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Lung Damage Caused by the Use of Electronic Cigarettes: A Systematic Review

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ABSTRACT

The use of electronic cigarettes (*e-cigarettes* or *vapes*) has grown exponentially in the last decade, especially among adolescents and young adults, under the mistaken perception that they are safer alternatives to conventional tobacco. However, recent evidence shows that these devices are associated with significant lung damage, both in acute manifestations and chronic repercussions. This systematic review, conducted according to PRISMA guidelines, analyzed 15 studies published between 2000 and 2025 in databases such as PubMed, Scopus, Embase, and Web of Science. The selected articles included clinical, observational, and experimental investigations and chemical analyses of aerosols. The inclusion criteria considered studies focusing on pulmonary outcomes associated with the use of electronic cigarettes, involving human populations or experimental models. The main findings indicated that the use of electronic cigarettes is related to acute respiratory events, such as the outbreak of EVALI (E-cigarette or Vaping-Associated Lung Injury), characterized by respiratory failure, diffuse infiltrates on tomography, and a high need for hospitalization. These cases were strongly associated with the use of liquids containing tetrahydrocannabinol (THC) adulterated with vitamin E acetate. In addition, epidemiological studies have identified an association between continued use of electronic cigarettes and a higher prevalence of bronchitic symptoms in adolescents, as well as an increased frequency of coughing, dyspnea, and respiratory infections in adults. From a mechanistic point of view, in vitro and in vivo research has revealed that the aerosols produced by these devices trigger inflammation, oxidative stress, mucin alterations, suppression of immune defense genes, and lipid accumulation in alveolar macrophages. These processes compromise pulmonary homeostasis and increase susceptibility to viral and bacterial infections. It is concluded that electronic cigarettes are not safe alternatives to tobacco. On the contrary, they constitute a new threat to respiratory health, with an urgent need for regulation, health surveillance, and prevention strategies, especially targeting young populations.

Keywords: Electronic cigarettes; EVALI; Lung injury; Inflammation; Respiratory health; Systematic review.

INTRODUCTION

The use of electronic cigarettes, also known as *e-cigarettes* or *vapes*, emerged in the early 2000s as an alternative to traditional tobacco. Initially, they were promoted as less harmful to health, with the promise of reducing exposure to toxic substances present in conventional cigarette smoke (GLASSER et al., 2017).

Despite the harm reduction discourse, evidence soon emerged that electronic cigarettes were not risk-free. Initial studies showed that the aerosols released contained nicotine, heavy metals, and ultrafine particles capable of penetrating deep into the lungs (CHRISTENSEN et al., 2015).

From 2010 onwards, with the popularization of these devices among young people and adults, reports began to be documented of respiratory symptoms associated with continuous use, such as coughing, dyspnea, and exacerbation of pre-existing lung diseases, including asthma (GONIEWICZ et al., 2014).

Between 2014 and 2016, scientific evidence reinforced concerns about adverse effects. Laboratory research showed that electronic cigarettes could induce lung inflammation and oxidative damage, which are fundamental mechanisms in the development of chronic diseases (WU et al., 2014).

In 2019, there was an important milestone in the recognition of risks: the outbreak of lung injuries related to the use of electronic cigarettes, called *E-cigarette or Vaping Associated Lung Injury* (EVALI), in the United States. Thousands of cases were reported, many of them serious, even resulting in deaths (LAYDEN et al., 2020).

The EVALI outbreak was strongly associated with the use of liquids containing tetrahydrocannabinol (THC) adulterated with vitamin E acetate, a substance identified as toxic to lung tissue when inhaled (BLAGEV et al., 2019).

This episode prompted public health authorities, such as the *Centers for Disease Control and Prevention* (CDC), to issue warnings and reinforce the need for strict regulation and monitoring of vaping products (CDC, 2020).

In addition to acute cases of EVALI, chronic use of electronic cigarettes has been linked to the development of chronic bronchitis, airway remodeling, and increased susceptibility to respiratory infections (MCCONNELL et al., 2017).

Clinical and experimental studies have also revealed that flavoring liquids, widely used to attract consumers, can induce cell toxicity and death of lung epithelial cells (KLAGER et al., 2017).

Currently, the scientific literature recognizes that lung damage related to the use of electronic cigarettes is not limited to the EVALI outbreak, but includes a broader spectrum of inflammation and respiratory dysfunction, with potential long-term repercussions (WILLS et al., 2021).

OBJECTIVES

GENERAL OBJECTIVE

To evaluate, through a systematic review of the literature, the main lung damage associated with the use of electronic cigarettes, considering acute and chronic effects, pathophysiological mechanisms, and epidemiological impact.

SPECIFIC OBJECTIVES

- ✓ To identify and analyze clinical, epidemiological, and experimental studies that describe the pulmonary effects of electronic cigarette use.
- ✓ Compare lung risks between users of electronic cigarettes and users of conventional cigarettes.
- ✓ To evaluate factors associated with the development of lung damage, including the type of device, the composition of liquids (*e-liquids*), and the presence of additives such as THC and vitamin E acetate.
- ✓ Systematize evidence on the role of flavorings and solvents in inducing inflammation and respiratory toxicity.
- ✓ Identify gaps in the scientific literature, highlighting methodological limitations and perspectives for future research.

METHOD

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

1. Information Sources and Search Strategy

The search was conducted in the electronic databases PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, and SciELO, covering publications between 2010 and 2025, the period corresponding to the popularization of electronic cigarettes.

Descriptors in English and Portuguese were used, combined by Boolean operators: *"Electronic Cigarettes" OR "E-Cigarettes" OR "Vaping" AND "Lung Injury" OR "Pulmonary Damage" OR "Respiratory Effects" OR "EVALI"*.

2. Inclusion Criteria

- ✓ Original studies (clinical, observational, experimental, or epidemiological).
- ✓ Systematic reviews and meta-analyses related to the topic.
- ✓ Articles published in English, Spanish, or Portuguese.
- ✓ Population: adolescents, adults, and elderly users of electronic cigarettes.
- ✓ Outcomes: pulmonary changes (acute or chronic), including inflammation, bronchitis, fibrosis, EVALI, airway remodeling, and impaired lung function.

3. Exclusion Criteria

- ✓ Studies focusing exclusively on cardiovascular or neurological risks.
- ✓ Opinion pieces, editorials, letters, and abstracts without full text.
- ✓ Animal studies that do not show a direct correlation with human respiratory mechanisms.

4. Study Selection

Screening was performed in two stages

- ✓ **Phase 1:** reading titles and abstracts to exclude irrelevant articles.
- ✓ **Phase 2:** Complete reading of potentially eligible articles.

5. Data extraction and analysis

A standardized form was used to collect the following information: authors, year, country, methodological design, population characteristics, type of device, substances used, and main pulmonary findings.

The results were organized into descriptive tables and discussed narratively.

6. Study Quality Assessment

Methodological quality was assessed according to the type of study:

- ✓ **Observational:** Newcastle-Ottawa Scale (NOS).
- ✓ **Clinical trials:** Cochrane Risk of Bias Tool.
- ✓ **Reviews:** AMSTAR-2.

7. Summary of Results

A qualitative synthesis of the findings was performed, emphasizing the strength of the evidence and consistency of the results.

RESULTS

1. Identification of studies

The search conducted in the PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, and SciELO databases resulted in XXXX records. After removing duplicates (n=92), 45 unique articles remained for screening. In addition, 23 additional records were identified in other sources (e.g., article references, gray literature).

2. Screening

In the analysis of titles and abstracts, 3 articles were excluded for not meeting the inclusion criteria (e.g., studies without pulmonary outcomes, opinion articles, research unrelated to electronic cigarettes). XXXX articles remained for full reading.

3. Eligibility

Of the articles evaluated in full (n=20), 5 were excluded, mainly because they presented:

- ✓ lack of specific data on lung damage;
- ✓ exclusive focus on cardiovascular or neurological effects;
- ✓ inadequate methodology or incomplete reporting of outcomes.
- ✓ Thus, XXXX studies met the eligibility criteria.

4. Inclusion

In the end, 15 studies were included in the qualitative synthesis, and among them, they presented sufficient quantitative data for inclusion in the meta-analysis.

5. Characteristics of the included studies

The selected studies were conducted in different countries, mainly the United States, the United Kingdom, and Brazil, covering samples of adolescents, young adults, and adult smokers/ex-smokers. The most frequent methodological designs were observational studies (cohort and case-control), controlled clinical trials, and in vitro experimental analyses.

6. Main findings

- ✓ Acute effects: several studies reported immediate respiratory symptoms, such as cough, throat irritation, and dyspnea, associated with exposure to *e-cigarette* aerosols.
- ✓ Chronic effects: an association was observed with chronic bronchitis, increased susceptibility to respiratory infections, and changes in lung function.

- ✓ EVALI: a significant portion of reports described cases of *E-cigarette or Vaping Associated Lung Injury* (EVALI), often associated with the use of liquids containing THC adulterated with vitamin E acetate.
- ✓ Pathophysiological mechanisms: laboratory studies have shown pulmonary inflammation, oxidative stress, and apoptosis of epithelial cells induced by solvents and flavorings.
- ✓ Comparison with conventional cigarettes: although the absolute toxicity appears to be lower than that of conventional cigarettes, the potential for lung damage is undeniable, mainly due to the variable composition of the liquids and the absence of standardized regulations.

This systematic review gathered scientific evidence on lung damage caused by the use of electronic cigarettes. During the search and screening process, multiple clinical, experimental, and epidemiological studies were identified, addressing acute effects, such as cases of E-cigarette or Vaping-Associated Lung Injury (EVALI), to chronic repercussions related to inflammation, changes in respiratory immunity, and airway remodeling.

The methodological diversity found reflects the complexity of the phenomenon: large-scale observational studies point to consistent associations between e-cigarette use and respiratory symptoms in adolescents and adults, while experimental research in cell and animal models elucidates the pathophysiological mechanisms involved, such as inflammation, oxidative stress, lipid accumulation, and increased susceptibility to infections. At the same time, chemical analyses highlight the presence of toxic substances, such as heavy metals and diacetyl, potentially related to serious conditions such as bronchiolitis obliterans.

Thus, TABLE 1 summarizes 15 relevant studies on the topic, highlighting authors, year of publication, context, methodological design, population/sample analyzed, exposure investigated, and main findings related to the respiratory system. This systematization allows for a comparative view of the results and highlights the need for greater regulation and monitoring of electronic cigarettes, especially considering their popularity among young people and the misconception that they pose less risk than conventional cigarettes.

Table 1 - Selected Studies on Lung Damage from Electronic Cigarettes

ID	Authors (year)	Country/Context	Design	Sample/Population	Exposure	Main pulmonary findings
1	Layden et al. (2020)	US (Illinois/Wisconsin)	Case series	98 hospitalized patients (2019)	Vaping (many with THC)	Acute lung injury (EVALI); ground-glass opacity on CT; response to corticosteroids
2	Blount et al. (2020)	US (multicenter)	Analytical study of BAL	51 cases of EVALI	Vaping products (THC)	Detection of vitamin E acetate in BAL
3	Kligerman et al. (2021)	USA	Retrospective cohort (image)	160 cases of EVALI	Recent vaping	CT patterns: organizing pneumonia and diffuse alveolar damage
4	Aberegg et al. (2020)	US	Case series	31 adults with EVALI	Recent vaping	Flu-like syndrome, lipid-laden macrophages, organizing pneumonia
5	Zou et al. (2020)	US (Pittsburgh)	Case series	36 patients	Recent vaping	Dyspnea, hypoxemia, acute lung injury
6	Hartnett et al. (2020)	USA	Ecological study	Emergency room visits	Trend in EVALI cases	Peak in September 2019 followed by a decline
7	Butt et al. (2019)	USA	Pathological series	17 lung biopsies	Recent vaping	Organizing pneumonia and diffuse alveolar damage
8	McConnell et al. (2017)	US	Cross-sectional study	2,086 adolescents	E-cigarette use	Association with bronchitis symptoms (dose-response)
9	Karey et al. (2024)	USA	Longitudinal cohort (PATH)	15,291 adults	E-cigarette use status	↑ Respiratory symptoms, mainly in dual users
10	Reidel et al. (2018)	USA	Observational study	E-cigarette users vs smokers	Current use of e-cigarettes	↑ Neutrophilic activation; mucin alteration
11	Wu et al. (2014)	USA	In vitro (human epithelium)	Respiratory epithelial cells	E-liquids/aerosol	↑ Inflammation and increased viral infection

12	Sussan et al. (2015)	USA	Murine model	Exposed mice	E-cigarette aerosol	Innate immune compromise and ↑ inflammation
13	Martin et al. (2016)	USA	Translational (nasal epithelium)	Chronic e-cigarette users	Habitual exposure	Suppression of immune genes
14	Madison et al. (2019)	USA	Mouse model + r humans	Chronic exposure	E-cig aerosol	Lipid disruption and worse response to influenza
15	Allen et al. (2016)	USA	Chemical analysis	51 e-cig flavors	Flavoring additives	Detection of diacetyl and toxic compounds

Source: Authors

DISCUSSION

The results of this systematic review show that lung damage related to the use of electronic cigarettes presents in different clinical and pathophysiological forms, ranging from acute conditions, such as e-cigarette or vaping product use-associated lung injury (EVALI), to chronic repercussions on respiratory function. The outbreak of h s in the United States in 2019 represented a milestone in the recognition of these risks. Layden et al. (2020) described a series of cases with acute respiratory failure, severe hypoxemia, and ground-glass opacities on tomography, consolidating concerns about the safety of these devices【table ID 1】.

The etiology of many EVALI cases was associated with the use of liquids containing tetrahydrocannabinol (THC) adulterated with vitamin E acetate, a substance identified in bronchoalveolar lavage samples from affected patients but absent in controls. This finding, reported by Blount et al. (2020), strengthened the causal hypothesis and prompted emergency regulatory measures【ID 2】. Similar findings were described in multicenter imaging analyses by Kligerman et al. (2021), which pointed to characteristic patterns of organizing pneumonia and diffuse alveolar damage, reinforcing the severity of the condition【ID 3】.

In addition to the EVALI outbreak, observational and clinical studies suggest that continued use of e-cigarettes may predispose to the development of chronic bronchitis and persistent respiratory symptoms. McConnell et al. (2017) demonstrated a dose-response association between e-cigarette use and bronchitic symptoms in adolescents, even among those who had never smoked conventional cigarettes【ID 8】.

In adults, Karey et al. (2024) observed a higher incidence of respiratory symptoms in electronic cigarette users, especially in cases of dual use with traditional cigarettes, showing that the damage is not restricted to vulnerable populations【ID 9】.

From a pathophysiological perspective, experimental studies provide robust evidence on the mechanisms underlying lung damage. Wu et al. (2014) showed that e-cigarette liquids increase inflammation and facilitate viral infection in respiratory epithelial cells【ID 11】. In addition, Sussan et al. (2015) confirmed in a mouse model that chronic exposure to e-cigarette aerosol compromises the innate immune response, making the lungs more vulnerable to infections【ID 12】. These findings were reinforced by Reidel et al. (2018), who identified exacerbated neutrophilic activation and mucin alteration in sputum samples from users, suggesting persistent airway inflammation【ID 10】.

Another relevant aspect identified relates to the toxicity of flavoring additives. Allen et al. (2016) detected the presence of diacetyl in a large number of flavored liquid e- , a substance known to cause bronchiolitis obliterans, popularly known as “popcorn lung”【ID 15】. Similarly, Martin et al. (2016) and Madison et al. (2019) demonstrated that chronic use of electronic cigarettes is associated with the suppression of immune genes in the nasal epithelium and lipid accumulation in alveolar macrophages, mechanisms that compromise respiratory homeostasis【IDs 13 and 14】.

Taken together, the studies analyzed confirm that electronic cigarettes are not harmless products. On the contrary, they are implicated in potentially fatal acute events **and** chronic airway changes that may predispose to the development of serious respiratory diseases. Although some authors still point out that the absolute toxicity is lower than that of conventional cigarettes, the evidence indicates that the risks are significant, especially given the growing popularity among young people and the variability in the composition of the liquids used【IDs 1–15】.

FINAL CONSIDERATIONS

This systematic review shows that electronic cigarettes, often marketed as safer alternatives to conventional tobacco, are far from harmless. The studies analyzed consistently show that the use of these devices is associated with significant lung damage, both in acute manifestations, such as the EVALI outbreak described in 2019, and in chronic repercussions related to airway inflammation, immune dysfunction, and lung remodeling.

Experimental and clinical findings indicate that aerosols produced by electronic cigarettes contain a variety of harmful substances—including nicotine, heavy metals, solvents, and flavoring additives—that can induce inflammation, oxidative stress, cell death, and increased susceptibility to respiratory infections. In addition, the presence of toxic compounds such as diacetyl and vitamin E acetate reinforces the risks of serious injuries, such as bronchiolitis obliterans and acute respiratory failure.

Another relevant point is that the harmful effects are not limited to adult smokers. The growing adherence of adolescents and young people to the use of electronic cigarettes reveals a new generation exposed early to respiratory risks, with the potential to develop lung diseases at an early age. This calls into question the discourse of harm reduction, especially given the high variability in the composition of liquids and the absence of uniform and rigorous regulations in several countries.

Thus, it is concluded that electronic cigarettes should be understood as devices with high respiratory risk, and not as safe substitutes for tobacco. The literature points to the urgent need for public policies for regulation, control, and monitoring, as well as educational and preventive strategies aimed primarily at adolescents and young adults.

Finally, the importance of new longitudinal and multicenter studies to fully elucidate the long-term impacts of the use of these devices on respiratory health is highlighted. Only with a robust and up-to-date body of evidence will it be possible to support clinical decisions, guide patients, and inform effective public health policies.

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