Review Article

VAPING TRENDS AMONG ADOLOSCENTS: UNDERSTANDING THE RISE OF E CIGARETTES IN YOUTH CULTURE

ABSTRACT

Electronic cigarettes (e-cigarettes) have emerged as a contentious topic due to their rising popularity among adolescents and young adults, alongside growing concerns regarding their health implications. This review synthesizes current literature on various dimensions of e-cigarette use, encompassing initiation and progression among youth, respiratory complications, mental health implications, effects on fertility, and their role in smoking cessation. Research indicates a significant rate of e-cigarette initiation among adolescents, influenced by demographic factors such as age, cohabitation with tobacco users, and predisposing psychosocial traits including sensation-seeking behavior and externalizing mental health issues. Respiratory health concerns associated with e-cigarettes include notable cases of EVALI, characterized by severe lung injuries linked to certain e-liquid additives. Aerosols from e-cigarettes are implicated in impairing lung function, disrupting mucociliary clearance, and compromising immune responses, thereby heightening susceptibility to respiratory infections. Furthermore, e-cigarette use is associated with elevated levels of depressive symptoms and anxiety among adolescents, though longitudinal studies indicate complex bidirectional relationships necessitating further investigation. In terms of fertility, studies highlight potential adverse effects on male reproductive health, including disruptions in testicular morphology, decreased sperm counts, and altered hormone levels. While e-cigarettes offer a potential harm reduction strategy for adult smokers, their increasing prevalence among youth and potential health risks underscore the imperative for continued research and regulatory oversight to mitigate adverse respiratory, mental health, and reproductive outcomes, as well as to clarify their role in smoking cessation efforts.

KEYWORDS: Electronic cigarettes, Adolescents, Nicotine, Progression, Respiratory complications

INTRODUCTION

Electronic cigarettes, often known as e-cigarettes, are devices that heat a fluid, typically consisting of propylene glycol or glycerol (glycerin), nicotine, and flavoring ingredients, to deliver an aerosol (also referred to as vapor) to users. This current form was invented in the early 2000s by Hon Lik, a Chinese pharmacist. "An electronic atomization cigarette that functions as substitutes [sic] for quitting smoking and cigarette substitutes," according to the US patent submission describes the e-cigarette device[1]. In the United States, e-cigarettes, or electronic cigarettes, have grown more prevalent. In contrast to conventional cigarettes, e-cigarettes work by aerosolizing nicotine and other components upon inhalation, as opposed to by smoking tobacco [2]. As compared with standard cigarette smokers, the lack of combustion in e-cigarettes certainly decreases their susceptibility to toxins. However, secondhand or thirdhand exposure could occur to both users and non-users if they come into close physical touch with the device's components or breathe in secondhand aerosol [3].

Most E- cigarettes contain nicotine which is the primary ingredient in tobacco and contributes to addiction through its distinctive impact on nicotinic acetylcholine receptors (nAChRs), which influences reward systems and related psychomotor and cognitive processes[4] .The reality that smoking predominantly starts in adolescence, the concurrent development of nicotine dependence and mood disorders, and the fact that nicotine may trigger stress and exacerbate depression and anxiety[5]. This shows that the adolescent brain is predisposed to nicotine dependency, which is consistent with the notion that responses to psychoactive chemicals change innately during this developmental phase[6].

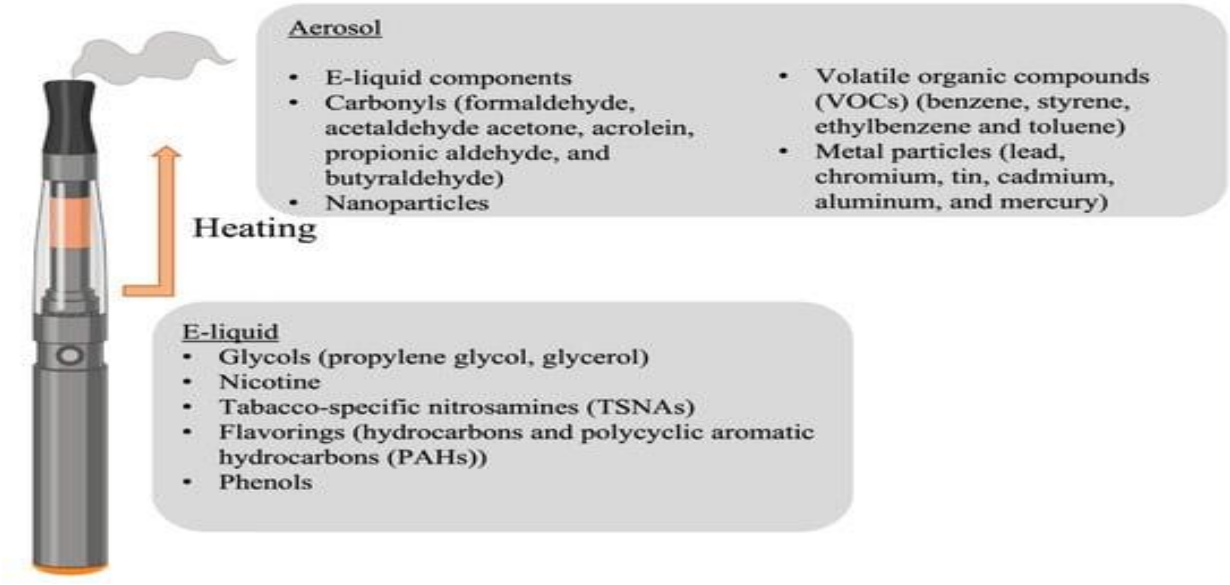


Fig: 1 Exposure of heating

The study by Vivekananda rajah et al. (2019) explores the effects of cigarette smoke exposure on nicotinic acetylcholine receptors (nAChRs) in the brainstem, as well as its impacts on cardiac,

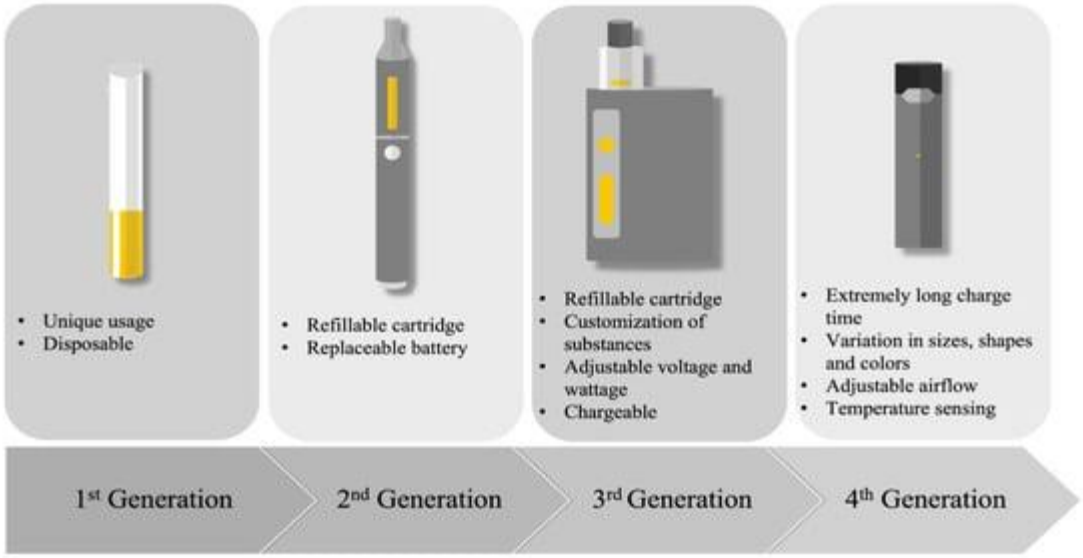
respiratory, and sleep functions. The research investigates how cigarette smoke alters nAChR expression, potentially influencing physiological processes such as cardiovascular regulation, respiratory control, and sleep patterns. This study underscores the broader implications of cigarette smoke on neurological and physiological health, highlighting significant areas of concern related to smoking-related health effects. E-cigarette usage has been linked to exacerbations of pre-existing respiratory disorders such as asthma, acute pneumonias, and pulmonary diseases such as EVALI/VAPI (vaping-associated pulmonary damage)[7]. There are dangers associated with nicotine in e-cigarettes, including potential worsening of ischemic diseases and disruption of the blood-brain barrier due to doses of nicotine that can surpass those in regular cigarettes. Studies also point to inflammation and oxidative stress as possible causes of the increased risk of stroke and cerebrovascular damage linked to e-cigarette usage [8].

- **TYPES OF E- CIGARETTES**

E-cigarettes have changed substantially since they were first introduced to the market. The devices, which go by many names, were produced in a wide variety of forms, dimensions, and kinds. At present, four generations of electronic cigarettes have been created. Its fundamental parts are still a cartridge that holds a fluid, an atomizer that heats the e-liquid to generate an aerosol, a sensor that activates the device, and a battery that supplies the current required to heat the atomizer.

Due to its lack of recharge ability and refill ability, the initial generation of e-cigarettes were primarily intended for a single use. The second generation evolved to include devices with refillable e-liquid cartridges and replaceable batteries. The third generation allowed users to alter the ingredients in the e-liquid and was intended to last for several uses. Fourth-generation e-cigarettes, or Pod-Mods, came in a plethora of sizes, styles, and colours and had every feature of their predecessors.[34]

Currently, over 500 brands and 8000 flavours have been sold in the e-cigarette industry, which is constantly changing. Young adults have taken a strong interest in these gadgets. On the contrary, 85% of persons between the ages of 18 and 29 reported trying vaping in 2018, and exposure to marketing is directly linked to vaping use. Nonetheless, new pricing and licensing measures have resulted in a decline in the prevalence of e-cigarettes. Varied age groups have varied perceptions about using e-cigarettes. Adolescents and young adults may view the use of these devices as popular on the one hand. In reality, 40% of adolescents who use e-cigarettes have never smoked. The e-cigarette was proposed as an introduction to traditional cigarettes based on these results . However, for older users, switching to e-cigarettes was a help in quitting traditional cigarettes. This resulted from the widespread perception that using electronic cigarettes is less dangerous than smoking traditional cigarettes. However, because e-cigarettes contain a variety of chemicals, users are exposed to compounds that may have an adverse effect on their overall health.[34]



- **Fig: 2 Types of e- Cigarettes**

- **EPIDEMOLOGY OF E- CIGARETES**

Electronic cigarettes (e-cigarettes), developed by Chinese pharmacist Hon Lik in the early 2000s, function by heating a solution containing propylene glycol or glycerol (glycerin), nicotine, and flavorings to produce an inhalable aerosol, commonly referred to as vapor. Marketed as a substitute or aid for quitting smoking, these devices entered the market with claims of reduced harm compared to traditional cigarettes and the ability to be used in smoke-free areas. Despite their rapid adoption, significant gaps remain in understanding their health impacts, efficacy for smoking cessation, and overall public health consequences. The complexity of e-cigarette products, which continue to evolve rapidly, coupled with diverse marketing practices worldwide, underscores the need for robust scientific research to assess their safety profiles, particularly concerning long-term exposure to aerosolized nicotine, flavorings, and other components. Of concern are reports of unintended nicotine ingestion, particularly among children, highlighting safety risks associated with refillable e-cigarette cartridges [1].

Furthermore, questions persist about the potential for e-cigarettes to initiate nicotine addiction in non-tobacco users and influence smoking behaviors. Future research must encompass a comprehensive evaluation of e-cigarettes' effects on tobacco use patterns, quit rates, secondhand exposure risks, and broader public health impacts to inform evidence-based regulations aimed at protecting both users and non-users alike. It is still entirely unknown what brain mechanisms, specifically which subtypes of nicotinic receptors are involved, mediate the long-term effects of nicotine in vivo [2].

According to a report published in 2011, based on a consumer-based survey, during 2009 and 2010, the percentage of adults who tried these goods more than doubled, and knowledge of these

products increased across all demographic categories. 11 Even more concerning, according to the CDC, the percentage of students in grades 6 through 12 who use e-cigarettes increased from 3.3% to 6.8% between 2011 and 2012[9].

Adolescents who were mostly Hispanic and who made up the sample of a different study by Barrington-Trimis et al. (2015) were roughly similar in number. Once the remaining sociodemographic characteristics were considered, boys were twice as likely as girls to report using e-cigarettes currently. It was shown that there were no further statistically significant relationships between sociodemographic traits and e-cigarette or cigarette use. Twenty-four percent of teenagers said they had used e-cigarettes at any point in their lives; 9.6% said they had done so in the last 30 days (about 4 and a half weeks), and 14.4% said they had. Remarkably, a smaller percentage of teenagers had smoked cigarettes: 5.7% of teenagers now smoked and 13.0% had smoked in the past. Of the individuals who use e-cigarettes, 44.2% of former users and 40.5% of current users have never used a cigarette. 33.0% of current e-cigarette users and 66 teenagers (3.2% of the sample overall) indicated dual-current usage of cigarettes and e-cigarettes. After adjusting for sociodemographic characteristics, there was a high correlation found between current cigarette smoking and prior and present e-cigarette use[10].

Most current e-cigarette users indicated regular use, and many exclusive e-cigarette users reported using flavored e-cigarettes in 2019. Reported e-cigarette use was exceedingly common among students in middle and high school in 2019.

8837 middle school students and 10 097 high school students participated in the survey. There were 66.3% responses. It was projected that 10.5% of middle school pupils and 27.5% of high school students currently use e-cigarettes. 63.6% of high school students and 65.4% of middle school students reported using e-cigarettes exclusively, while 34.2% of high school students and 18.0% of middle school students reported using them frequently [11].

An estimated 59.1% of high school students and 54.1% of middle school students who currently use e-cigarettes reported using JUUL as their regular brand during the previous 30 days, or roughly four and a half weeks; 13.8% of high school students and 16.8% of middle school students reported not using a regular brand. An estimated 72.2% of high school students and 59.2% of middle school students who now use just e-cigarettes reported using flavored ones; the most popular tastes were fruit, menthol or mint, and candy, desserts, or other sweets[11].

- **INITIATION AND PROGRESSION**

In research by Harlow et al. (2022), 23,167 person-waves were supplied by 9,584 youngsters who were inexperienced to cigarettes and e-cigarettes at wave 1. Initiating e-cigarettes accounted for 12% of the person-waves exposed throughout the research period; combustible cigarette smoking accounted for 7% of the person-waves begun; 917 reported currently smoking (4% per person-wave); 2,152 (22%) were lost to follow-up. Additionally, it was discovered that young people who started using e-cigarettes were older on average, more likely to live with a tobacco user, had a higher sensation-seeking score, were more likely to have externalizing mental health issues, had previously consumed cannabis, alcohol, or other tobacco products, performed worse

academically, were more likely to initiate the use of cigarettes, and were more likely to think that e-cigarettes are less risky than conventional cigarettes than adolescents people who never initiated[12]. As evidenced by a positive response to at least one of the two survey items on e-cigarette dependence, 28.4% of young people who had never used cigarettes or e-cigarettes were vulnerable. When the demographics of susceptible and non-susceptible children were compared, it was found that susceptible kids reported ever used marijuana, alcohol, or other tobacco products, and were somewhat older and more likely to be male. Race and school did not affect susceptibility. After six months, 3.7% of children reported using e-cigarettes for the previous 30 days (about 4 and a half weeks), while 8.9% of kids had started using them. Comparatively, 6. Months later, 0.9% of adolescents reported having smoked cigarettes for 30 days in the past. 3.1% of young people had started smoking traditional cigarettes. Findings show a substantial univariate relationship between follow up e-cigarette outcomes and e-cigarette susceptibility factors [13]. Out of 4100 eligible students, 3396 (82.8%) gave their consent and that of their parents to participate in the study. Each level higher on the 4-level baseline vaping frequency continuum, after controlling for baseline smoking, was linked to correspondingly higher odds of smoking more frequently and heavily by follow-up; these relationships held true in covariate-adjusted analyses. When comparing baseline infrequent smokers to baseline nonsmokers, the positive correlation between baseline vaping and follow-up smoking frequency was larger. More frequent vaping was linked to a higher risk of heavy and frequent smoking six months later in this study of teenagers. Adolescence behaviours related to smoking, which are prominent in this study among vapers, have been associated to an increased likelihood of developing nicotine dependence as an adult.5. While some young people use e-cigarettes to stop smoking, vaping did not result in baseline smokers smoking less. However, more research is necessary because the driving force for vaping was not assessed [14].The onset of smoking cigarettes and the progression to regular use are linked to symptoms of depression. It's unclear if there are any parallels between the onset of teenage e-cigarette use and depressive symptoms. Six research findings on indicators of depression among adolescents were included in a recent review on e-cigarette use and adolescent psychological wellness. Uncertain findings were found about the correlation between using electronic cigarettes and depressive episodes. Adolescents who reported lifetime or past 30-day exclusive e-cigarette use had a greater proportion of indicators of depression than those who never used e-cigarettes, according to four longitudinal investigations. Comparatively, a cross-sectional study discovered that while exclusive lifetime e-cigarette use was not linked to depressive symptoms, exclusive lifetime conventional cigarette use was. Only one of the six included studies used a series of tests and found a reciprocal correlation between e-cigarette use and depression symptoms. Stated differently, a higher likelihood of e-cigarette initiation (or ever use) 12 months later was predicted by higher depressive symptoms. A faster rise in depressive symptoms over the course of a year was linked to sustained e-cigarette use, which was defined as past 30-day use at both 6-month and 12-month follow-ups. According to a more recent longitudinal study of adolescents, the number of days that teens used e-cigarettes increased more quickly over the span of 30 months when they had higher levels of depression symptoms, but not

when they first started using them. The collective results of these studies highlight the significance of extended follow-up times and longitudinal designs, as well as the need to look into the connections between changes in e-cigarette use and depression over time. The longitudinal relationship between e-cigarette use and indicators of adolescent depression over a span of three years and seven time points was examined in this prospective cohort survey study. Moustafa et al. 2021 speculated that e-cigarette use would be related to changes in depression symptoms and that depression symptoms would increase in tandem with the progression of adolescent e-cigarette use. The results may be used to identify young people who are more inclined to make advance in using e-cigarettes and to assist the design of prevention and intervention initiatives [15].

- **RESPIRATORY COMPLICATIONS**

In 2019, the United States saw the start of the EVALI (Electronic cigarette Associated Lung Injury) pandemic, with users reporting pneumonia and severe respiratory symptoms. Nicotine-containing e-liquids and vitamin E acetate were shown to be associated with the outbreak. Because e-cigarettes may be adjusted, there are worries that this might lead to serious and permanent lung transplants. In 2019, 27.5% of US high school students reported using e-cigarettes. With the exception of menthol and tobacco flavours, the FDA outlawed all flavoured cartridge-based electronic nicotine delivery systems (ENDS).Pathogenicity associated with EVALI and the SARS-CoV-2 infection involves reduced neutrophil function, pro-inflammatory cytokine overexpression, and a cytokine storm that results in multiple organ failure. It has also been found that exposure to e-cigarette aerosol reduces the expression of genes related to motility and cilia assembly in epithelial cells that line the airway. In contrast to those who never smoked over half of e-cigarette users (who were otherwise healthy) had lipid-laden macrophages in their lungs. These macrophages were substantially linked to inflammatory cytokines (IL4 and IL10) [16]. Considering vitamin E acetate is known to be a very hazardous substance that may be causing vape-related illnesses and fatalities, research on how it affects vapers' lungs is noteworthy. A pattern implies lipoid pneumonia, which can arise when oils or components high in lipids are aerosolized into the airways, leading to inflammation and impaired function. The intricate network of extracellular membranes on the respiratory epithelium is necessary for breathing and life. In order to stabilize the lung against collapse and aid in lung expansion, surfactant membranes establish a stable monolayer at the air-liquid interface by lowering surface tension. Lung oil disrupts the phase coexistence of lung surfactant, causing lipid phases to coexist in an orderly or disordered manner [17]. Aerosols from e-cigarettes that contain nicotine may negatively affect a number of the lungs' host defence systems. It has been demonstrated that α7 nicotinic acetylcholine receptors (α7 nAChRs) control the activity of the cystic fibrosis trans membrane conductance regulator (CFTR) in the airways in a mouse model. When nicotine is exposed, α7nAChR activity is down regulated, which affects CFTR function and mucociliary clearance (MCC)[18]. In addition to nicotine, lung function may be negatively impacted by inhaling particles and flavourings included in e-cigarette aerosols. It has been determined that e-

cigarette aerosols include ultrafine particles, and lung parenchyma and airways may be harmed by submicron particles. Some ultrafine particles—particles smaller than 100 nm—have the ability to damage DNA, trigger the generation of pro-inflammatory cytokines, and compromise the immune system by generating free radicals. Furthermore, it has been shown that breathing in ultrafine particles raises the incidence of asthma flare-ups. High temperatures produced by e-cigarette devices may trigger the creation of formaldehyde, which might have harmful consequences on the lungs. Flavours in e-cigarettes may potentially change cellular redox balances in the airways by boosting pro-inflammatory cytokines [19]. Kumar et al 2016 employed Sino-Nasal Outcome Test (SNOT-22) scores and evaluated nasal MCC of patients recruited from a smoking cessation clinic in which they were allocated to either non-e-cigarette cessation treatment or e-cigarettes in a randomized single-blind clinical experiment. Subjects randomized to the e-cigarette group at three months had nasal MCC and sino-nasal symptoms that were considerably worse than those assigned to the non-e-cigarette group [20]. The flavouring compounds included in ENDS have a significant impact on the cytotoxic effects of e-liquids and e-liquid aerosols. Additionally, exposure to ENDS aerosol may elevate the expression of β-defences genes in human bronchial epithelial cells (HBE), indicating a proinflammatory reaction. Using an in vitro HBE model, lvorings may compromise the integrity of the epithelium and damage the barrier function. It has been established that e-liquids containing cinnamondehyde inhibit the immune function of the epithelium, neutrophils, and natural killer cells in a dose-response manner, leading to dysfunction of the macrophage phagocytic activity and impaired bactericidal effect. Specific ENDS flavorings may trigger a proinflammatory response by increasing the secretion of IL-8 in HBE and fibroblasts, which will in turn have a chemotactic effect on neutrophils. According to recent research, exposure to ENDS extract may reduce neutrophil extracellular trap formation, reduce ROS generation, and decrease neutrophil chemo taxis [21].

MENTAL HEALTH IMPLICATIONS

There was a strong correlation between smoking and detrimental effects such as depression and anxiety. The substantial incidence of this association in adolescents is demonstrated by the strong link between smoking and affective disorders as well as the significant danger that smoking poses for affective disorders. For instance, smoking start, exploration, regular consumption, recurrence and nicotine reliance have all been prospectively correlated to early anxiety and depression in adolescence. Additionally, a long-term investigation of the relationship between smoking and bad affect in teenagers revealed that stress, anxiety and depression were not just outcomes of smoking but also etiological risk factors for smoking [22].

Increased smoking reward expectancies were associated with a 17% rise in depressive symptoms from mid-to late-adolescence, and this increase was projected to translate into a 23% increase in the risks of smoking progression. These results provide a first look at reward-related mechanisms

that could take place in the early stages of smoking acquisition in young people who exhibit higher symptoms of sadness. Adolescents who are despondent and prone to smoking are highlighted by expectations that smoking has many advantages. When designing smoking prevention programs for young people with depression, it's crucial to focus on these expectations of reward. Over the course of three years, an average of 25% of adolescents experienced clinically significant levels of depressive symptoms. Evaluating the subgroup's expectations for smoking rewards might help identify those adolescents who are most at risk of starting to smoke. Since between 30% and 60% of persons enrolled in smoking cessation programs had experienced significant depression in the past.[23] Using data from the risk behaviour survey, Chadi et al. (2019) examined the relationship between depressed symptoms among high school adolescents (n = 26,821) who used single or dual-use EC. Based to the findings, self-harm thoughts and depressed symptoms were correlated with 9.1% of exclusive EC users (compared to those who don't) (AOR = 1.23, 95% CI: 1.03–1.47) and 1.37, 95% CI: 1.19–1.57).11 30.7% of participants said they had been depressed for more than two weeks, and 17.3% said they had thought about trying suicide at least once in the previous year. In comparison with non-users, 11 EC alone and dual EC and marijuana users reported higher levels of depressive symptoms and suicide. [24] Sustained use of electronic cigarettes over a 12-month period was related with an acceleration of increase in depression symptoms over time when compared to non-tobacco product usage. This relationship among youths who use e-cigarettes that contain nicotine could have been due to nicotine's mood-deregulating effects. Among the general population of youths who use e-cigarettes with or without nicotine, the relationship between prolonged e-cigarette use and increases in depression symptoms might be explained by one of many processes. Adolescents who use e-cigarettes may fail to develop adequate coping strategies to buffer against affective triggers (e.g., problem solving, communication, and seeking social support) because they rely on e-cigarette use as a (maladaptive) coping mechanism that provides temporary relief but no long-term mental health benefit. Alternatively, instead of partaking in pro-social, healthy recreational activities (such joining groups after school or playing sports), which can help avoid depression and improve overall well-being. [25] Another study found that teenagers with high externalizing difficulties were much more likely to start using e-cigarettes, combustible cigarettes, or both than teenagers with low externalizing problems. Adolescents who had a lot of internalizing issues were more likely to start using e-cigarettes than traditional cigarettes, or vice versa. When it comes to externalizing issues vs internalizing issues, this correlation is more reliable. Resolving mental health issues may be a viable avenue to stop teenagers from starting to use nicotine and/or tobacco products. [26] A recent comprehensive study of vaping and mental health comorbidities in children found that vaping is consistently related with depression, suicidality, attention-deficit/hyperactivity disorder (ADHD), and conduct disorder in teenagers. It's possible that different methods led to the conclusion that ADHD was linked to EC usage in teenagers but not in young adults. Alternatively, because of neurobiological and psychological variables, ADHD may be a risk factor for the beginning of EC in teens that is diminished by early adulthood. Adolescents with untreated ADHD are known to be more likely to use drugs,

such as ECs, due to social media and accessibility, whereas younger people with ADHD are more likely to use other substances, such alcohol. The observed difference might potentially be explained by improvements in self-regulation brought about by brain maturity.[27]

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- **FERTILITY**

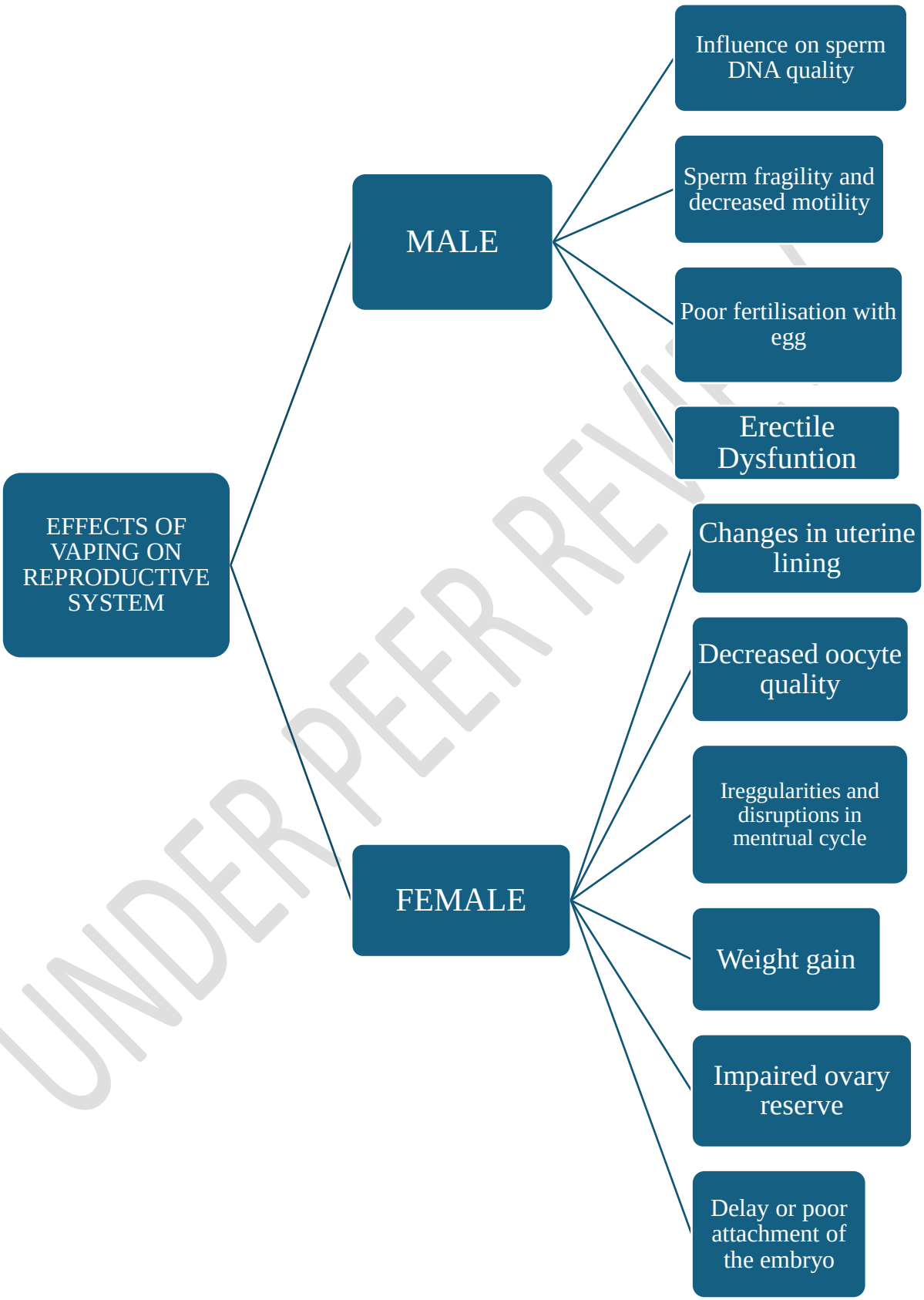
According to recent studies, using electronic cigarettes can have a detrimental effect on one's genitourinary system, which might lead to issues with sexual health. The usage of e-cigarettes may potentially impact fertility. According to a survey, the number of sperm in e-cigarette users is comparatively lower than that of non-users (147 million against 91 million). A comprehensive analysis reveals the paucity of information on the effects of e-cigarettes on the female reproductive system. However, research employing animal models indicates that e-cigarettes may be detrimental to female sexual health.[28] The term "secondhand smoke," or "environmental cigarette smoke," refers to the air-diluted combination of side stream (SCS), which may age more quickly in an indoor setting, and mainstream (MCS) smoke inhaled by active smokers. The most significant anomaly connected to the ECS in epididymal spermatozoa was the lack of a tail, which is thought to indicate sperm fragility and is connected to unsuccessful fertilization. Note that the ECS dosages used in the aforementioned research resulted in a total suspended particulate (TSP) of about 100 mg/m3 air, which is extremely high and not representative of normal human exposures. Smokers can really produce a cloud of smoke that has a TSP of 2-4 mg/m3 of air. Other experimental research that exposed male mice to MCS or SCS assessed the quality of sperm DNA and reproductive end points. The findings indicated that male exposure to secondhand smoke may have an impact on sperm motility and fertilization rates, and that MCS and SCS had varied impacts on the genetic integrity and function of sperm.[29] Youth wellbeing depends on their sexual health. The World Health Organization (WHO) defines sexual health as "a state of physical, emotional, mental, and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction, or infirmity." This definition is crucial. Furthermore, sexual health is a wide topic that has to be taken into account in a comprehensive manner. Adolescents who have healthy sexual health are less likely to have depression and drug abuse problems.[30]

DISCUSSION:

In a research study conducted using an animal model, El Golli et al. released the first paper addressing the impact of e-cigarette refill liquids, both with and without nicotine, on rat testes. Wistar rats weighing 160 ± 20 g were given intraperitoneal injections of electronic cigarette refill liquid every day for four weeks. The findings demonstrated that e-cigarette refill fluids, whether or not they included nicotine, caused oxidative stress in rat testes, which significantly increased the activity of antioxidant enzymes such glutathione S-transferase, catalase, and superoxide

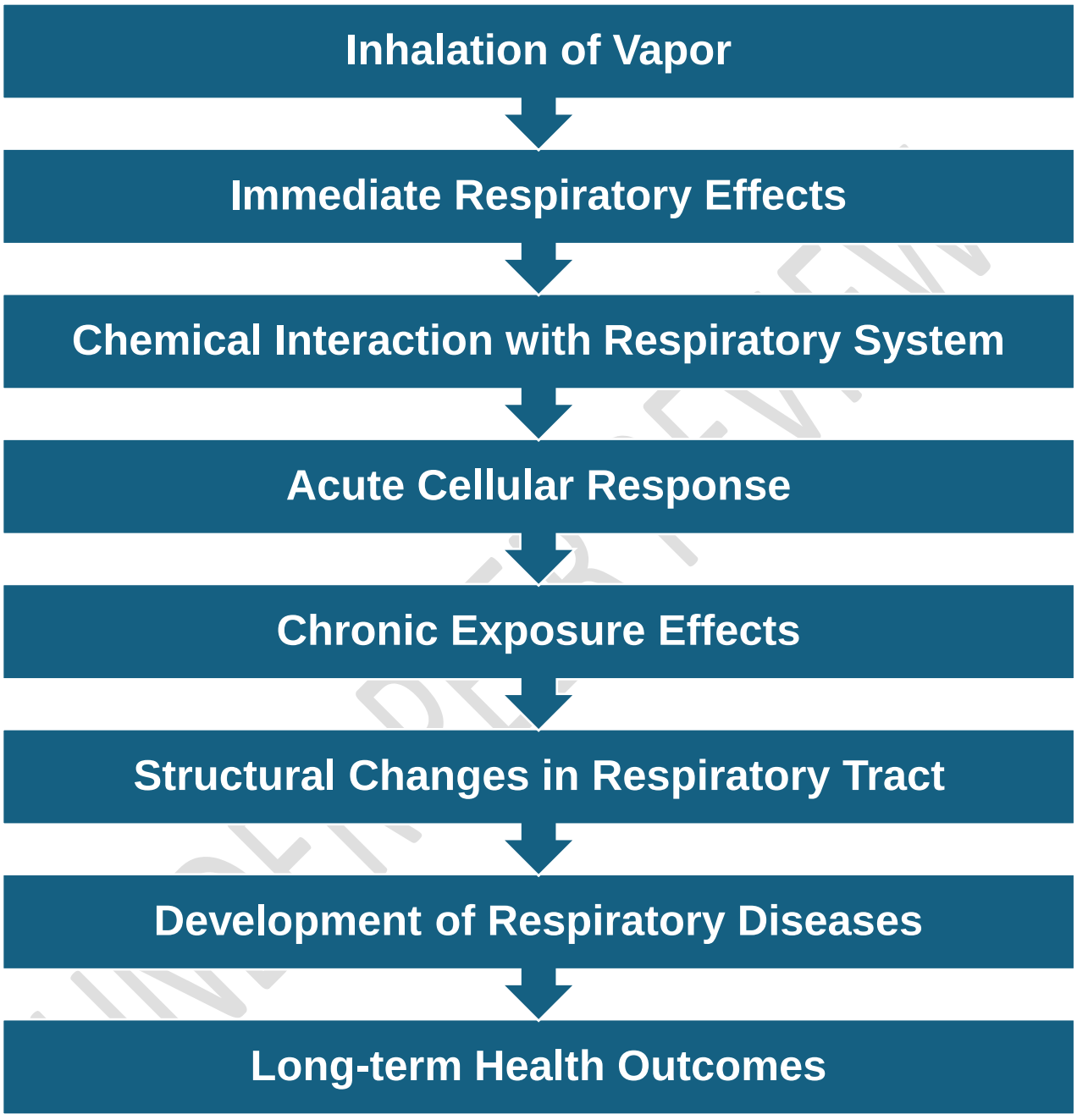
dismutase. Testicular tube contents were disorganized and germ cells prematurely shed from the seminiferous epithelium, among other histopathologically-driven alterations in testis morphology. Mostly androgens, hormones have a comprehensive control over the shape and function of the testes. Because e-liquid exposure reduced the messenger RNA (mRNA) expression of two important steroidogenesis enzymes, cytochrome P450scc and 17β-Hydroxysteroid dehydrogenases (17β-HSD), circulating testosterone levels decreased significantly (by 50% and 30%, respectively). The number and viability of sperm extracted from the epididymis cauda were much lower.[31] Another study found that exposure to e-liquid reduced the amount of epididymal spermatozoa in both liquids with and without nicotine. Remarkably, the sperm counts in the rat treated with the non-nicotine fluid were 32.3 ± 3.0 million/mL and 38.4 ± 0.9 million/mL, respectively, lower than in the other group treated with nicotine. Comparing the vitality of sperm for exposed rats yielded similar results, with 27.0% ± 4.6% and 42.8% ± 5.1% of viable sperm, respectively. The results of a morphological research showed a statistically significant increase in the proportion of aberrant sperm, 43.0% ± 1.0% vs. 30.2% ± 1.8% vs. 24.0% ± 0.9%, notably in the rats exposed to the nicotine-free liquid compared to the liquid containing nicotine vs. control. Both experimental groups showed a significant drop in circulating testosterone levels following four weeks of therapy. The experimental rats' epididymides showed impacts of the e-liquid on their oxidative state.[32] The impact of smoking or e-vapor exposure on male rat fertility was also examined in a research conducted by Wawryk-Gawda et al. Smoking and e-vapor exposure caused the seminiferous epithelium to undergo morphological and functional alterations, including vacuolization, decreased spermatogenesis, and increased spermatogonia and spermatocyte death. Furthermore, minor alterations in the morphology of sperm were noted. Rats exposed to conventional cigarette smoke showed more significant alterations, whereas the effects of vapor on male reproductive systems were marginally less pronounced.[33] The influence of e-cigarette use on intrinsic oocyte quality and oocyte genome integrity is not demonstrated, in contrast to sperm. Nonetheless, some evidence points to ovarian dysfunction in animal models that have been exposed to e-cigarettes. Indeed, the ovaries of female rats exposed to e-cigarette fluid showed a lower proportion of normal follicles. These animals also had altered hormone levels, as seen by the decreased release of estrogen. In mice exposed to e-cigarette vapour, the results of conception and fertilization were also impacted. Smoking was linked to fewer oocytes being recovered from female donors during oocyte retrieval procedures as well as a worse response to ovarian stimulation.[34] Pre-clinical investigations using C57BL/6J mice were conducted to investigate the effects of e-cigarettes on pregnancy start, second-generation fetal reproductive health, implantation, and future offspring health. Using the computerized whole-body inhalation system for animal models, SCIREQ in Expose, these mice were exposed to aerosols from electronic cigarettes. They received two puffs per minute for three hours of exposure, lasting around two seconds each. There were no flavourings and a blend of propylene glycol and vegetable glycerine with 24 mg/mL of nicotine in the liquid. It was 245 °C when the vapour was produced. After mating, females were exposed to e-cigarettes five days a week for four months, running concurrently with control mice. This

resulted in a fertility trial. Five days following the appearance of the copulatory plug (day 5.5), pregnant mice were put to death. This was done in order to examine the effects of e-cigarettes on the implantation process. Prior to mating, virgin mice were exposed to vapor for four weeks. Pregnant mice exposed to vapor had a slightly smaller litter size per litter, but there were no variations in the pups' weights. When compared to the control group, dams exposed to e-cigarette vapor had a three- to four-day delay in the commencement of their first litter. The embryo attachment was delayed in the mice due to pre-mating and post-pregnancy exposure to e-cigarette vapor. Hemorrhagic blood cells were seen at the implantation sites in the experimental mice, and by day 5.5 of pregnancy, only one embryo had implanted in ten dams.[35] In the subsequent experiment, pregnant C57BL/6J mice were exposed to e-cigarette nicotine vapor. This study aimed to investigate the impact of e-cigarette exposure during periods of high brain growth, but it also measured the influence on pup weight. The atomizer, battery, and 510-T tank cartridges were utilized with Joyetech 510-T electronic cigarettes. 2.4% nicotine in propylene glycol (PG) or 0% nicotine/PG was included in the fluid. From day 15 to 19, pregnant mice were exposed to vapors with or without nicotine content, once a day for around 20 minutes.[36] Additionally, from postnatal day 2 to 16, pups were exposed in the same manner. A daily exposure to nicotine of 2.1 mg was estimated. In comparison to both the 2.4% nicotine/PG and the untreated mice, the mean weight of the pups exposed to 0% nicotine/PG vapors throughout prenatal life was considerably lower on the first day of postnatal life. After seven days of postnatal exposure to nicotine vapor, the mean weight of the pups was much less than that of the untreated control mice. Despite only being exposed to the fumes once a day for around 20 minutes, the mice's weight was negatively impacted by the exposure. Considering the primary goal of the study, the findings suggested that long-lasting behavioral alterations may be brought about by exposing mice to vaporized nicotine at a phase of fast brain development.[36] An increasing number of animal experimentation studies indicate that nicotine in ENDS modifies DNA methylation, causes birth abnormalities, lowers birth weight, and impacts the development of the offspring's heart and lungs. According to a sizable population-based cohort research conducted in the US in 2014, 5% of expectant mothers were current users of ENDS, and the majority of them were also smokers.[37]

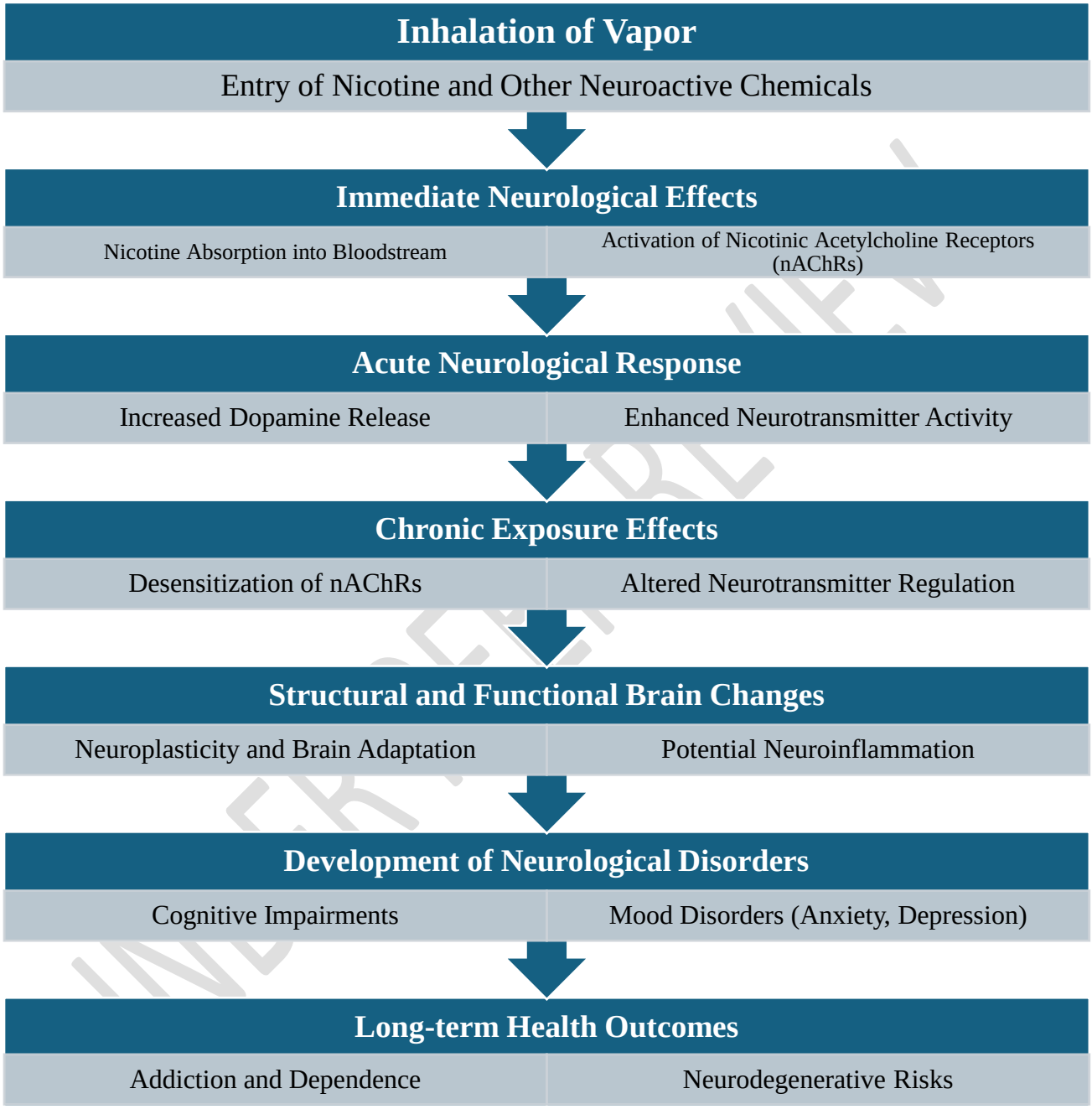


PATHOPHYSIOLOGY

Respiratory Pathophysiology



Neurological Pathophysiology



- **CESSATION OF E CIGARETTES**

  Although electronic cigarettes, also known as electronic nicotine delivery systems or e-cigarettes, are heavily advertised as smoking cessation tools, the evidence supporting this claim has not held up to scrutiny. There were no differences in the 6-month stop rates between e-cigarettes with and without nicotine and a nicotine patch in one randomized experiment. Longitudinal studies based on a population have similarly failed to find any links between using e-cigarettes and stopping.

  E-cigarette usage was notably higher among women, young adults, and those with lower levels of education. Compared to nonusers, a higher percentage of e-cigarette users at baseline (69.0% vs. 57.9%; P =.046) reported smoking their first cigarette less than 30 minutes after waking up. There was no significant correlation found between baseline e-cigarette use and a higher intention to stop smoking.[38]

  Compared to placebo ECs, there is evidence from two trials that ECs assist smokers in quitting permanently. For similar reasons, the absence of difference in ECs' impact from nicotine patches shown in one experiment is questionable. When compared to placebo ECs and nicotine patches, ECs seem to assist smokers who are unable to completely quit in cutting back on their cigarette intake; nevertheless, the aforementioned limitations also impact the reliability of this conclusion. Furthermore, this data is further limited by the absence of a biochemical evaluation of the real decrease in smoking consumption. There is no proof that using EC for a brief period of time increases your risk of illness.[39]

  There exist several plausible reasons for the observed association between e-cigarette usage and reduced cessation rates in this meta-analysis that integrates observational and clinical research. The fact that e-cigarettes are widely accessible consumer goods may be significant when thinking about them as a possible smoking cessation tool. Comparing the scenario to the discrepancies between licensed NRT medicines' clinical efficacies in clinical trials and their real-world application in nonclinical settings may shed light on the matter. [40] There exist several plausible reasons for the observed association between e-cigarette usage and reduced cessation rates in this meta-analysis that integrates observational and clinical research. The fact that e-cigarettes are widely accessible consumer goods may be significant when thinking about them as a possible smoking cessation tool. The scenario can be comparable to the discrepancies between licensed NRT medicines' clinical efficacies for quitting smoking in clinical studies and their real-world use in nonclinical contexts.[41]

CONCLUSION

This review highlights the significant health implications associated with electronic cigarette (e-cigarette) use, focusing on epidemiology, initiation and progression, respiratory complications, mental health effects, and fertility.

Epidemiologically, e-cigarettes, developed by Hon Lik in the early 2000s, have quickly gained popularity as smoking cessation aids and substitutes for traditional cigarettes. Despite their widespread use, there remain substantial gaps in our understanding of their long-term health impacts and effectiveness in helping people quit smoking. Reports show a growing prevalence of e-cigarette use among adolescents, raising concerns about nicotine addiction and secondhand exposure risks. The potential for e-cigarettes to influence smoking behaviors highlights the need for more research to inform regulations that protect both users and non-users. The initiation and progression of e-cigarette use among adolescents is alarming. Studies indicate that starting to use e-cigarettes is associated with older age, living with tobacco users, higher sensation-seeking scores, and externalizing mental health issues. Additionally, e-cigarette use has been linked to a higher likelihood of starting to smoke traditional cigarettes, suggesting a gateway effect. These findings underscore the importance of targeted interventions to prevent e-cigarette use among vulnerable youth.

Respiratory and mental health complications associated with e-cigarette use have emerged as significant public health concerns. The 2019 outbreak of EVALI (Electronic Cigarette or Vaping Product Use-Associated Lung Injury) highlighted the potential for severe respiratory symptoms, including pneumonia, linked to e-cigarette use. Nicotine-containing e-liquids and additives such as vitamin E acetate have been implicated in these adverse effects. E-cigarette aerosols, which contain ultrafine particles, flavorings, and other harmful substances, can compromise lung function and elevate the risk of respiratory diseases. Concurrently, the mental health implications of e-cigarette use are profound, particularly among adolescents. Research demonstrates a strong correlation between e-cigarette use and symptoms of depression, anxiety, and suicidal ideation. Adolescents with higher levels of depressive symptoms are more likely to initiate and continue using e-cigarettes, suggesting a bidirectional relationship. Using e-cigarettes as a coping mechanism for emotional distress may impede the development of healthy coping strategies, exacerbating mental health issues. These findings underscore the urgent need for stricter regulations on e-cigarette products and integrated prevention and intervention programs that address both the physical and mental health risks associated with e-cigarette use.

Fertility concerns related to e-cigarette use have also been documented. Studies show that e-cigarette use may adversely affect sperm count and quality, potentially impacting male fertility. Animal models suggest that exposure to e-cigarette liquids, both with and without nicotine, can cause oxidative stress and changes in the testes, leading to reduced testosterone levels and impaired sperm viability. Although research on the effects of e-cigarettes on female reproductive health is limited, preliminary findings suggest potential risks. These implications for

reproductive health underscore the necessity for further research to fully understand the impact of e-cigarettes on fertility.

In conclusion, while e-cigarettes are often promoted as safer alternatives to traditional cigarettes, the emerging evidence points to significant health risks across multiple areas. The rapid increase in e-cigarette use, particularly among adolescents, coupled with the potential for respiratory, mental health, and reproductive complications, necessitates robust scientific research and stringent regulatory measures. Public health efforts must focus on preventing e-cigarette initiation, especially among youth, and addressing the broader implications for individual and population health.

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