

Review Article

Vaping Products And Asthma In Youths: A Review Of The Prospective Study

Sheida Khosravaniardakani^{1*}

1. Student Research Committee, Shiraz University Of Medical Sciences, Shiraz, Iran.

***Corresponding author: Sheida Khosravaniardakani.** Student Research Committee, Shiraz University Of Medical Sciences, Shiraz, Iran. Email: sh20091367@gmail.com, <http://orcid.org/0000-0002-4581-4134>

Abstract:

Objective: In this review, we explore the known and suspected toxicity of electronic cigarettes (e-cigarettes) in adolescents and young adults to raise awareness of the dangers and identify issues associated with their usage and its association with asthma.

Methods: Narrative review.

Results: E-cigarettes, sometimes known as "vaping," are becoming increasingly popular among children. E-cigarettes produce a vapor from a solution containing a psychoactive chemical, most often nicotine or tetrahydrocannabinol (THC), as well as flavorings and other additives that users inhale. According to the Monitoring the Future study, e-cigarette usage has increased dramatically among teenagers since its debut in the early 2000s. Over 40% of high school seniors reported use in the previous year. Adolescents are particularly exposed to the dangers of e-cigarettes because they are targeted as new users with commercials and flavoring chemicals, and they are not using them to quit smoking. The pulmonary dangers of vaping are quickly becoming apparent, with the most concerning being the disease known as e-cigarette/vaping-associated lung injury (EVALI). Extrapulmonary effects, including cardiovascular, immunologic, and neurodevelopmental impacts, have also been documented in recent investigations. Many of these effects will almost certainly be dose-dependent. To reduce or eliminate new e-cigarette initiation, public health activities are urgently needed to help current e-cigarette users trying to quit.

Conclusion: While we were looking for cohort studies, such studies are not released yet but we firmly support the prohibition of e-cigarette flavorings and advertising focused on teenagers, and we urge doctors to be aware of the growing pandemic.

Keywords: E-cigarettes, vape, nicotine, Asthma.

Submitted: 15 January 2022, Revised: 13 March 2022, Accepted: 21 March 2022

Background:

E-cigarettes are smoking devices that have been commercially available since 2004. The idea behind making them is to induce a sense of smoking while providing an intermittent supply of nicotine without breathing the ashes. They come in many shapes and sizes, but their purpose is the same: to imitate other smoking devices such as pipes, cigars, and of course cigarettes (1-2). A vape is a device in which a specific liquid is converted to vapor, and a person experiences the sensation of smoking by inhaling this vapor. Using this

device is called "vaping" (2-3). In fact, every vape generally has a liquid that is produced by steam heat (2). The pulmonary effects of vaping have just recently been studied. A mass e-cigarette/vaping-associated lung injury (EVALI) was authorized recently in 2019 (3). Increased consumption among middle and high school students appears to be driven by advertising activities and flavored items aimed at attracting teenagers and young adults (4). Because many teenagers who vape are nicotine-naïve, they are not utilizing e-cigarettes as smoking

cessation devices. As they were initially promoted, the risks to the pediatric population are more significant. The general population believes that vaping poses low health hazards (5), which has aided in its widespread adoption, reversing a long-term drop in nicotine usage in the United States, a previous public health success. The pathologic implications of vaping are discussed and the unique issues that this avoidable harm poses to teenagers and youth (1-5).

Adolescents and challenges:

Adolescents are particularly vulnerable to the effects of vaping. Adolescents have historically been targeted by cigarette advertisements and have had much higher rates of tobacco use initiation. Teenage use of vaping devices has increased dramatically in the last decade, with more than 40% of high school seniors reporting use in the previous year (1, 6).

Every year, more than 24 million adolescents were exposed to vaping commercials (7, 8), which commonly feature adolescents (7). We have noticed an upsurge in adolescent vaping as e-cigarette companies have increased their advertising budgets. Although e-cigarettes were first introduced as well as many contemporary commercials for smoking cessation solutions are aimed at youngsters who are not already using nicotine products; for example, there are over 1 million posts about e-cigarettes on Instagram, with many of the ads generated by e-cigarette manufacturers (7). A significant majority of advertising has a vital sexual component, with female models posing in suggestive stances or wearing provocative apparel (9). The FDA has cited JUUL, the largest e-cigarette firm, for direct marketing to adolescents (10). Adolescents are more attracted to flavors and showy technology. A burgeoning culture has sprung up around developing new flavors and varieties. This marketing tactic is similar to the ad campaigns for "flavored cigarettes" that target teenagers (11).

Adolescent vaping cessation has also been linked to the flavor of e-cigarettes, motivating the development of appealing flavors to boost youth vaping (12). Large and flashy devices, frequently paired with e-liquid designed to create an impenetrable vapor cloud, draw attention to users and can be utilized by youths who want to stand out and perform for others.

Electronic cigarette components

The liquid vaporized in e-cigarettes ("e-liquid") ingredients are as follows: psychoactive drugs, solvents, and flavoring compounds, all of which might pose health hazards when used alone or in combination. Nicotine is an addictive alkaloid and the most prevalent psychoactive element in e-liquids. Humans have ingested nicotine for hundreds of years. Nicotine can be found in one of two chemical forms in vaping liquid. Nicotine freebase, sometimes known as "pure nicotine," is an unprotonated form of nicotine that may be easily inhaled and absorbed via the lungs. High amounts of nicotine freebase, on the other hand, are unpleasant to ingest, prompting the development of a new formulation, nicotine salt. Smoking, especially smoking nicotine, is one of the leading causes of death and preventable diseases worldwide. Smoking nicotine increases the risk of a variety of health problems, some of which can be fatal. The most important risk factor for lung cancer is smoking. Cancers of the mouth, throat, larynx, esophagus, intestine, bladder, cervix, kidney, liver, stomach, and pancreas are other cancers that are caused by smoking (12,13). Nicotine is complexed with an acid, generally benzoic acid, in its protonated state. After that, the crystal is dissolved in the vaping liquid. This benzoic acid salt allows for significantly larger nicotine concentrations in e-liquids, fifty milligrams of nicotine is usually permitted dose for such products, accompanying increases in the nicotine dose absorbed by the user, resulting in increased addictive potential (13). In terms

of volume, the principal constituent in e-liquids is a solvent made up of propylene glycol (PG) and vegetable glycerin (VG) (14).

The ratio between these liquids impacts nicotine delivery by diluting the nicotine to the appropriate concentration and allowing for a consistency that can be readily inhaled. There are over 7000 e-liquid flavoring ingredients on the market, and flavoring mixes are frequently made up of custom blends of compounds with unknown toxicologic characteristics (15).

Diacetyl (2,3-butanediol), a buttery taste utilized in food flavorings and e-liquids due to its advantageous chemical features, has been linked to bronchiolitis obliterans in a workplace outbreak among microwave popcorn employees (16). Terpenes, a naturally occurring aromatic oil derivative of isoprene, are another flavoring ingredient commonly employed in e-liquid (14, 17). The formation of hazardous aldehydes during the heating of the e-liquid has also been a source of concern however, the clinical significance of this has yet to be determined (18).

To act as an e-cigarette, the e-liquid must have specific physiochemical properties. A tank or pod holds the e-liquid and is connected to a coil that warms and vaporizes the components in most e-cigarettes. Too thick liquid can clog the heating components or fail to evaporate properly. Vitamin E acetate (or tocopheryl acetate) is a thickening agent commonly used in THC-containing e-liquids. Vitamin E acetate has been linked to the EVALI outbreak, according to the CDC (19). Vitamin E acetate was discovered in numerous samples of THC-containing e-liquid consumed by patients who later had lung symptoms, according to the New York State Department of Health in September 2019. (20). Finally, unregulated and handmade e-liquids impede understanding the toxicity of e-liquids. Some users consider e-cigarettes a hobby, creating their liquids and custom-making e-cigarette machinery to

sell to members of online e-cigarette communities via Instagram or Twitter (Mackey et al., 2015). These e-liquid mixtures' components are entirely unknown and unregulated (21).

E-cigarette/vaping associated lung injury

The Centers for Disease Control and Prevention (CDC) has received reports of over 2800 cases of lung injury from vaping, including over 60 confirmed deaths, since the outbreak began in 2019. (19). EVALI is identified using the CDC diagnostic criteria, which include recent vaping, lung infiltrates on chest imaging, and the absence of infectious pulmonary symptoms; however, many people with EVALI also use other inhalational medications (22).

Many questions concerning EVALI's genesis, diagnosis, and therapy remain unresolved. Fibrinous pneumonitis, widespread alveolar damage, and organized pneumonia were all seen in these cases, all of which are indications of acute toxic lung injury (23, 24). The damage patterns described are consistent with lung injury induced by poisons or chemicals. EVALI sufferers indicate they only use nicotine-based products, despite the fact that vitamin E acetate and THC-containing vaping products have been "strongly linked" to the epidemic (19). The cause of the injury is unknown. Patients with EVALI usually have a variety of abnormalities on chest imaging examinations such as X-ray and computed tomography (CT). Widespread bilateral ground-glass opacities, areas of consolidation, centrilobular nodules, septal thickening, pleural effusions, crazy paving, and the atoll or reverse halo sign have all been observed in the setting of EVALI (25, 26). These symptoms are not specific to any pathogenic condition, posing further diagnostic challenges in situations when EVALI is suspected. As a result, they must be assessed in the context of a clinical setting. THC or nicotine-containing e-liquids were widely bought from unregulated

sources by the majority of EVALI patients. Vitamin E acetate (3, 27, and 28), a thickening ingredient commonly seen in THC-containing e-liquid acquired from unregulated sources, was detected in many of these e-liquids. Although some of these THC e-liquids have been branded as "Dank Vapes," numerous other black/gray market firms have copied this branding (29). The removal of harmful exposure is the most critical priority, and patients should be actively encouraged to stop vaping. With the discontinuation of vaping, most patients see clinical improvement (30).

Severe pulmonary dysfunction, such as hypoxia or respiratory distress, should be admitted to the hospital for treatment. Corticosteroids have been shown to help alleviate symptoms. In Wisconsin, 65% of patients said their "respiratory improvement was related to the use of glucocorticoids," although this is complicated by many patients' concomitant discontinuation of vaping (3).

As a result, the Centers for Disease Control and Prevention (CDC) has issued a recommendation to support corticosteroid usage in most patients until other infectious causes are investigated (22). Following up with these individuals once they have been diagnosed is equally crucial. Many individuals who have developed EVALI have continued to vape, and additional help in quitting may be required. Patients should see either their primary care physician or a lung specialist regularly.

Asthma:

Despite the ongoing debate regarding the effectiveness of e-cigarettes as smoking cessation aids, asthmatic patients who currently smoke are regularly advised by their health care providers to switch to e-cigarettes as a safer alternative (31). Polls reveal that asthmatic children are more likely to use e-cigarettes than their non-asthmatic peers, which is concerning. In a recent study of 6089 US high school students, e-cigarette

use was found to be linked to asthma on its own (32). In a similar study of 35,904 South Korean high school students, researchers observed a stronger correlation between e-cigarette use and asthma, as well as the fact that asthmatic vapers missed school more frequently owing to severe asthma symptoms (33). According to the Florida Youth Tobacco Survey, 33% of asthmatic children aged 11 to 17 were exposed to secondhand e-cigarette aerosol, which has been related to an increased risk of asthma episodes (34). Furthermore, preliminary data from vaping-related lung disease cases in Illinois and Wisconsin suggests that asthmatic individuals are affected at a greater rate than predicted (3).

At the University of North Carolina, we recently published two case reports of teenage asthmatic e-cigarette users who required veno-venous extracorporeal membrane oxygenation due to life-threatening status asthmaticus (35). The existing data suggest that vaping is frequent among teenage asthmatic patients and that these users may be more vulnerable to the negative consequences of vaping. Limited research suggests that e-cigarettes may exacerbate the chronic obstructive pulmonary disease. According to survey data from a population of high school students in South Korea, Vaping was linked to an increased risk of being diagnosed with asthma and more missed school days due to asthma (36, 37).

According to a study of 2086 youths, those who had previously vaped were twice as likely to experience bronchitis symptoms as those who had never vaped (38). In a laboratory setting, e-cigarette use in asthmatic patients altered lung function and inflammation (39). E-cigarette fluid also increased airway hyperactivity, mucin formation, cytokine production, protease expression, and distal airway enlargement in mice (40). Individuals who utilize these products to stop smoking report that their asthma symptoms have improved (41).

Conclusion:

Adolescents are especially susceptible to e-cigarette-related pulmonary damage, addiction, and other health issues. They're unique in that they're largely smokers who are attempting to quit, rather than smokers who are trying to quit. Teens are prime candidates for nicotine addiction, which increases the risk of cigarette smoking. As a result, the growing rates of nicotine addiction are concerning. Most long-term smokers are committed by the time they reach the age of 18, and those who have developed a nicotine addiction find it difficult to quit (42).

Companies that manufacture and sell e-cigarettes use sophisticated and well-developed marketing techniques to specifically target teenagers. Preventing main use in adolescents and young adults is the most important step in decreasing the long-term effects of nicotine exposure. It is critical to support efforts to reduce the initiation of nicotine and THC use among adolescents, such as regulations limiting advertising directed at adolescents, prohibiting the sale of flavored vaping liquids, and prohibiting the sale of e-cigarettes to minors, in order to mitigate the effects of the adolescent vaping epidemic. To reduce combustible cigarette smoking, further study is needed to evaluate the long-term safety of products on the market. Smoking cessation e-cigarette products should only be supplied to adults since only a small percentage of teenagers use e-cigarettes for that purpose. We are also looking forward to continued research into the toxicity of particular e-cigarette components in terms of short- and long-term pulmonary consequences. As more knowledge regarding the toxicity and harmful pulmonary and extrapulmonary effects becomes known, we urgently demand suitable content limitations.

References:

1. Johnston LD, Miech RA, O'Malley PM, Bachman JG, Schulenberg JE, Patrick ME. Monitoring the Future National Survey Results on Drug Use, 1975-2018: Overview, Key Findings on Adolescent Drug Use. Institute for Social Research. 2019 Jan.
2. Miech R, Johnston L, O'Malley PM, Bachman JG, Patrick ME. Trends in adolescent vaping, 2017–2019. *New England Journal of Medicine*. 2019 Oct 10;381(15):1490-1.
3. Layden JE, Ghinai I, Pray I, Kimball A, Layer M, Tenforde MW, Navon L, Hoots B, Salvatore PP, Elderbrook M, Haupt T. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin. *New England journal of medicine*. 2020 Mar 5;382(10):903-16.
4. Dai H, Hao J. Exposure to advertisements and susceptibility to electronic cigarette use among youth. *Journal of Adolescent Health*. 2016 Dec 1;59(6):620-6.
5. Anand V, McGinty KL, O'Brien K, Guenther G, Hahn E, Martin CA. E-cigarette use and beliefs among urban public high school students in North Carolina. *Journal of Adolescent Health*. 2015 Jul 1;57(1):46-51.
6. Gentzke AS, Creamer M, Cullen KA, Ambrose BK, Willis G, Jamal A, King BA. Vital signs: tobacco product use among middle and high school students—United States, 2011–2018. *Morbidity and Mortality Weekly Report*. 2019 Feb 15;68(6):157.
7. Duke JC, Lee YO, Kim AE, Watson KA, Arnold KY, Nonnemaker JM, Porter L. Exposure to electronic cigarette television advertisements among youth and young adults. *Pediatrics*. 2014 Jul 1;134(1):e29-36.
8. Mantey DS, Cooper MR, Clendennen SL, Pasch KE, Perry CL. E-cigarette marketing exposure is associated with e-cigarette use among US youth. *Journal of Adolescent Health*. 2016 Jun 1;58(6):686-90.
9. Ritter SL. Heating up the debate: e-cigarettes and Instagram.

10. FDA. 2019. FDA warns JUUL Labs for marketing unauthorized modified risk tobacco products, including in outreach to youth; [accessed 2019 Oct 3]. <https://www.fda.gov/news-events/press-announcements/fdawarns-juul-labs-marketing-unauthorized-modified-risk-tobacco-products-including-outreach-youth> Carpenter CM, Wayne GF, Pauly JL, Koh HK, Connolly GN. New cigarette brands with flavors that appeal to youth: tobacco marketing strategies. *Health Affairs*. 2005 Nov;24(6):1601-10.
11. Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine & tobacco research*. 2015 Jul 1;17(7):847-54.
12. Goldenson NI, Leventhal AM, Stone MD, McConnell RS, Barrington-Trimis JL. Associations of electronic cigarette nicotine concentration with subsequent cigarette smoking and vaping levels in adolescents. *JAMA pediatrics*. 2017 Dec 1;171(12):1192-9.
13. Varlet V, Farsalinos K, Augsburger M, Thomas A, Etter JF. Toxicity assessment of refill liquids for electronic cigarettes. *International journal of environmental research and public health*. 2015 May;12(5):4796-815.
14. Allen JG, Flanigan SS, LeBlanc M, Vallarino J, MacNaughton P, Stewart JH, Christiani DC. Flavoring chemicals in e-cigarettes: diacetyl, 2, 3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental health perspectives*. 2016 Jun;124(6):733-9.
15. Kreiss K, Gomaa A, Kullman G, Fedan K, Simoes EJ, Enright PL. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. *New England Journal of Medicine*. 2002 Aug 1;347(5):330-8.
16. Meehan-Atrash J, Luo W, Strongin RM. Toxicant formation in dabbing: the terpene story. *ACS omega*. 2017 Sep 30;2(9):6112-7.
17. Khlystov A, Samburova V. Flavoring compounds dominate toxic aldehyde production during e-cigarette vaping. *Environmental science & technology*. 2016 Dec 6;50(23):13080-5.
18. CDC. 2020. Outbreak of lung injury associated with the use of e-cigarette, or vaping, products [Internet]; [accessed 2020 Jun 22]. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html
19. Sun LH. Contaminant found in marijuana vaping products linked to deadly lung illnesses, tests show. *Washington Post* [Internet]. <https://www.washingtonpost.com/health/2019/09/05/contaminant-found-vaping-products-linked-deadly-lung-illnesses-state-federal-labs-show>. 2019.
20. Mackey TK, Miner A, Cuomo RE. Exploring the e-cigarette e-commerce marketplace: Identifying Internet e-cigarette marketing characteristics and regulatory gaps. *Drug and alcohol dependence*. 2015 Nov 1;156:97-103.
21. Siegel DA, Jatlaoui TC, Koumans EH, Kiernan EA, Lauer M, Cates JE, Kimball A, Weissman DN, Petersen EE, Reagan-Steiner S, Godfred-Cato S. Update: interim guidance for health care providers evaluating and caring for patients with suspected e-cigarette, or vaping, product use associated lung injury—United States, October 2019. *Morbidity and Mortality Weekly Report*. 2019 Oct 18;68(41):919.
22. Sommerfeld CG, Weiner DJ, Nowalk A, Larkin A. Hypersensitivity pneumonitis and acute respiratory distress syndrome from e-cigarette use. *Pediatrics*. 2018 Jun 1;141(6).
23. Arter ZL, Wiggins A, Hudspath C, Kisling A, Hostler DC, Hostler JM. Acute eosinophilic pneumonia following electronic cigarette use. *Respiratory medicine case reports*. 2019 Jan 1;27:100825.
24. Henry TS, Kligerman SJ, Raptis CA, Mann H, Sechrist JW, Kanne JP. Imaging

- findings of vaping-associated lung injury. *AJR Am J Roentgenol.* 2020 Mar 8;214(3):498-505.
25. Mukhopadhyay S, Mehrad M, Dammert P, Arrossi AV, Sarda R, Brenner DS, Maldonado F, Choi H, Ghobrial M. Lung biopsy findings in severe pulmonary illness associated with E-cigarette use (vaping) A report of eight cases. *American journal of clinical pathology.* 2020 Jan 1;153(1):30-9.
 26. Christiani DC. Vaping-induced acute lung injury. *New England Journal of Medicine.* 2020 Mar 5;382(10):960-2.
 27. Pray IW, Atti SK, Tomasallo C, Meiman JG. E-cigarette, or Vaping, Product Use–Associated Lung Injury Among Clusters of Patients Reporting Shared Product Use—Wisconsin, 2019. *Morbidity and Mortality Weekly Report.* 2020 Mar 6;69(9):236.
 28. Grady D. Dank Vapes, TKO and other THC vaping brands are linked to illnesses, CDC says. *New York Times.* 2019.
 29. Kalininskiy A, Bach CT, Nacca NE, Ginsberg G, Marraffa J, Navarette KA, McGraw MD, Croft DP. E-cigarette, or vaping, product use associated lung injury (EVALI): case series and diagnostic approach. *The Lancet Respiratory Medicine.* 2019 Dec 1;7(12):1017-26.
 30. Polosa R, Campagna D, Sands MF. Counseling patients with asthma and allergy about electronic cigarettes: an evidence-based approach. *Annals of Allergy, Asthma & Immunology.* 2016 Feb 1;116(2):106-11.
 31. Schweitzer RJ, Wills TA, Tam E, Pagano I, Choi K. E-cigarette use and asthma in a multiethnic sample of adolescents. *Preventive medicine.* 2017 Dec 1;105:226-31.
 32. Clapp PW, Jaspers I. Electronic cigarettes: their constituents and potential links to asthma. *Current allergy and asthma reports.* 2017 Nov;17(11):1-3.
 33. Bayly JE, Bernat D, Porter L, Choi K. Secondhand exposure to aerosols from electronic nicotine delivery systems and asthma exacerbations among youth with asthma. *Chest.* 2019 Jan 1;155(1):88-93.
 34. Bradford LE, Rebuli ME, Ring BJ, Jaspers I, Clement KC, Loughlin CE. Danger in the vapor? ECMO for adolescents with status asthmaticus after vaping. *Journal of Asthma.* 2020 Nov 1;57(11):1168-72.
 35. Cho JH, Paik SY. Association between electronic cigarette use and asthma among high school students in South Korea. *PloS one.* 2016 Mar 4;11(3):e0151022.
 36. Kim SY, Sim S, Choi HG. Active, passive, and electronic cigarette smoking is associated with asthma in adolescents. *Scientific reports.* 2017 Dec 19;7(1):1-8.
 37. McConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, Unger J, Samet J, Leventhal A, Berhane K. Electronic cigarette use and respiratory symptoms in adolescents. *American journal of respiratory and critical care medicine.* 2017 Apr 15;195(8):1043-9.
 38. Kotoulas SC, Pataka A, Domvri K, Spyrtatos D, Katsaounou P, Porpodis K, Fouka E, Markopoulou A, Passa-Fekete K, Grigoriou I, Kontakiotis T. Acute effects of e-cigarette vaping on pulmonary function and airway inflammation in healthy individuals and in patients with asthma. *Respirology.* 2020 Oct;25(10):1037-45.
 39. Garcia-Arcos I, Geraghty P, Baumlin N, Campos M, Dabo AJ, Jundi B, Cummins N, Eden E, Grosche A, Salathe M, Foronjy R. Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner. *Thorax.* 2016 Dec 1;71(12):1119-29.
 40. Solinas A, Paoletti G, Firinu D, Di Pino M, Tusconi M, Mura JF, Del Giacco S, Marongiu F. Vaping effects on asthma: results from a web survey and clinical investigation. *Internal and Emergency Medicine.* 2020 Jun;15(4):663-71.
 41. Zhu SH, Melcer T, Sun J, Rosbrook B, Pierce JP. Smoking cessation with and without assistance: a population-based analysis. *American journal of preventive medicine.* 2000 May 1;18(4):305-11.

