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Review Article

## Vaping: From Public Health Crisis to Impacting SARS-CoV-2 Pandemic - ②

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## ABSTRACT

**Objective:** Electronic cigarette use has increased tremendously from being introduced about over a decade ago till now. While there were continued concerns about its growing use, incidences of lung injuries and deaths related to vaping brought further attention to the topic. Our objectives are to highlight the ill effects of e-cigarette use on health, discuss lung injuries, CDC guidelines, and explore evidence suggesting the correlation of vaping on individuals who develop SARS-CoV-2 related symptoms.

**Methods:** This is a review paper. Various search engines, including MEDLINE Pubmed, CINAHL Complete, OVID, were searched for this review paper.

**Results:** The majority of the population using e-cigarettes are adolescents and young adults. E-cigarettes can cause harmful effects on individuals' health and have a further risk for addiction to nicotine and other substances. In 2019 and early 2020, E-cigarette or Vaping Associated Lung Injuries (EVALI) numbers grew rapidly. A definitive cause of vaping-related lung injuries or deaths is yet to be determined and is under investigation; Vitamin E Acetate is implicated in several cases. Severe respiratory compromise caused deaths. In 2020, COVID-19 pandemic started, which also led to symptoms of serious acute respiratory syndrome. Besides coexisting medical conditions, it is unclear if vaping can exacerbate lung injury due to SARS-COV and leave these otherwise healthy adolescents and young adults more vulnerable.

**Conclusion:** It is not disputed that there is less chemical exposure in e-cigarette use; however, they are not as harmless as projected. As e-cigarettes have been on the market only for the last 13-14 years, besides vaping-related lung injuries, the long-term effects of e-cigarette use need further exploration and continued research as well. During the SARS-CoV-2 pandemic, it is important to look into if vaping can cause more deleterious effects if someone contracts COVID-19.

## INTRODUCTION

After Herbert A. Gilbert's first smokeless non-tobacco cigarette in 1963, it took 40 years until Hon Li rediscovered electronic cigarettes in 2003. With this device, a vaporized form of nicotine liquid solution could be created with an atomizer, hence the name "electronic atomizing cigarette" [1-3]. In research and healthcare, e-cigarettes are commonly referred to as Electronic Nicotine Delivery Systems (ENDS) [3]. It was believed that many cancerous substances, including tar, were eliminated as compared to traditional cigarettes, and therefore, it was projected as a much safer option [3]. These electronic cigarettes got introduced in the United States in 2007 [4]. Since then, electronic cigarettes and e-liquids have gained popularity rapidly due to a variety of reasons beyond the above-perceived health benefits. The largest consuming groups have been young adults and adolescents. Within three years, several brands were available in the U.S. [1]. E-cigarettes were added to National Tobacco Youth Survey in 2014, and since 2014, it has been the most frequently used tobacco product by young population [5].

In 2019, there were growing concerns about lung injuries related to the use of e-cigarettes and vape products, and this continued to be a concern and topic of discussion until early 2020 when the rise of the SARS-CoV-2 pandemic gained attention due to the growing crisis. The Covid-19 virus is noted to have milder symptoms in youth unless there are pre-existing medical conditions. The World Health Organization (WHO) has issued warnings about risks of contracting Coronavirus due to lung injury from smoking, sharing vape products, waterpipe, sheesha, or hukkah [6]. This article also looks into existing evidence if vaping could predispose individuals to more severe symptoms.

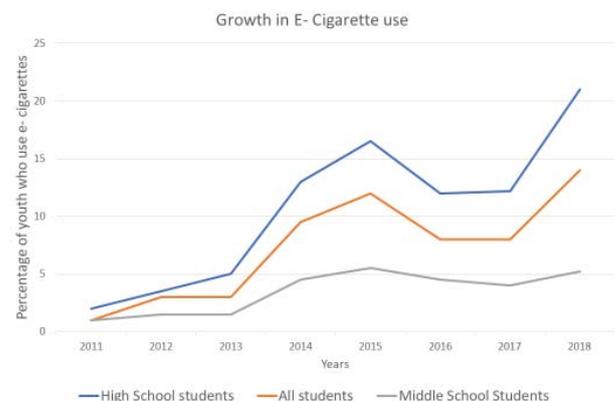
## METHODS

For this literature review, we used various search engines, including MEDLINE PubMed, CINAHL Complete, and OVID. The keywords used for the search included vaping, e-cigarettes, SARS-CoV-2, and COVID-19. With keywords, vaping and e-cigarettes, 29,133 results were discovered. In advanced search, we included keywords vaping, e-cigarettes, and vaping related lung injuries and this reduced results to 1,418 and when SARS-CoV-2 was added to the search, results decreased to 87. We further focused our review on the impact of vaping and e-cigarettes among youth, who otherwise are

considered at low risk for SARS-CoV-2 pandemic.

### Progression of vape product use

During 2011-2015, e-cigarette use increased by 900% among U.S. middle and high school students [5]. Some decline in use was noticed around 2015-2017 [4,5]. However, use was again noticed to be trending upwards between 2017-2018, where it increased 78% among high school students, from 11.7% in 2017 to 20.8% in 2018 [7]. The current figure estimates that 1 in every five high school students and 1 in 20 middle school students use e-cigarettes, which is more than 3.6 million U.S. youth [4,7]. School students often use these e-cigarettes not just because they are advertised as safer or involving fewer risks but also because they are trying to "fit in," contents used in vape could be modified and the contents used are easier to hide from parents. Boys are twice more likely to use e-cigarettes than girls. 30.7% of e-cigarette users start smoking in less than six months as compared to 8.1% of non-users [8]. 66% of users are using only flavored e-cigarettes, 13.2% are using nicotine, and 5.8% marijuana, close to 15% either did not know or chose some other responses [8]. This is to be kept into consideration that vaping products could be bought only by individuals who are older than 18 years old.



**Source:** National Youth Tobacco Survey, 2011- 2018 [9]

One study from 2016 reported that in adult's prevalence of e-cigarette use is close to 4.5%, which is about 10.8 million adult e-cigarette users in the United States. Of the e-cigarette users, 15% were never-cigarette smokers. The prevalence was highest between

ages 18 to 24 years (9.2%), translating to approximately 2.8 million users in this age range, and 51.2% were younger than 35 years, more than half of the population that was using. This study also indicated that the age-standardized prevalence of e-cigarette use was high among men; Lesbian, Gay, Bisexual, and Transgender (LGBT) persons; current combustible cigarette smokers; and those with chronic health conditions. A prevalence is noted to be around 4.5%, which corresponds to 10.8 million adult e-cigarette users in the United States [10]. As per Euromonitor International, around the globe, more than 35 million people are likely using electronic cigarettes and related products [11]. This is despite the fact that several countries are trying to regulate sales of these products. Internationally, around 41 countries have banned sales of e-cigarettes, 66 countries allow selling e-cigarettes but 32 out of those are regulating the nicotine content of these e-cigarettes [12].

### Mechanism of e-cigarettes

The basic mechanism of e-cigarettes involves heating coil activating to aerosolize the e-cigarette solution to form an emission, which is described as an aerosol or vapor, is inhaled from the mouthpiece [3].

In less than two decades of their existence, vaping devices have gone through several modifications. First-generation e-cigarette resembled a traditional cigarette, often having a disposable or have a reloadable cartridge for repeated uses. Second-generation e-cigarettes are known as vapes or vape pens (with medium size tank devices). These tanks were used as a refillable reservoir for the electronic cigarette liquid (e-liquid). Further evolution of e-cigarettes led to the introduction of vape mods [3]. These vape mods have several features, including variable voltage settings, display screens, interchangeable cartridges or other components, Bluetooth syncing, and more. This has been both fascinating and lucrative for the new generation. These changes give the ability to control the wattage and voltage of the heater. In turn, individuals can control the amount and intensity of vapor inhalation. In fact, these modern devices used by millennials and Gen-Z, no longer resemble traditional or previous generations of e-cigarettes, and they are labeled as third-generation e-cigarettes. E-cigarettes that are Bluetooth enabled can also keep track of the amount of vaping by an individual in a day.

### Electronic nicotine delivering systems/ vape devices/ e-cigarettes



**Source:** U.S. Department of Health and Human Services, Center for disease control and prevention (CDC)

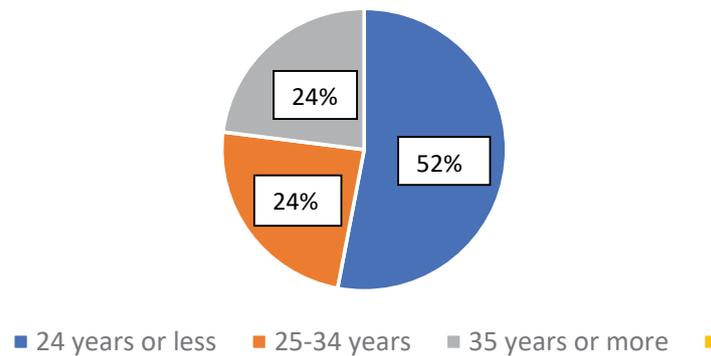
The number of identified/partially identified components in tobacco and tobacco smoke totals 9582, and about 70 of them could cause cancers, including nicotine, hydrogen cyanide, lead, benzene, carbon monoxide, radioactive elements like uranium [13]. It is known that e-cigarettes contain fewer harmful particles than traditional cigarettes. However, so far, contents delivered in e-cigarettes are not standardized [13,14]. Most E-cigarettes are labeled as containing

nicotine, flavoring agents, and organic compounds. Manufacturers do not have to report all e-cigarette ingredients. Until recently, there were no regulations mandating reporting of all ingredients in the U.S. [8]. In the last two years, U.S. Food and Drug Administration has proposed new rules including, regulations of flavors of tobacco products, regulations of premium cigars, tobacco product standard for nicotine level of combusted cigarettes, content and format of substantial equivalence report and most recently, as of September 25, 2019, premarket tobacco application and recordkeeping requirement [15]. These rules are not in effect yet.

Nicotine is highly addictive, and it can lead to other substance use in the future [16]. It is considered as one of the “gateway drugs” along with alcohol and marijuana [17]. As the grey matter in the brain continues to evolve until the mid-twenties, it can impact the developing brain negatively by cognitive impairment, including impaired learning, attention, and memory [18]. Conventional cigarettes’ nicotine absorption is around 1 mg, and blood levels of nicotine reach between 15 to 30 ng/ml [19, 20]. On the other hand, e-cigarette solutions (as advertised by brands) can have concentrations between 0 and 24 mg/mL of nicotine. Recently, one leading brand of the e-cigarette took it to an alarming level as it advertised containing nicotine concentration as high as 59 mg/mL along with the presence of benzoic acid [21,22]. Ghosh, et al. [23] discussed JUUL-type ENDS have nicotine salts, protonated with benzoic acid, can lead to increased cytoplasmic calcium ions and cytotoxicity. Gholap, et al. [24] also suggest that protonated form of nicotine salts have higher nicotine absorption and sensory effects than nicotine base. They highlight on the importance of different forms nicotine, as they can play significant role in nicotine addiction. Like any addiction, nicotine addiction depends on the amount of nicotine one is exposed to and the adaption of receptors. Hence, the concentrated forms of these nicotine-based e-cigarettes liquids can enhance the immediate effect, increase risks of addiction, and further long-term effects on memory and other cognitive impairment as described above. Flavoring agents like diacetyl are chemical that has been linked to serious lung disease. Not much is known about the impact of other additives like propellants, solvents, and oils (organic compounds, propylene glycol, and vegetable glycerin) when consumed in larger amounts [3,22]. They also have suspended ultrafine particles and heavy metals like tin, lead, and nickel [25,26]. The invisible harmful suspended ultrafine byproduct particles of the e-cigarettes could affect the surroundings, thus leading to risks of secondhand and thirdhand smoke, against the advertised and assumed notions of safety for non-smokers around the subject. Hence, it is important to stress upon that e-cigarette use is not as safe as it is projected [18].

As mentioned above, the ability to change cartridges and components easily allows replacing nicotine or flavored e-liquids with cannabis products such as Tetrahydrocannabinol (THC) or Cannabinoid Oil (CBD oil). Particularly Tetrahydrocannabinol (THC), which is a primary psychoactive component of cannabis. Also, concentrations of THC achieved through the vaping device could be substantially high, along with the same principle as nicotine. Chronic, high amounts of cannabis use can also cause significant memory impairment, decreased motivation, impaired judgment, a decline in academic performance, increased paranoia, worsening of symptoms of depression and anxiety. The human body has an endocannabinoid system, and its receptors are widely distributed throughout the brain. Hence, endogenous cannabinoids (anandamide and 2- arachidonoyl glycerol) act on cannabinoid receptors in these parts of the brain

Age Distribution of EVALI confirmed or probable cases



**Figure 1:** Age Distribution of EVALI confirmed or probable cases.

to produce mind-altering effects; for example, amygdala (panic/paranoia), hippocampus (memory impairment), neocortex (altered judgment, attention, and thinking), nucleus accumbens (euphoria) [27]. As so far, e-liquid contents are not standardized; there are times when THC content could be more than recommended doses, especially if bought off the streets. This can cause profound impairments and further risks of addiction too.

### E-cigarette, or Vaping, Product use Associated Lung Injury (EVALI) crisis

While there were already concerns about an epidemic of e-cigarette use in the last few years, vaping-related pulmonary injuries had brought this rapid use to another limelight in 2019, and it was now considered a public health crisis.

According to a CDC report generated on February 2020, 2807 cases of E-cigarette, or Vaping, Product Use Associated Lung Injury (EVALI) were reported to CDC from 50 states (all but Alaska), the District of Columbia, and 2 U.S. territory. This number included 68 deaths in a total of 29 states throughout the country. In January 2020, out of a total of 2668 hospitalized cases of EVALI, 15% of them were less than 18 years of age, the largest group was 18-24 years of age comprise 37% of all the cases, and 24% were noted to be between 25- 34 years of age. Almost 76% of cases are less than 35 years old [28] (Figure). This corroborates findings that e-cigarettes and vaping products are more common in the younger population like described above [29].

A large number of patients who had used THC-containing vaping products have led to EVALI cases. However, reviewing the data gives mixed reports. Based on data from January 2020, where 82% of cases reported using Tetrahydrocannabinol (THC)-containing products in the three months preceding symptom onset, and only 33% of them used THC-containing products alone. A total of 57% of cases used vaping products that contained nicotine, and 14% used nicotine only. The median age of EVALI patients who died was around 49.5 years [29].

### Presentation of EVALI

The initial respiratory symptoms are non-specific, including nonproductive cough, pleuritic chest pain, or shortness of breath (in 95% of patients), which can appear over several days to several weeks

before hospitalization. Other findings might include tachycardia (55%), tachypnea (45%), fever, chills, or fatigue (85%) in patients; reported gastrointestinal findings like nausea, vomiting, abdominal pain, and diarrhea (77%) had preceded respiratory findings in some cases [30]. Most patients have been hospitalized with hypoxemia (pulse oximetry <95% was present in 57% patients) and, in some cases, has progressed to acute or subacute respiratory failure. Some have required respiratory support therapies ranging from supplemental oxygen to endotracheal intubation and mechanical ventilation. Some patients who were suspected of having infection were treated with antibiotics empirically and did not improve. In some cases, corticosteroids were able to alleviate the symptoms [30].

### SARS-CoV-2/ COVID-19 pandemic

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus-2 was identified in China in 2019. It reached the U.S. in early 2020 is still ongoing. The pandemic grew rapidly, causing mild to severe symptoms across the life span, particularly among the elderly or people with pre-existing medical conditions. The COVID-19 pandemic symptoms include fever, chills, cough, breathing difficulties, fatigue, muscle aches, congestion, sore throat, runny nose, loss of taste or smell, nausea, and vomiting. The respiratory symptoms of this virus overlap with vaping-related lung injuries. In the early 2020, when the public health crisis due to EVALI cases was ongoing in the U.S. and new cases were still reported in substantial numbers, SARS-CoV2 started to spread. There are concerns if initial cases of SARS-CoV-2 might have been missed as vaping-related lung injuries. Other concerns are, if this pandemic overshadowed identifying EVALI cases promptly and attention that is needed to look into regulating contents of e-cigarettes and vaping devices.

Individuals who smoke are at higher risk for respiratory tract-related viral infections. Smoking can cause endothelial dysfunction and increased free radical concentration. Smokers can present with varying degree of lung injury after heavy and chronic use, from bronchiolitis, pneumonia, pulmonary emphysema, chronic bronchitis, tuberculosis, or to even lung cancers [31]. Those who have chronic respiratory illnesses like chronic obstructive pulmonary diseases can be a vulnerable population for viral infections. So, if exposed to the SARS-CoV-2 virus, these individuals can have acute decompensation

to existing respiratory conditions. Hence, specialists in the field have suggested smokers might have higher odds of COVID-19 infections or for its complications. Sharma et al. elaborated on the findings of Zhang et al., where they speculated a correlation of increased ACE2 gene expression, gene encoding the receptor for SARS-CoV-2, in both SARS-CoV-2 and smokers airway epithelial cells [32,33]. The raised levels of TMPRSS2 protease, which can promote viral entry in the cells, are also observed in the small airways of smokers. Smokers are noticed have elevated thrombosis related markers like D-dimers and C-Reactive Protein (CRP) [31]. These markers are also raised in COVID-19 patients and one of the fatal complication of COVID-19 pandemic is Disseminated Intravascular Coagulation (DIC). These initial observations and opinions still need to be backed up by more evidence. There are concerns if vaping can contribute to increased inflammatory response making these individuals with respiratory compromise more susceptible when exposed to the virus [34].

Researchers are also considering if there could be increased risks due to shared vape devices or secondary smoke/vapor. So far, no clear evidence is available suggestive of virus transmission through vapors [34].

### Recommendations and Guideline [28]

- CDC continues to recommend refraining from using E-cigarettes.
- Adolescents, young adults, and parents should be aware of types of e-cigarettes, their ill effects, possible lung injuries from vape products, and suggested possibilities of smoking and vaping, further complicating lung infections pandemic.
- School teachers and staff should also enforce similar rules for any tobacco product like cigarettes and discuss the impact of vaping products.
- Physicians should closely screen and provide education to adolescents and adults about the effects of vaping.
- These e-cigarettes should not be bought from off the streets, and people should not modify e-cigarette products or add any other substances that are not intended by the manufacturer.
- E-cigarette products should never be used by adolescents, young adults, pregnant women, or adults who do not currently use tobacco products.
- If attempting to quit, adults should use evidence-based smoking cessation treatments. They should be enrolled in counseling and use FDA-approved medications. Those who need help quitting tobacco products, including e-cigarettes, should contact their medical provider.

### CONCLUSIONS

E-cigarettes and vape products are widely accepted among youth due to perceived fewer ill-effects, easier use, faster and large amounts of nicotine and THC delivered. There are overlapping respiratory symptoms of vaping-related lung injury and SARS-CoV-2. It is well known that smokers are at higher risk for viral infections, and super-imposed viral infections might exacerbate chronic respiratory symptoms. The experts suggest some initial correlation between viral expression and vaping/smoking based on similar gene expressions. However, more research and evidence are needed to establish a direct correlation.

### DISCLOSURES

The author has received honorariums for writing and reviewing manuscripts from American Physician Institute.

### AUTHOR'S CONTRIBUTION

The author is responsible for reviewing the literature, evaluated the data, and wrote the manuscript.

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