e-cigarettes, it is crucial not to overlook the potential efficacy of these devices in assisting with the cessation of tobacco smoke. However, further research of all dimensions of vaping exposure is critical, especially regarding the impact on individuals in close proximity who may indirectly deal with the effects of this health-hazardous behavior.

8. Discussion

The influence of electronic cigarettes on tobacco cessation is a subject of debate, marked by conflicting evidence. Some studies propose that such devices can serve as effective tools for encouraging smoking cessation, while others argue the opposite. A meta-analysis of five controlled clinical trials discovered that, in comparison to nicotine replacement therapy or a placebo, electronic cigarettes demonstrated superiority in promoting smoking cessation. However, the level of confidence in this evidence was regarded as being relatively low. Notably, the potential of electronic cigarettes as quit-smoking tools hinges on specific ingredients in their composition, with nicotine [14] and non-tobacco flavorings [18] being highlighted in several studies. Nicotine in electronic cigarettes serves as an alternative for that in conventional cigarettes, alleviating withdrawal symptoms. Additionally, maintaining access to menthol or mint-flavored e-cigarettes was identified as a factor supporting their role in smoking cessation.

Curiously, three studies contrasted the efficacy of electronic cigarettes to nicotine cessation aids that is approved by the FDA [107], raising questions considering the confirmed position of the latter. Despite lacking FDA approval as smoking cessation tools, some studies assert the safety of e-cigarettes for smokers unable to quit using other medications like Varenicline and Bupropion [19] . Conversely, a study within the PATH Study cohort discovered that among those attempting to quit, individuals utilizing electronic cigarettes exhibited a reduced rate of cigarette abstinence lasting 12 months or more

compared to non-users. Another review determined that the proof supporting the effectiveness of electronic cigarettes for quitting smoking or their safety as alternatives is insufficient and may pose harm.

Considering the positive outcomes of electronic cigarettes in aiding tobacco cessation, it remains a concern due to its adverse effects on the respiratory system, particularly the lungs, where vapor deposition and exposure to harmful chemicals occur (Hart, 2022). Notably, detrimental consequences such as inflammation and irritation in the upper respiratory tract, nausea, and vomiting have been highlighted by Sapru et al. (2020). These effects compromise the immune system [76], increasing vulnerability to respiratory infections. Prolonged e-cigarette use can significantly impact normal vascular function [62], with studies suggesting potential impairment of aortic endothelial function, leading to cardiovascular dysfunction (Olfert et al., 2017). Mood irregularities, impaired impulse regulation, and the risk of stroke and seizure are additional concerns, influencing synaptic formation and affecting attention and learning. Research indicates adverse effects on anxiety, depression, and concentration, particularly in adolescents with developing brains [21]. Furthermore, e-cigarettes may adversely affect fertility, causing reduced sperm production and increased sperm death in males [86], and a decrease in estrogen release and ovarian follicle development in females [88]. Oral health is also at risk, with research linking electronic cigarette use to increase likelihood of self-reported dental attrition due to oral infections [92]. Despite potential oral health impacts, individuals attempting to quit tobacco smoking may find the benefits of e-cigarettes outweighing the short-term risks [90]. Overall, the dual nature of electronic cigarettes, offering both advantages and drawbacks, emphasizes the importance of considering an individual's health status to ascertain the proportion between probable advantages and hazards.

9. Conclusion

To conclude, the impact of electronic cigarettes on tobacco cessation remains a contentious topic marked by contradictory evidence, with numerous studies presenting conflicting and inconclusive findings. While using e-cigarettes as a means to quit smoking is a viable option, it is crucial to take into account the drawbacks linked to their usage, given the associated risks. Consequently, when opting for an electronic cigarette as a tool to overcome tobacco dependence, careful consideration of an individual's health becomes paramount.

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References

1. Tobacco. (2023, July 31). https://www.who.int/news-room/fact-sheets/detail/tobacco
2. Flor, L. S., Reitsma, M. B., Gupta, V. K., Ng, M., & Gakidou, E. (2021, January 21). The effects of tobacco control policies on global smoking prevalence. Nature Medicine. https://doi.org/10.1038/s41591-020-01210-8
3. What are the effects of secondhand and thirdhand tobacco smoke? | National Institute on Drug Abuse. (2021, April 12). National Institute on Drug Abuse. https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/what-are-effects-secondhand-thirdhand-tobacco-smoke
4. Tiwari RK, Sharma V, Pandey RK, Shukla SS. Nicotine Addiction: Neurobiology and Mechanism. J Pharmacopuncture. 2020 Mar 31;23(1):1-7. doi: 10.3831/KPI.2020.23.001. PMID: 32322429; PMCID: PMC7163392.
5. Bal, S., Dalai, R., Sethi, S., & Darshan, V. (2019). Different forms of Tobacco and its Bad Effects on Our Health and Society. Indian Journal of Public Health Research & Development . Nov2019, Vol. 10 Issue 11, p409-412. 4p.
6. Hajdusianek, W., Żórawik, A., Waliszewska-Prosół, M., Poręba, R., & Gać, P. (2021, June 16). Tobacco and Nervous System Development and Function—New Findings 2015–2020. Brain Sciences. https://doi.org/10.3390/brainsci11060797
7. US Department of Health and Human Services. Smoking Cessation: A Report of the Surgeon General—Executive Summary. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.

8. Livingstone-Banks, J., Lindson, J., Hartmann-Boyce, J., & Aveyard, P. (2021). Effects of interventions to combat tobacco addiction: Cochrane update of 2019 and 2020 reviews. Department of Health, National Institute for Health Research. https://doi.org/10.1111/add.15769

9. Noncommunicable Diseases and Mental Health. (2023). PAHO/WHO | Pan American Health Organization. https://www.paho.org/en/noncommunicable-diseases-and-mental-health#gsc.tab=0

10. Introduction | National Institute on Drug Abuse. (2021, August 3). National Institute on Drug Abuse. https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/introduction

11. Patnode CP, Henderson JT, Thompson JH, Senger CA, Fortmann SP, Whitlock EP. Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation in Adults, Including Pregnant Women: A Review of Reviews for the U.S. Preventive Services Task Force. Evidence Synthesis No. 134. AHRQ Publication No. 14-05200-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2015.

12. Kulik MC, Lisha NE, Glantz SA. E-cigarettes associated with depressed smoking cessation: a cross-sectional study of 28 European Union countries. Am J Prev Med. 2018; 54:603–609.

13. Hajek P. Electronic cigarettes have a potential for huge public health benefit. BMC Med. 2014; 12:225.

14. Kotz D, Jackson S, Brown J, Kastaun S. The Effectiveness of E-Cigarettes for Smoking Cessation. Dtsch Arztebl Int. 2022 Apr 29;119(17):297-301. doi: 10.3238/arztebl.m2022.0162. PMID: 35384835; PMCID: PMC9450504.

15. Levett JY, Filion KB, Reynier P, Prell C, Eisenberg MJ. Efficacy and Safety of E-Cigarette Use for Smoking Cessation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Am J Med. 2023 Aug;136(8):804-813.e4. doi: 10.1016/j.amjmed.2023.04.014. Epub 2023 May 5. PMID: 37148992. https://pubmed.ncbi.nlm.nih.gov/37148992/

16. Hajek, P., Phillips-Waller, A., Przulj, D., Pesola, F., Myers Smith, K., Bisal, N., Li, J., Parrott, S., Sasieni, P., Dawkins, L., Ross, L., Goniewicz, M., Wu, Q., McRobbie, H., (2019). A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy. New England Journal of Medicine, (), NEJMoa1808779–. doi:10.1056/NEJMoa1808779

17. Trial Tests E-cigarettes against Nicotine Replacement. (2019, March 8). National Cancer Institute. https://www.cancer.gov/news-events/cancer-currents-blog/2019/e-cigarettes-nrt-smoking-cessation-clinical-trial

18. Mok Y, Jeon J, Levy DT, Meza R. Associations Between E-cigarette Use and E-cigarette Flavors With Cigarette Smoking Quit Attempts and Quit Success: Evidence From a U.S. Large, Nationally Representative 2018-2019 Survey. Nicotine Tob Res. 2023 Feb 9;25(3):541-552. doi: 10.1093/ntr/ntac241. PMID: 36250607; PMCID: PMC9910159.

19. Thomas KH, Dalili MN, Lopez-Lopez JA, Keeney E, Phillippo DM, Munafò MR, et al.Comparative clinical effectiveness and safety of tobacco cessation pharmacotherapies and electronic cigarettes: asystematic review and network meta-analysis of randomized controlled trials. Addiction. 2022;117:861–76.https://doi.org/10.1111/add.15675876THOMASET AL.

20. Chen R, Pierce JP, Leas EC, Benmarhnia T, Strong DR, White MM, Stone M, Trinidad DR, McMenamin SB, Messer K. Effectiveness of e-cigarettes as aids for smoking cessation: evidence from the PATH Study cohort, 2017-2019. Tob Control. 2023 Aug;32(e2):e145-e152. doi: 10.1136/tobaccocontrol-2021-056901. Epub 2022 Feb 7. PMID: 35131948; PMCID: PMC10423520.

21. Get the Facts on E-cigarettes | Know the Risks: E-cigarettes & Young People | U.S. Surgeon General's Report. (n.d.). Know the Risks: E-Cigarettes and Young People | U.S. Surgeon General's Report. https://e-cigarettes.surgeongeneral.gov/getthefacts.html#:~:text=E%2Dcigarettes%20create%20an%20aerosol,as%20marijuana%2C%20and%20other%20drugs.&text=Stores%20the%20e%2Dliquid.

22. Marqués, P., Piqueras, L., & Sanz, M. (2021). An updated overview of e-cigarette impact on human health. Respiratory Research, 22(1). https://doi.org/10.1186/s12931-021-01737-5

23. Sapru, S., Vardhan, M., Li, Q., Guo, Y., Li, X., & Saxena, D. (2020). E-cigarettes use in the United States: reasons for use, perceptions, and effects on health. BMC Public Health, 20(1). https://doi.org/10.1186/s12889-020-09572-x

24. Tips for Coping with Nicotine Withdrawal and Triggers. (2022, January 3). National Cancer Institute. https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco/withdrawal-fact-sheet#:~:text=Yes.,trying%20to%20quit%20tobacco%20use.

25. World Health Organization: WHO. (2023, September 28). E-cigarettes contain hazardous substances, addictive and harmful. https://www.who.int/thailand/news/feature-stories/detail/e-cigarettes-contain-hazardous-substances--addictive-and-harmful#:~:text=E%2Dcigarettes%20delivers%20nicotine,Nicotine%20is%20a%20toxic%20substance

26. Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics. (2023, December 20). Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics. Annual Review of Pharmacology and Toxicology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2946180/

27. National Academies Press (US). (2018, January 23). Toxicology of E-Cigarette constituents. Public Health Consequences of E-Cigarettes - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK507184/

28. National Academies Press (US). (2018, January 23). Toxicology of E-Cigarette constituents. Public Health Consequences of E-Cigarettes - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK507184/

29. Xiè wén. (2023b, October 22). VG and PG in vape - Effects and Implications. RELX-PH. https://relxnow.ph/blogs/vape-knowledge/vg-and-pg-in-vape-effects-and-implications#:~:text=What%20Is%20the%20Difference%20between,smoother%20inhales%20and%20denser%20clouds

30. Baassiri, M., Talih, S., Salman, R., Karaoghlanian, N., Saleh, R., Hage, R. E., Saliba, N. A., & Shihadeh, A. (2017). Clouds and "throat hit": Effects of liquid composition on nicotine emissions and physical characteristics of electronic cigarette aerosols. Aerosol Science and Technology, 51(11), 1231–1239. https://doi.org/10.1080/02786826.2017.1341040

31. Andrews, T. (2023, December 5). Top tips for maximum vape flavour. OK Vape. https://okvape.co.uk/blog/vaping-beginners/top-tips-for-maximum-vape-flavour/#:~:text=Propylene%20glycol%20tends%20to%20be,balanced%2050PG%2F50VG%20e%20liquid

32. Foley, D. (2022, February 1). The Ultimate Guide to PG VG Ratios. The London Vape Company. https://www.thevapecig.co.uk/news/the-ultimate-guide-to-pg-vg-ratios

33. UNC Gillings School of Global Public Health. (2019, November 26). Fruit and candy flavors make young people perceive e-cigarettes as less harmful - UNC Gillings School of Global Public Health. https://sph.unc.edu/sph-news/fruit-and-candy-flavors-make-young-people-perceive-e-cigarettes-as-less-harmful/#:~:text=Most%20e%2Dcigarettes%20contain%20nicotine,milk%20and%20lemon%20crumble%20cake

34. The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review. (2023, December 20). The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review. Nicotine & Tobacco Research. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9356694/

35. Small, R., & Green, B. (2012). Skin care products. In Elsevier eBooks (pp. 286–297). https://doi.org/10.1016/b978-1-4377-0580-5.00024-8

36. Influence of E-Liquid Humectants, Nicotine, and Flavorings on Aerosol Particle Size Distribution and Implications for Modeling Respiratory Deposition. (2023, December 20). Influence of E-Liquid Humectants, Nicotine, and Flavorings on Aerosol Particle Size Distribution and Implications for Modeling Respiratory Deposition. Frontiers in Public Health. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8968757/

37. Unlocking the potential of Ethanol-Based E-Liquid Bases – AIRTEK VAPE. (2023, September 11). https://airtekvape.com/unlocking-the-potential-of-ethanol-based-e-liquid-bases/#:~:text=Ethanol%20serves%20several%20advantageous%20purposes,more%20intense%20and%20vibrant%20flavors

38. Guvendiren, M., Purcell, B. P., & Burdick, J. A. (2012). Photopolymerizable systems. In Elsevier eBooks (pp. 413–438). https://doi.org/10.1016/b978-0-444-53349-4.00227-2

39. Prentice, D. E., & Majeed, S. (1978). Oral toxicity of polyethylene glycol (PEG 200) in monkeys and rats. Toxicology Letters, 2(2), 119–122. https://doi.org/10.1016/0378-4274(78)90084-x

40. How to choose your e-liquid's PG/VG ratio. (n.d.). https://www.aromes-et-liquides.fr/en/content/89-choose-the-right-pgvg-ratio-for-your-e-liquid#:~:text=As%20we%20said%20earlier%2C%20an,on%20the%20device%20you%20use

41. Xie Wen. (2023c, October 22). VG and PG in vape - Effects and Implications. RELX-PH. https://relxnow.ph/blogs/vape-knowledge/vg-and-pg-in-vape-effects-and-implications#:~:text=It's%20a%20clear%2C%20viscous%20liquid,like%20a%20fuller%20vapor%20experience

42. National Academies Press (US). (2018b, January 23). Toxicology of E-Cigarette constituents. Public Health Consequences of E-Cigarettes - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK507184/

43. Yao, Q., Wu, Y., Li, H., Zeng, X., Zhang, T., Li, G., Zhou, B., Zhang, L., Ding, H., & Ye, Y. (2012). Ionized water for improving smoking quality of cigarettes and application thereof. SciSpace - Paper. https://typeset.io/papers/ionized-water-for-improving-smoking-quality-of-cigarettes-1g9neii2cd

44. El-Hage, R., El-Hellani, A., Salman, R., Talih, S., Shihadeh, A., & Saliba, N. A. (2020). Vaped humectants in E-Cigarettes are a source of phenols. Chemical Research in Toxicology, 33(9), 2374–2380. https://doi.org/10.1021/acs.chemrestox.0c00132

45. Wagener, T. L., Leavens, E. L. S., Mehta, T., Hale, J., Shihadeh, A., Eissenberg, T., Halquist, M. S., Brinkman, M. C., Johnson, A. L., Floyd, E. L., Ding, K., Hage, R. E., & Salman, R. (2020). Impact of flavors and humectants on waterpipe tobacco smoking topography, subjective effects, toxicant exposure and intentions for continued use. Tobacco Control, 30(4), 366–372. https://doi.org/10.1136/tobaccocontrol-2019-055509

46. Bo, C., Xiaoying, Z., Qing, Y., Tiandong, Z., Qianxu, Y., Lei, Y., Yong, L., Guofu, Z., & Hongming, Y. (2015). Humectant for cigarettes and application thereof. SciSpace - Paper. https://typeset.io/papers/humectant-for-cigarettes-and-application-thereof-1r568qkod7

47. Gülşen A, Uslu B. Health Hazards and Complications Associated with Electronic Cigarettes: A Review. Turk Thorac J. 2020 May;21(3):201-208. doi: 10.5152/TurkThoracJ.2019.180203. PMID: 32584238; PMCID: PMC7311157.

48. About Electronic Cigarettes (E-cigarettes). (2023, October 31). Centers for Disease Control and Prevention.

49. Patnode CP, Henderson JT, Thompson JH, Senger CA, Fortmann SP, Whitlock EP. Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation in Adults, Including Pregnant Women: A Review of Reviews for the U.S. Preventive Services Task Force. Evidence Synthesis No. 134. AHRQ Publication No. 14-05200-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2015.

50. Ogunwale, Mumiye A et al. (2017) Aldehyde Detection in Electronic Cigarette Aerosols. ACS omega 2(3): 1207-1214. doi: 10.1021/acsomega.6b00489].

51. US Food and Drug Administration. Want to Quit Smoking? FDA-Approved and FDA-Cleared Cessation Products Can Help. FDA. 2022 Jul 21; Available from: https://www.fda.gov/consumers/consumer-updates/want-quit-smoking-fda-approved-and-fda-cleared-cessation-products-can-help

52. American Lung Association. Health Risks of E-Cigarettes and Vaping. American Lung Association; 2020.

53. Baystate Health. What Does Vaping Do to Your Body?. www.baystatehealth.org. October 4, 2022. Available from: https://www.baystatehealth.org/news/2021/11/what-does-vaping-do-to-your-body

54. Karanwal, A. Lung Cancer Awareness - PRIME Hospital. www.primehealth.ae. [cited 2023 Dec 7]. Available from: https://www.primehealth.ae/prime-medical-center/health-blog/lung-cancer-awareness

55. Broderick S. What Does Vaping Do to Your Lungs?. John Hopkins Medicine; 2021. Available from: https://www.hopkinsmedicine.org/health/wellness-and-prevention/what-does-vaping-do-to-your-lungs

56. Ghosh A, Coakley RC, Mascenik T, Rowell TR, Davis ES, Rogers K, et al. Chronic E-Cigarette Exposure Alters the Human Bronchial Epithelial Proteome. American Journal of Respiratory and Critical Care Medicine. 2018 Jul;198(1):67–76.

57. Gotts JE, Jordt SE, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? BMJ. 2019 Sep 30;366:l5275. Available from: https://www.bmj.com/content/366/bmj.l5275

58. Bowler RP, Hansel NN, Jacobson S, Graham Barr R, Make BJ, Han MK, et al. Electronic Cigarette Use in US Adults at Risk for or with COPD: Analysis from Two Observational Cohorts. Journal of General Internal Medicine. 2017 Sep 7;32(12):1315–22. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5698219/

59. Wang L, Wang Y, Chen J, Liu P, Li M. A Review of Toxicity Mechanism Studies of Electronic Cigarettes on Respiratory System. International Journal of Molecular Sciences. 2022 May 1;23(9):5030

60. Callahan-Lyon P. Electronic cigarettes: human health effects. Tobacco Control. 2014 Apr 14;23(suppl 2):ii36–40.

61. Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol. 2014;34(3):509–15.

62. Chronic e-cigarette use impairs endothelial function on the physiological and cellular levels. Arteriosclerosis, Thrombosis, and Vascular Biology. DOI: 10.1161/ATVBAHA.121.317749

63. Alzahrani T, Pena I, Temesgen N, Glantz SA. Association Between Electronic Cigarette Use and Myocardial Infarction. Am J Prev Med. 2018 Oct;55(4):455-461. doi: 10.1016/j.amepre.2018.05.004. Epub 2018 Aug 22. Erratum in: Am J Prev Med. 2019 Oct;57(4):579-584. PMID: 30166079; PMCID: PMC6208321.

64. Moheimani RS, Bhetraratana M, Yin F, Peters KM, Gornbein J, Araujo JA, Middlekauff HR. Increased Cardiac Sympathetic Activity and Oxidative Stress in Habitual Electronic Cigarette Users: Implications for Cardiovascular Risk. JAMA Cardiol. 2017 Mar 1;2(3):278-284. doi: 10.1001/jamacardio.2016.5303. PMID: 28146259; PMCID: PMC5626008.

65. Espinoza-Derout J, Shao XM, Lao CJ, Hasan KM, Rivera JC, Jordan MC, Echeverria V, Roos KP, Sinha-Hikim AP, Friedman TC. Electronic Cigarette Use and the Risk of Cardiovascular Diseases. Front Cardiovasc Med. 2022 Apr 7;9:879726. doi: 10.3389/fcvm.2022.879726. PMID: 35463745; PMCID: PMC9021536.

66. Olfert IM, DeVallance E, Hoskinson H, Branyan KW, Clayton S, Pitzer CR, Sullivan DP, Breit MJ, Wu Z, Klinkhachorn P, Mandler WK, Erdreich BH, Ducatman BS, Bryner RW, Dasgupta P, Chantler PD. Chronic exposure to electronic cigarettes results in impaired cardiovascular function in mice. J Appl Physiol (1985). 2018 Mar 1;124(3):573-582. doi: 10.1152/japplphysiol.00713.2017. Epub 2017 Nov 2. PMID: 29097631; PMCID: PMC5899271.

67. El-Mahdy MA, Mahgoup EM, Ewees MG, Eid MS, Abdelghany TM, Zweier JL. Long-term electronic cigarette exposure induces cardiovascular dysfunction similar to tobacco cigarettes: role of nicotine and exposure duration. Am J Physiol Heart Circ Physiol. 2021 May 1;320(5):H2112-H2129. doi: 10.1152/ajpheart.00997.2020. Epub 2021 Feb 19. PMID: 33606584; PMCID: PMC8163641.

68. Benowitz NL, Fraiman JB. Cardiovascular effects of electronic cigarettes. Nat Rev Cardiol. 2017 Aug;14(8):447-456. doi: 10.1038/nrcardio.2017.36. Epub 2017 Mar 23. PMID: 28332500; PMCID: PMC5519136.

69. Fuoco FC, Buonanno G, Stabile L, Vigo P. 2014. Influential parameters on particle concentration and size distribution in the mainstream of e-cigarettes. Environ. Pollut. 184:523–29

70. Pope CA 3rd, Burnett RT, Krewski D, Jerrett M, Shi Y, et al. 2009. Cardiovascular mortality and exposure to airborne fine particulate matter and cigarette smoke: shape of the exposure-response relationship. Circulation 120:941–48

71. Ikonomidis, I., Vlastos, D., Kourea, K., Kostelli, G., Varoudi, M., Pavlidis, G., Efentakis, P., Triantafyllidi, H., Parissis, J., Andreadou, I., Iliodromitis, E., & Lekakis, J. (n.d.). Electronic cigarette smoking increases arterial stiffness and oxidative stress to a lesser extent than a conventional cigarette: An acute and chronic study. AHA Journals. https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.117.029153

72. Chaumont M, de Becker B, Zaher W, Culié A, Deprez G, Mélot C, Reyé F, Van Antwerpen P, Delporte C, Debbas N, Boudjeltia KZ, van de Borne P. Differential Effects of E-Cigarette on Microvascular Endothelial Function, Arterial Stiffness and Oxidative Stress: A Randomized Crossover Trial. Sci Rep. 2018 Jul 10;8(1):10378. doi: 10.1038/s41598-018-28723-0. PMID: 29991814; PMCID: PMC6039507.

73. Madison, M. C., Landers, C. T., Gu, B.-H., Chang, C.-Y., Tung, H.-Y., You, R., Hong, M. J., Baghaei, N., Song, L.-Z., Porter, P., Putluri, N., Salas, R., Gilbert, B. E., Levental, I., Campen, M. J., Corry, D. B., & Kheradmand, F. (2019, October 1). Electronic cigarettes disrupt lung lipid homeostasis and innate immunity independent of nicotine. The Journal of clinical investigation. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6763255/#:~:text=Together%2C%20our%20findings%20reveal%20that,poor%20response%20to%20infectious%20challenge

74. Chuquimia, O. D., Petursdottir, D. H., Periolo, N., & Fernández, C. (2013, January). Alveolar epithelial cells are critical in protection of the respiratory tract by secretion of factors able to modulate the activity of pulmonary macrophages and directly control bacterial growth. Infection and immunity. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3536158/

75. Lab study: E-cigarettes may damage body's ability to fight infection. (n.d.). https://www.research.va.gov/currents/0120-E-cigarettes-damage-bodys-ability-to-fight-infection.cfm

76. Derewicz, M. (2020, November 12). Are e-cigarette users at greater risk of poor immune response to flu, COVID? | Newsroom. Newsroom. https://news.unchealthcare.org/2020/11/are-e-cigarette-users-at-greater-risk-of-poor-immune-response-to-flu-covid/#:~:text=The%20suppressed%20expression%20of%20important,less%20effective%20in%20these%20groups

77. UNC Gillings School of Global Public Health. (2022, July 7). Fourth-generation vaping devices increase risk to immune cells - UNC Gillings School of Global Public Health. https://sph.unc.edu/sph-news/fourth-generation-vaping-devices-increase-risk-to-immune-cells/

78. Kalininskiy, A., Kittel, J. A., Nacca, N., Misra, R. S., Croft, D., & McGraw, M. D. (2021). E-cigarette exposures, respiratory tract infections, and impaired innate immunity: a narrative review. Pediatric Medicine, 4, 5. https://doi.org/10.21037/pm-20-97

79. Keith, R. J., & Bhatnagar, A. (2021). Cardiorespiratory and immunologic effects of electronic cigarettes. Current Addiction Reports, 8(2), 336–346. https://doi.org/10.1007/s40429-021-00359-7

80. Miyashita, L., & Foley, G. (2020). E-cigarettes and respiratory health: the latest evidence. The Journal of Physiology, 598(22), 5027–5038. https://doi.org/10.1113/jp279526

81. Chen, I., Todd, I., & Fairclough, L. (2019). Immunological and pathological effects of electronic cigarettes. Basic & Clinical Pharmacology & Toxicology, 125(3), 237–252. https://doi.org/10.1111/bcpt.13225

82. Wick, K. D., Fang, X., Maishan, M., Matsumoto, S., Spottiswoode, N., Sarma, A., Simoneau, C. R., Khakoo, M., Langelier, C., Calfee, C. S., Gotts, J. E., & Matthay, M. A. (2022). Impact of e-cigarette aerosol on primary human alveolar epithelial type 2 cells. American Journal of Physiology-lung Cellular and Molecular Physiology, 323(2), L152–L164. https://doi.org/10.1152/ajplung.00503.2021

83. Snoderly, H. T., Nurkiewicz, T. R., Bowdridge, E. C., & Bennewitz, M. F. (2021). E-Cigarette use: device market, study design, and emerging evidence of biological consequences. International Journal of Molecular Sciences, 22(22), 12452. https://doi.org/10.3390/ijms222212452

84. Montjean, D., Godin Pagé, M.-H., & Bélanger, M.-C. (2023, March 18). An Overview of E-Cigarette Impact on Reproductive Health. NCBI. from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10053939/

85. Int J Environ Res Public Health. (2020, August 24). The Effects of E-Cigarette Vapor Components on the Morphology and Function of the Male and Female Reproductive Systems: A Systematic Review. NCBI. Retrieved December 20, 2023, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7504689/

86. Gawda, E., Zarobkiewicz, M., Chapek, K., & Chylińska-Wrzos, P. (2019, December). Histological changes in the reproductive system of male rats exposed to cigarette smoke or electronic cigarette vapor | Request PDF. ResearchGate. from

https://www.researchgate.net/publication/338173357_Histological_changes_in_the_reproductive_system_of_male_rats_exposed_to_cigarette_smoke_or_electronic_cigarette_vapor

87. Edinburgh International Conference Centre. (2017). Fertility 2017. https://srf-reproduction.org/wp-content/uploads/2017/01/Fertility-2017-Final-Programme-and-Abstracts.pdf

88. Chen, T., Wu, M., Dong, Y., & Kong, B. (2022, April 8). Effect of e-cigarette refill liquid on follicular development and estrogen secretion in rats. NCBI. Retrieved December 20, 2023, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8988604/

89. Wetendorf, M., Randall, L., Lemma, M., & Hurr, S. (2019, September 5). E-Cigarette Exposure Delays Implantation and Causes Reduced Weight Gain in Female Offspring Exposed In Utero. PubMed. Retrieved December 20, 2023, from https://pubmed.ncbi.nlm.nih.gov/31598571/

90. Holliday R, Chaffee BW, Jakubovics NS, Kist R, Preshaw PM. Electronic Cigarettes and Oral Health. J Dent Res. 2021 Aug;100(9):906-913. doi: 10.1177/00220345211002116. Epub 2021 Mar 25. PMID: 33764176; PMCID: PMC8293737.

91. Alhajj, M.N., Al-Maweri, S.A., Folayan, M.O. et al. Oral health practices and self-reported adverse effects of E-cigarette use among dental students in 11 countries: an online survey. BMC Oral Health 22, 18 (2022). https://doi.org/10.1186/s12903-022-02053-0

92. AlQobaly, L., Abed, H., Alsahafi, Y. A., Sabbah, W., & Hakeem, F. F. (2022, July 1). Does smoking explain the association between use of e-cigarettes and self-reported periodontal disease? Journal of Dentistry. https://doi.org/10.1016/j.jdent.2022.104164

93. Wisniewski DJ, Ma T, Schneider A. Nicotine induces oral dysplastic keratinocyte migration via fatty acid synthase-dependent epidermal growth factor receptor activation. Exp Cell Res. 2018 Sep 15;370(2):343-352. doi: 10.1016/j.yexcr.2018.06.036. Epub 2018 Jun 30. PMID: 29966661; PMCID: PMC6108942.

94. Isik Andrikopoulos G, Farsalinos K, Poulas K. Electronic Nicotine Delivery Systems (ENDS) and Their Relevance in Oral Health. Toxics. 2019; 7(4):61. https://doi.org/10.3390/toxics7040061

95. Almeida-Da-Silva, C. L. C., Dakafay, H. M., O'Brien, K., Montierth, D., Xiao, N., & Ojcius, D. M. (2021, June 1). Effects of electronic cigarette aerosol exposure on oral and systemic health. Biomedical Journal. https://doi.org/10.1016/j.bj.2020.07.003

96. Banks E, Yazidjoglou A, Brown S, Nguyen M, Martin M, et al. Electronic cigarettes and health outcomes: systematic review of global evidence. Report for the Australian Department of Health. Canberra: National Centre for Epidemiology and Population Health, 2022. Available from: https://nceph.anu.edu.au/research/projects/health-impacts-electronic-cigarettes#health_outcomes.

97. G. B. D. Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet, 2017; 390(10100):1345-422. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28919119

98. National Academies of Sciences Engineering and Medicine. Public health consequences of e-cigarettes. The National Academies Press, Washington, DC 2018. Available from: http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx.

99. Winnall, WR, Greenhalgh, EM & Scollo, MM. 18.6.9 Exposure to secondhand e-cigarette emissions. In Greenhalgh, EM, Scollo, MM and Winstanley, MH [editors]. Tobacco in Australia: Facts and issues. Melbourne: Cancer Council Victoria; 2023. Available from: https://www.tobaccoinaustralia.org.au/chapter-18-e-cigarettes/18-6-the-health-effects-of-e-cigarette-use/18-6-9-exposure-to-secondhand-e-cigarette-emissions

100. Melstrom P, Sosnoff C, Koszowski B, King BA, Bunnell R, et al. Systemic absorption of nicotine following acute secondhand exposure to electronic cigarette aerosol in a realistic social setting. International Journal of Hygiene and Environmental Health, 2018; 221(5):816-22. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29853292

101. Alnajem, A., Redha, A., Alroumi, D. et al. Use of electronic cigarettes and secondhand exposure to their aerosols are associated with asthma symptoms among adolescents: a cross-sectional study. Respir Res 21, 300 (2020). https://doi.org/10.1186/s12931-020-01569-9

102. Islam, T., Braymiller, J. L., Eckel, S. P., Liu, F., Tackett, A. P., Rebuli, M. E., Barrington-Trimis, J. L., & McConnell, R. (2022, January 10). Secondhand nicotine vaping at home and respiratory symptoms in young adults. Thorax. https://doi.org/10.1136/thoraxjnl-2021-217041

103. Huang J, Feng B, Weaver SR, et al.. Changing perceptions of harm of e-cigarette vs cigarette use among adults in 2 US national surveys from 2012 to 2017. JAMA Netw Open 2019; 2: e191047.

104. Madison MC, Landers CT, Gu BH, et al.. Electronic cigarettes disrupt lung lipid homeostasis and innate immunity independent of nicotine. J Clin Invest 2019; 129: 4290–4304.

105. Nath S, Geraghty P. Should we worry about children's exposure to third-hand by-products generated from electronic nicotine delivery systems? ERJ Open Res. 2020 Jul 20;6(2):00194-2020. doi: 10.1183/23120541.00194-2020. PMID: 32714967; PMCID: PMC7369463.

106. Chen H, Li G, Allam VSRR, et al.. Evidence from a mouse model on the dangers of thirdhand electronic cigarette exposure during early life. ERJ Open Res 2020; 6: 00022-2020.

107. New York State. TalkToYourPatients.ny.gov [Internet]. Talktoyourpatients.health.ny.gov. Available from: https://talktoyourpatients.health.ny.gov/medication

108. Know the risks of e-cigarettes for young people | Know the risks: e-cigarettes & young people | U.S. Surgeon General's report. (n.d.). Know the Risks: E-Cigarettes and Young People | U.S. Surgeon General's Report. https://e-cigarettes.surgeongeneral.gov/knowtherisks.html#

109. Melissa A. Burmeister, PhD Assistant Professor Department of Pharmaceutical Sciences Ashley Hawthorne, PharmD, BCCCP Assistant Professor Department of Pharmacy Practice Abby J. Weldon, PhD Assistant Professor Department of Pharmaceutical Sciences Jennifer White, PharmD Assistant Professor Department of Pharmacy Practice William Carey University School of Pharmacy Biloxi, Mississippi. (2022, May 13). Adverse Neurologic Effects of Electronic Cigarette Use. U.S.Pharmacist. https://www.uspharmacist.com/article/adverse-neurologic-effects-of-electronic-cigarette-use

110. E-cigarette Aerosol Exposure Induces Neurotoxic Accumulation of. (2023, January 31). Columbia University Mailman School of Public Health. https://www.publichealth.columbia.edu/research/centers/niehs-center-environmental-health-justice-northern-manhattan/news-events/newsbriefs/summer-2021/recent-research-shows-metals-e-cigarette-aerosol-vape-clouds-could-cause-damage-central-nervous-system

111. Esteban-Lopez, M., Perry, M. D., Garbinski, L. D., Manevski, M., Andre, M., Ceyhan, Y., Caobi, A., Paul, P., Lau, L. S., Ramelow, J., Owens, F., Souchak, J., Ales, E., & El-Hage, N. (2022). Health effects and known pathology associated with the use of E-cigarettes. Toxicology Reports, 9, 1357–1368. https://doi.org/10.1016/j.toxrep.2022.06.006

112. A. Ruszkiewicz, J., Zhang, Z., Gonçalves, F. M., Tizabi, Y., T. Zelikoff, J., & Aschner, M. (2020). Neurotoxicity of e-cigarettes. Food Chem Toxicol, 32145355. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7089837/