

Nicotine vaping was not the cause of e-cigarette, or vaping, product use-associated lung injury in the United States

EVALI (E-cigarette, or Vaping, product use-Associated Lung Injury) was an outbreak of severe and sometimes fatal lung injury in North America between mid-2019 and early 2020 [1]. It occurred among young people who vaped black-market tetrahydrocannabinol (THC) oils contaminated with vitamin E acetate (VEA).

Fourteen percent of EVALI cases reported vaping nicotine only [1]. This finding has been used to make the claim that nicotine products can cause EVALI.

Australian health departments, for example, have warned about a link between nicotine vaping products and the outbreak of EVALI [2, 3]. Media reports still link EVALI to nicotine vaping in an alarming way [4]. This messaging shapes public perceptions of the risks of vaping nicotine and adversely influences public policy on e-cigarettes [5].

Vaping is the most popular aid for quitting or reducing smoking in Australia [6], the United Kingdom [7] and the United States [8] and is more effective than nicotine replacement therapy [9]. There are likely to be substantial benefits for public health if more Australian smokers switched to vaping nicotine [10]. However, unfounded claims about a link with EVALI and restrictive Australian policies justified by this claim reduce the uptake of e-cigarettes in Australia to the detriment of public health.

1 | WHAT IS EVALI?

EVALI is a form of acute respiratory distress syndrome which causes breathing difficulty, shortness of breath and chest pain. In the US outbreak, it led to 2807 hospitalisations and 68 deaths by February 2020 [1]. The diagnosis of EVALI is based on recent vaping, radiological findings, absence of infection and 'no evidence in the medical record of alternative plausible diagnoses' [11].

In January 2020, the US Centers for Disease Control and Prevention (CDC) concluded that EVALI was strongly linked to vitamin E acetate [12]. VEA is a thickening or cutting agent that was added to THC (cannabis) vape oils by black-market dealers. The CDC stated that

other causes were possible, but no other causal agent has been identified.

It is highly implausible that nicotine vaping products played a role in EVALI. First, because there are good reasons to doubt that 14% of EVALI cases in the United States vaped nicotine only. Second, VEA is not soluble in nicotine e-liquids and has never been detected in nicotine e-liquids. [13] Third, no potential causal agent in nicotine vapes has been identified. Fourth, nicotine vaping products remained unchanged before, during and after the outbreak.

Because of the inherent implausibility of EVALI being caused by e-cigarettes, 75 multi-disciplinary experts petitioned the CDC to change the name of the disease [14]. The name is misleading as it falsely implies that all vaping devices cause this disorder, when the only identified cause has been THC vaping products contaminated with vitamin E acetate. A more accurate name would be VALI (Vaping Associated Lung Injury).

2 | UNDER-REPORTING OF THC USE

Self-reports denying THC use are often unreliable because of stigma, parental disapproval, legal ramifications, fear of job loss and/or fear of loss of insurance coverage (a particular problem in the United States) [15, 16]. In one study, over two-thirds of frequent cannabis users tested positive after claiming that they had not used cannabis in the past week [16].

This under-reporting was likely to have occurred during the EVALI outbreak. Unsurprisingly, some cases who initially denied using THC, were later found to have used THC after interviews with social contacts or after testing of biological specimens [12, 17, 18].

According to the CDC, misreports of THC use in the EVALI outbreak might be due to recall bias, social desirability bias, patients not knowing the content of the vaping products they used or that they 'might be hesitant to reveal use of substances that are not legal in their state' [19]. At the time of EVALI, cannabis was still illegal in 38 US states.

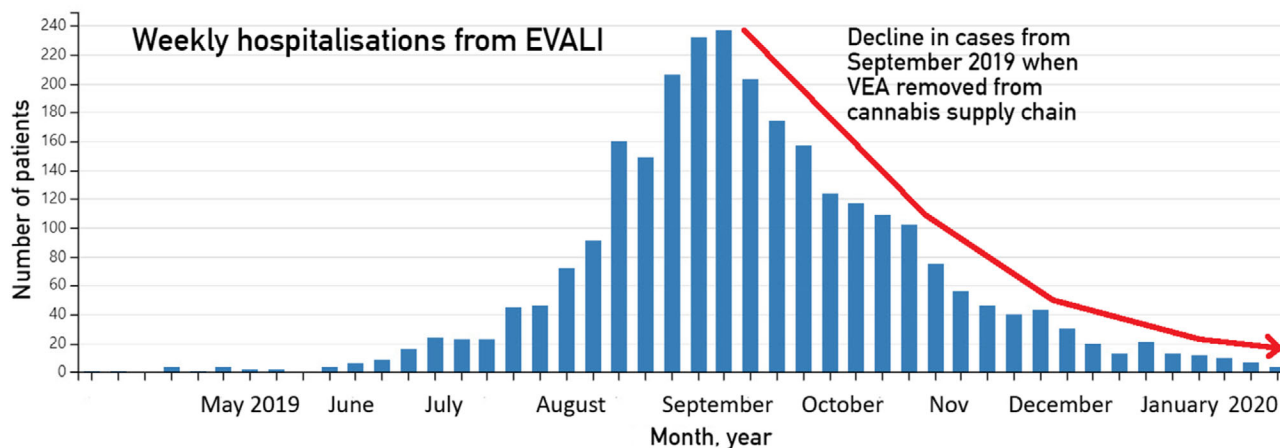


FIGURE 1 Timeline of hospitalisations for e-cigarette, or vaping, product use-associated lung injury (EVALI). VEA, vitamin E acetate

3 | TEMPORAL AND GEOGRAPHICAL PATTERNS

The localised geography and temporal pattern of the outbreak were consistent with a contaminated supply chain for illicit THC products. Case numbers rose rapidly to a peak and then disappeared in early 2020 when VEA was eliminated (Figure 1).

It is highly implausible that commercial nicotine vaping products caused this pattern of EVALI cases. There have been no verified cases of EVALI from vaping nicotine before or after the outbreak and no remedial changes were made to the composition of nicotine vaping products.

It is significant that confirmed cases of EVALI occurred almost exclusively in North America. Vaping nicotine is popular in dozens of countries and there were an estimated 82 million vapers worldwide in 2021 [20].

There was one case of EVALI in the United Kingdom despite a high prevalence of nicotine vaping [21]. Two cases in Australia misattributed to EVALI are discussed below.

4 | MISDIAGNOSIS OF EVALI

According to the CDC, 'EVALI is a diagnosis of exclusion with an intentionally sensitive case definition, and it is possible that cases caused by other etiologies could be misattributed to EVALI' [22].

It is therefore possible that some patients in the EVALI case series may have had other causes for their condition. Many patients did not have a full medical workup that could comprehensively exclude other possible causes.

Two recent cases of severe acute respiratory distress syndrome in Australia that were attributed to nicotine

vaping did not meet the EVALI case definition because other plausible diagnoses were present [23]. In addition, VEA was not detected in e-liquid and biological samples.

The first case in September 2020 involved a Sydney adolescent who had been using illicit nicotine vaping products purchased from convenience stores [23]. She developed urinary symptoms, initially treated with intravenous antibiotics. She subsequently developed pulmonary symptoms that progressed to acute respiratory distress.

One alternative diagnosis in this case was urosepsis triggering a lung injury [24]. Other possible causes were an allergic sensitisation reaction (eosinophils were found in the lung fluid) or a toxic response to another undisclosed chemical. The patient had also used THC via a water pipe and benzodiazepines. Bronchoscopy and bronchial lavage were not performed.

A second case of putative EVALI was reported in the Australian media in February 2022 [25]. The patient was a 71-year-old man who had smoked a pack-a-day for four decades before switching to nicotine vaping 10 years previously. He had a raised white cell count and CRP and was treated initially with antibiotics for community pneumonia. The post-mortem confirmed advanced COPD and interstitial lung disease consistent with the effects of long-term smoking. The patient most likely developed a secondary lung infection as a complication of COPD, leading to acute respiratory distress syndrome.

5 | MISCOMMUNICATION OF EVALI RISK BY HEALTH AUTHORITIES

Some of the information from Australian governments about EVALI has been inaccurate and misleading.

The federal Health Department website has warned since September 2019 that ‘International evidence is emerging of a possible link between the use of e-cigarettes and lung disease’, referring to the EVALI outbreak [2]. The warning does not differentiate between vaping nicotine or THC and discourages the use of any vaping product.

Thirty-one Australian health professionals wrote to the Chief Medical Officer pointing out that this health advice was inaccurate [26]. However, it has remained unchanged even as the evidence against nicotine vaping as a causal agent continues to strengthen.

In March 2022, NSW Health launched the ‘Do you know what you are vaping?’ education campaign which claimed that ‘vaping has been linked to serious lung disease’ [3]. This messaging implies that nicotine vaping can cause EVALI, as no other serious lung harm has been caused by vaping.

In the United States, the CDC continued to suggest that nicotine vaping could cause EVALI long after the evidence against it strengthened [27]. It has now withdrawn its warnings about commercial nicotine vaping products [1].

Advice from the UK Government was much swifter and clearer. In October 2019, Public Health England stated that EVALI ‘is not a problem linked to long-term use of regulated nicotine vaping products’ [28].

According to Public Health England, misinformation about vaping and EVALI can have deadly effects. They wrote, ‘The responses we have seen to the problem in the US and in other countries may increase the already widespread misunderstanding about the relative safety of nicotine e-cigarettes, deterring smokers from switching and risk driving vapers who have switched back to smoking. There is a real risk therefore that such a reaction will mean people continue to smoke, which will undoubtedly put lives at risk’ [28].

6 | CONCLUSION

The EVALI outbreak in the United States was caused by vaping black-market THC oils contaminated with vitamin E acetate. Some of the small number of cases that reported vaping nicotine only are likely to have misreported their use of THC for fear of legal or social consequences because many cases of EVALI occurred in US states where cannabis is still illegal. Others may have been former smokers with other respiratory illnesses that were misdiagnosed as EVALI. It is time for Australian health authorities and media to correct the continued miscommunication of the causes of the EVALI outbreak as misinformation could potentially harm public health.

AUTHOR CONTRIBUTIONS

Each author certifies that their contribution to this work meets the standards of the International Committee of Medical Journal Editors.

CONFLICT OF INTEREST

Colin P. Mendelsohn was a Board member of the Australian Tobacco Harm Reduction Association (ATHRA), a health promotion charity, until January 2021. ATHRA received unconditional funding for establishment costs from small Australian vape businesses. Vape industry funding has not been accepted since March 2019. He is the author of a book, *Stop Smoking Start Vaping*. Alex Wodak is currently a board member of ATHRA. Wayne Hall has no conflicts to declare.

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