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SYSTEMATIC REVIEW

Long-Term Pulmonary Outcomes Following E-Cigarette or Vaping Product Use-Associated Lung Injury (EVALI): A Systematic Review

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ABSTRACT

Background: Electronic cigarette or vaping product use-associated lung injury (EVALI) emerged as a major public health concern during the 2019 outbreak in the United States, causing over 2,800 hospitalizations and 68 deaths. While acute manifestations are well described, evidence regarding long-term outcomes remains limited. **Objective:** To systematically evaluate long-term pulmonary outcomes following EVALI, including pulmonary function, radiological findings, persistent symptoms, healthcare utilization, mortality, and quality of life. **Methods:** This systematic review followed PRISMA 2020 guidelines and was prospectively registered in PROSPERO. PubMed, ScienceDirect, and Google Scholar were searched from inception to 12 June 2026. Studies reporting post-discharge outcomes in patients diagnosed with EVALI according to CDC criteria were included. Risk of bias was assessed using the Newcastle-Ottawa Scale and JBI Critical Appraisal Checklists. Due to substantial heterogeneity, findings were synthesized narratively. **Results:** Of 1,045 records identified, 14 reports representing 13 unique cohorts were included. Nine studies with follow-up ≥3 months formed the primary synthesis. Persistent respiratory symptoms were reported in 45-48% of survivors at 12 months. Radiological abnormalities persisted in 33% of patients at one year, including focal scarring in 11%. Reduced diffusing capacity for carbon monoxide (DLCO) was consistently observed. Cognitive impairment, depression, and anxiety affected up to 46%, 59%, and 62% of survivors, respectively. Rehospitalization reached 24% at one year, while cumulative three-year mortality was 7.3%. **Conclusion:** A subset of EVALI survivors experiences incomplete recovery, highlighting the need for long-term multidisciplinary follow-up and standardized prospective studies.

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Highlights

1. Pulmonary recovery after EVALI may remain incomplete despite substantial clinical and radiological improvement;
2. Persistent respiratory, cognitive, and functional impairments can continue months to years after EVALI.

BACKGROUND

Electronic cigarette or vaping product use-associated lung injury (EVALI) emerged as a major public health concern during the 2019 outbreak in the United States (Krishnasamy et al., 2020). By the conclusion of national surveillance, the outbreak had resulted in more than 2,800 hospitalized cases and 68 confirmed deaths nationwide (Center for Disease Control and Prevention, 2020; Krishnasamy et al., 2020). The outbreak predominantly affected adolescents and young adults and highlighted the potential for severe pulmonary toxicity associated with vaping products (Layden et al., 2020). Although substantial progress has been made in understanding the epidemiology, clinical presentation, and acute management of EVALI, increasing attention has shifted toward the long-term health consequences experienced by survivors after hospital discharge (Rebuli et al., 2023).

The pathological basis of EVALI encompasses a spectrum of lung injury patterns, most commonly lipoid pneumonia, organizing pneumonia, diffuse alveolar damage, and acute fibrinous and organizing pneumonia that reflecting toxic rather than infectious pulmonary injury (Butt et al., 2019). Toxicological and epidemiological investigations identified vitamin E acetate, a lipophilic additive prevalent in tetrahydrocannabinol-containing vaping products, as the principal etiological agent implicated in the 2019 outbreak, with evidence suggesting disruption of pulmonary surfactant function and induction of lipoid pneumonia-like alveolar injury (Blount et al., 2020). Beyond direct cytotoxic effects, these injury patterns involve alveolar epithelial damage, impaired alveolar–capillary gas exchange, and activation of pro-inflammatory and pro-fibrotic pathways.(Butt et al., 2019; Park et al., 2026) The potential for subacute fibrotic remodeling, persistent bronchiolar inflammation, and structural disruption of the alveolar-capillary interface provides a plausible biological rationale for incomplete pulmonary recovery and residual impairment beyond the acute illness (Rebuli et al., 2023).

Recovery following acute EVALI is often considered favorable because many patients demonstrate rapid clinical improvement after vaping cessation and appropriate treatment. However, accumulating longitudinal evidence suggests that pulmonary recovery may be incomplete in a subset of patients. Persistent respiratory symptoms, including dyspnea and exercise intolerance, have been reported months after the initial illness (Triantafyllou et al., 2021). Abnormal pulmonary function, particularly reductions in diffusing capacity for carbon monoxide (DLCO), has also been observed during follow-up evaluations, suggesting residual impairment despite apparent clinical recovery (Ahmad et al., 2020; Wei et al., 2021). Furthermore, prospective cohort studies have demonstrated ongoing respiratory and functional limitations among some EVALI survivors, alongside cognitive or mood symptoms in several cohorts, even after radiographic improvement has occurred (Blagev et al., 2026, 2022; Tannert Niang et al., 2025).

Despite these findings, the overall trajectory of pulmonary recovery following EVALI remains incompletely understood. Interpretation of the existing literature is complicated by substantial heterogeneity in study design, sample size, severity of the initial illness, outcome definitions, and duration of follow-up, which limits direct comparison across studies. Published follow-up studies have reported varying degrees of pulmonary recovery, ranging from near-complete resolution of symptoms and radiographic abnormalities to persistent respiratory impairment, functional limitations, and ongoing healthcare utilization (Blagev et al., 2026, 2022; Tannert Niang et al., 2025; Triantafyllou et al., 2021). Importantly, available evidence spans follow-up periods ranging from several weeks after discharge to as long as three years, making it difficult to distinguish early recovery trajectories from true long-term

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pulmonary sequelae. Furthermore, existing studies have predominantly examined individual outcome domains, including pulmonary function, radiological findings, symptom persistence, healthcare utilization, mortality, and quality of life, in isolation, thereby hindering a comprehensive understanding of long-term recovery following EVALI (Rebuli et al., 2023). Consequently, clinicians lack consolidated evidence regarding which abnormalities are most likely to resolve, persist, or contribute to long-term morbidity after EVALI.

OBJECTIVE

This systematic review aims to evaluate long-term health outcomes following EVALI by synthesizing evidence across pulmonary function, radiological, symptom, healthcare utilization, and quality-of-life domains after the acute episode. By accounting for variations in follow-up duration and distinguishing early post-discharge recovery from longer-term sequelae, this review seeks to characterize recovery trajectories and residual pulmonary impairment among EVALI survivors.

MATERIAL AND METHODS

Study Design

This systematic review was conducted to evaluate long-term pulmonary and extrapulmonary outcomes following electronic cigarette or vaping product use-associated lung injury (EVALI). The review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261429551.

The review question and eligibility criteria were developed according to the Population, Exposure, Comparison, Outcome, and Study Design (PICOS) framework. The population consisted of patients diagnosed with confirmed or probable EVALI according to Centers for Disease Control and Prevention (CDC) criteria. The exposure of interest was a previous episode of EVALI followed by post-discharge clinical follow-up. Comparators included baseline assessments, non-EVALI vaping controls, or no comparator when applicable. Outcomes of interest included pulmonary function, radiological findings, persistent respiratory symptoms, healthcare utilization, mortality, and quality-of-life measures. Eligible study designs included prospective cohort studies, retrospective cohort studies, case-control studies, including matched case-control designs, case series, and case reports with longitudinal follow-up data.

Eligibility Criteria

Studies were eligible for inclusion if they: (1) enrolled patients with confirmed or probable EVALI as defined by CDC diagnostic criteria; (2) reported at least one post-discharge outcome pertaining to pulmonary function, radiological findings, respiratory symptoms, healthcare utilization, mortality, or quality of life; and (3) provided follow-up data obtained after the acute illness episode. No restriction was placed on follow-up duration as an eligibility criterion; instead, studies were stratified during evidence synthesis according to follow-up duration, with studies reporting follow-up of ≥3 months constituting the primary synthesis and studies reporting follow-up of <3 months presented as supplementary descriptive evidence characterizing early recovery trajectories.

Studies were excluded if they: (1) reported only acute-phase findings without any post-discharge follow-up assessment; (2) evaluated vaping-related pulmonary conditions other than EVALI; (3) combined EVALI cases with other diagnoses without providing separate outcome data for EVALI patients; or (4) were review articles, editorials, commentaries, conference abstracts without full-text availability, animal studies, or in vitro investigations. Eligible studies were limited to those published

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in the English language. No minimum sample size threshold was applied as an eligibility criterion. Case reports and case series of any size were eligible for inclusion provided that individual patient-level follow-up data were reported and patients fulfilled CDC diagnostic criteria for confirmed or probable EVALI.

Information Sources and Search Strategy

A systematic literature search was conducted across PubMed/MEDLINE, ScienceDirect, and Google Scholar from database inception to 12 June 2026. Search terms were developed using a combination of controlled vocabulary, including Medical Subject Headings (MeSH) where applicable, and free-text keywords to capture concepts related to EVALI, pulmonary function, radiological findings, respiratory sequelae, quality of life, healthcare utilization, and long-term outcomes. Additional studies were identified through manual screening of reference lists from all eligible full-text articles retrieved during the search. The complete search strategies used for each database are presented in **Table 1**.

Table 1. Database search strategies

Database	Search strategy
PubMed	("EVALI"[MeSH Terms] OR "electronic cigarette or vaping product use-associated lung injury"[MeSH Terms] OR "EVALI"[tiab] OR "vaping-associated lung injury"[tiab] OR "e-cigarette lung injury"[tiab]) AND ("pulmonary function"[tiab] OR "spirometry"[MeSH Terms] OR "spirometry"[tiab] OR "diffusing capacity"[MeSH Terms] OR "DLCO"[tiab] OR "radiology"[tiab] OR "radiography"[MeSH Terms] OR "computed tomography"[tiab] OR "follow-up"[tiab] OR "long-term outcome"[tiab] OR "quality of life"[MeSH Terms] OR "mortality"[MeSH Terms] OR "readmission"[tiab] OR "hospitalization"[MeSH Terms])
ScienceDirect	(EVALI OR "vaping-associated lung injury") AND ("lung function" OR spirometry OR DLCO OR follow-up)
Google Scholar	(EVALI OR "vaping-associated lung injury") AND ("follow-up study" OR longitudinal) AND (spirometry OR DLCO OR "pulmonary function test")

Study Selection

All records retrieved from electronic database searches were imported into reference management software, where duplicate records were identified and removed prior to screening. Two reviewers independently screened titles and abstracts of all retrieved records against the predefined eligibility criteria. Potentially eligible studies subsequently underwent independent full-text assessment by both reviewers. Disagreements at any stage of the selection process were resolved through discussion and consensus. The complete study selection process, including the number of records identified, screened, excluded with reasons, and included, was documented and reported using a PRISMA 2020 flow diagram.

To prevent double-counting of participants, records originating from the same patient registry or cohort were identified as companion reports. Such reports were evaluated separately at the publication level to preserve individual study characteristics, but were treated as a single patient cohort during evidence synthesis to avoid overrepresentation of any one patient population.

Data Extraction

Structured data extraction was performed independently by two reviewers using a standardized, pre-piloted extraction form. Extracted variables included: publication characteristics (first author, year, journal, country); study design; sample size; participant demographics (age, sex); CDC case classification; vaping product type (tetrahydrocannabinol-containing, nicotine-containing, or unspecified); duration and timing of follow-up; pulmonary function outcomes (FEV_1, FVC, FEV_1/FVC ratio, DLCO, and other parameters); radiological findings; respiratory symptom persistence; healthcare utilization outcomes; mortality; quality-of-life measures; and principal study conclusions. Any discrepancies in extracted data between reviewers were resolved through discussion and consensus.

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Risk of Bias Assessment

Methodological quality was assessed independently by two reviewers for each included study, with the assessment tool selected according to study design. Cohort studies and matched case-control studies were evaluated using the Newcastle–Ottawa Scale (NOS), which appraises selection, comparability, and outcome domains. Case series were appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series, and individual case reports were assessed using the JBI Critical Appraisal Checklist for Case Reports. Disagreements in quality assessment were resolved through discussion and consensus. No study was excluded from the review solely on the basis of methodological quality; however, study quality was considered in the interpretation of findings and is reported alongside outcome data to contextualize the strength of evidence.

Data Analysis

A quantitative meta-analysis was not performed owing to substantial clinical and methodological heterogeneity among the included studies. Heterogeneity was present across multiple dimensions, including study design, sample size, severity of the initial EVALI episode, outcome definitions and measurement instruments, follow-up duration and timing, and reporting methods, which precluded meaningful statistical pooling of results.

Evidence was therefore synthesized narratively in accordance. Studies reporting follow-up durations of ≥3 months constituted the primary synthesis on the basis that they provide more representative evidence of long-term pulmonary sequelae, whereas studies with follow-up durations of <3 months were retained as supplementary evidence describing early post-discharge recovery trajectories.

Outcomes were synthesized across six pre-specified domains: (1) pulmonary function, (2) radiological findings, (3) persistent respiratory symptoms, (4) healthcare utilization, (5) mortality, and (6) quality of life. Findings across studies were compared to identify recurring patterns of recovery, persistent impairment, and residual sequelae following EVALI. Given the predominantly observational and descriptive nature of the included evidence and the absence of meta-analytic pooling, a formal assessment of the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework was not performed; the overall quality of evidence across domains is instead discussed narratively in the relevant sections.

RESULTS

Study Selection

The database search identified 1,045 records, including 111 records from PubMed, 473 from ScienceDirect, and 461 from Google Scholar. After removal of 178 duplicate records, 867 unique citations underwent title and abstract screening. A total of 850 records were excluded because they were unrelated to EVALI, did not report post-discharge outcomes, represented non-human studies, review articles, editorials, conference abstracts, or otherwise failed to meet the predefined eligibility criteria. Seventeen full-text articles were assessed for eligibility. Three reports were excluded following full-text review. One study was excluded because the study population did not fulfill the Centers for Disease Control and Prevention (CDC) case definition for EVALI and instead described chronic small-airway fibrosis/constrictive bronchiolitis as a distinct clinical entity. One report was excluded because the case series not meet the minimum eligibility threshold for inclusion, with follow-up limited to the subacute period. Another study was excluded because pulmonary function data were available only during hospitalization and no post-discharge follow-up outcomes were reported.

Fourteen reports fulfilled all eligibility criteria and were included in the qualitative synthesis. Among these, two reports originated from the same EVALI registry cohort comprising 41 unique patients but

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evaluated different follow-up time points (12 months and 36 months). These companion reports were retained separately to preserve outcome-specific information but were treated as a single cohort during evidence synthesis to avoid double counting of participants. Consequently, the final review included 14 reports representing 13 unique study cohorts. The study selection process is summarized in **Figure 1**.

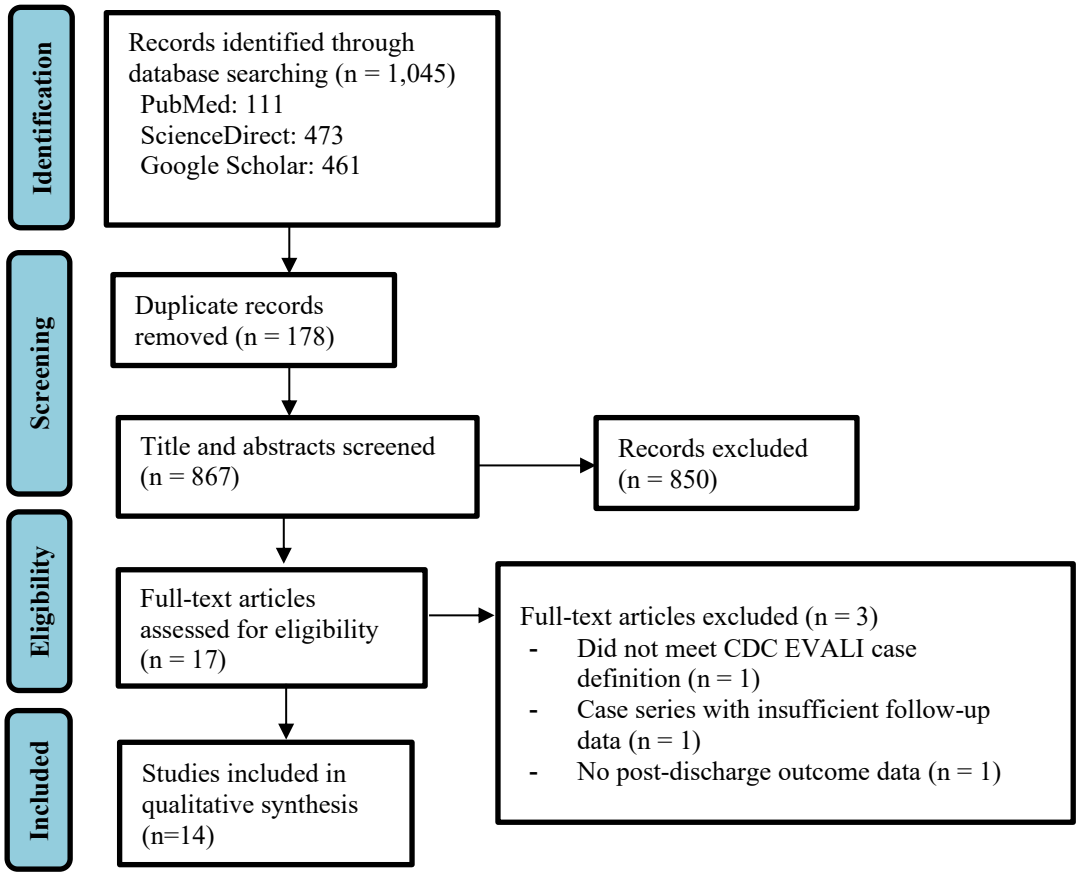


Figure 1. Diagram flow of literature search strategy for this systematic review

Characteristics of Included Studies

The included evidence consisted of prospective cohort studies, retrospective cohort studies, a matched case-control study, a case series, and four longitudinal case reports. Study sample sizes ranged from a single patient to 73 participants. Most studies enrolled adolescents and young adults, reflecting the demographic profile of the original EVALI outbreak. Follow-up duration varied substantially, ranging from approximately 4.5 weeks to 36 months after hospital discharge.

To facilitate interpretation of recovery trajectories, studies were stratified according to follow-up duration. Nine studies reported follow-up durations of at least three months and formed the primary synthesis evaluating long-term outcomes following EVALI. These studies included prospective and retrospective cohorts, a matched case-control study, and four longitudinal case reports, with follow-up periods ranging from 3 months to 3 years. Five additional studies reported shorter follow-up durations ranging from approximately 4.5 to 8 weeks and were retained as supplementary evidence describing early post-discharge recovery.

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Outcome assessment varied across studies. Pulmonary function outcomes included spirometry parameters (FEV1, FVC, FEV1/FVC ratio), diffusing capacity for carbon monoxide (DLCO), oscillometry, lung clearance index, and advanced imaging modalities such as hyperpolarized xenon-129 magnetic resonance imaging. Other frequently reported outcomes included radiological abnormalities, persistent respiratory symptoms, healthcare utilization, rehospitalization, mortality, cognitive symptoms, psychological sequelae, and continued vaping behavior. Detailed study characteristics are presented in **Table 2.**

Table 2. Characteristics of Included Studies

Study	Design	n	Age	Population	Follow-up	Outcomes Measured
A. Studies with Follow-up ≥3 Months						
Blagev et al., 2022(Blagev et al., 2022)	Prospective cohort	73	Mean 31 ± 11 years	EVALI survivors	12 months	Respiratory limitation (patient-reported), cognitive function, depression, anxiety, PTSD, vaping behavior
Triantafyllou et al., 2021(Triantafyllou et al., 2021)	Retrospective cohort	41	Median 21 years	EVALI survivors	12 months	Persistent symptoms, chest radiography, rehospitalization, mortality
Zhang et al., 2024(Zhang et al., 2024)	Retrospective cohort	41	Median 21 years	EVALI survivors	36 months	Mortality, emergency department visits, rehospitalization, radiological abnormalities, vaping behavior
Tannert Niang et al., 2025(Tannert Niang et al., 2025)	Prospective cohort	53	Not reported	NYC EVALI survivors	12–24 months	Persistent symptoms, activity limitations, healthcare utilization, vaping behavior
Eddy et al., 2020(Eddy et al., 2020)	Case report	1	18 years	Severe EVALI survivor (ICU)	8 months	Spirometry, oscillometry, lung clearance index, Xe129 MRI, chest CT
Wu et al., 2021(Wu et al., 2021)	Case report	1	56 years	Patient with EVALI	>6 months	FVC, DLCO, serial HRCT, respiratory symptoms
Nielsen et al., 2025(Ritzau Ishøj Nielsen et al., 2025)	Case report	1	19 years	Severe EVALI survivor (ICU, ECMO)	1.5 years	Serial spirometry (FEV1, FVC, FEV1/FVC), TLC, DLCO, chest HRCT
Blagev et al., 2026(Blagev et al., 2026)	Matched case-control	54	Young adults	EVALI survivors vs. 131 vape users without EVALI (matched controls)	≥12 months	Dyspnea, cognitive impairment, limitations in activities of daily living
Abdallah et al., 2023(Abdallah et al., 2023)	Retrospective cohort	41	Adolescents	Adolescents with EVALI	>3 months	FEV1, FVC, respiratory symptoms, oxygen requirement, corticosteroid response
B. Studies with Follow-up <3 Months						
Aberegg et al., 2020(Aberegg et al., 2020)	Case series	31	Median 24 years	Adults with EVALI	4.5–8 weeks	Residual symptoms, radiological opacities, spirometry
Wei et al., 2021(Wei et al., 2021)	Retrospective cohort	23	Adults	EVALI survivors	~1 month	DLCO, FEV1, FVC
Lee et al., 2021(Lee et al., 2021)	Retrospective cohort	8	Adolescents	Adolescents with EVALI	46.5 days	Serial spirometry, radiology, clinical symptoms

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Study	Design	n	Age	Population	Follow-up	Outcomes Measured
Carroll et al., 2020(Carroll et al., 2020)	Retrospective cohort	15 (11 follow-up)	Mean 17.1 years	Adolescents with EVALI	4.5 weeks	Spirometry, diffusion capacity, respiratory symptoms
Ahmad et al., 2020(Ahmad et al., 2020)	Case series	2	23 & 46 years	EVALI survivors	~2 month	DLCO, FEV1, FVC, TLC, serial chest CT

Risk of Bias Assessment

Methodological quality varied according to study design. Cohort and case-control studies generally demonstrated moderate methodological quality based on Newcastle–Ottawa Scale assessment. The most common limitations involved incomplete follow-up reporting, absence of non-exposed comparison groups, and potential selection bias. Case reports and case series fulfilled most Joanna Briggs Institute (JBI) appraisal criteria but remained inherently limited by small sample sizes and restricted generalizability. No study was excluded on the basis of methodological quality assessment.

Long-Term Pulmonary Outcomes Following EVALI

To facilitate interpretation of recovery trajectories, studies were stratified according to follow-up duration. Nine studies reporting follow-up periods ranging from 3 months to 3 years formed the primary synthesis of long-term outcomes, whereas five studies with shorter follow-up durations (approximately 4.5–8 weeks) were retained as supplementary evidence describing early recovery trajectories. A summary of long-term outcome findings is presented in **Table 3**.

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Table 3. Synthesis of Long-Term Outcomes Following EVALI

Study	Respiratory Outcomes	Radiological Outcomes	Rehospitalization / Mortality	Other Outcomes
Blagev et al., 2022(Blagev et al., 2022)	Respiratory limitation reported by 48% of patients (patient-reported)	–	–	Cognitive impairment 39%; depression/anxiety 59%; PTSD 62%; only 38% discontinued vaping
Triantafyllou et al., 2021(Triantafyllou et al., 2021)	Persistent symptoms in 45% of patients	Incomplete radiographic resolution in 6/18 patients (33%); focal scarring in 2 (11%)	Readmission 24%; mortality 4.9% within 1 year	Continued vaping use was documented
Zhang et al., 2024(Zhang et al., 2024)	–	Most radiological abnormalities improved; residual scarring remained in some cases	3-year mortality 7.3%; emergency department utilization increased to 38%	Continued vaping use was documented
Tannert Niang et al., 2025(Tannert Niang et al., 2025)	Respiratory symptoms were the most frequently reported symptom domain at interview waves 1–2	–	Not directly assessed; 16/33 (49%) reported a new diagnosis requiring care	15–29% of respondents reported vaping at each interview wave
Eddy et al., 2020(Eddy et al., 2020)	Persistent airflow obstruction and abnormal ventilation up to 8 months	CT findings improved but did not completely normalize	–	Xe129 MRI demonstrated persistent ventilation defects
Wu et al., 2021(Wu et al., 2021)	FVC improved; DLCO recovery was prolonged	Minimal residual fibrosis on HRCT	–	Symptoms improved following treatment
Nielsen et al., 2025(Ritzau Ishøj Nielsen et al., 2025)	Persistent airflow obstruction; FEV1 34–57% predicted across serial PFTs; DLCO 78% at 4.5 months	Radiological improvement on HRCT over time	–	Patient resumed vaping despite strong advisement against it; required ECMO support during acute phase
Blagev et al., 2026(Blagev et al., 2026)	Dyspnea was more frequent than in vaping controls	–	–	Cognitive impairment (46% vs 23%) and activity limitations (17% vs 2%) were more common than in controls
Abdallah et al., 2023(Abdallah et al., 2023)	Improvement in FEV1 and FVC during follow-up	–	Reduced oxygen requirement	Favorable response to corticosteroid therapy
Aberegg et al., 2020(Aberegg et al., 2020)	Abnormal spirometry in 44% of patients who underwent follow-up PFT	Residual opacities in 40% of patients	–	Residual symptoms remained common
Wei et al., 2021(Wei et al., 2021)	DLCO remained reduced in most patients during early follow-up	–	–	Suggested persistent alveolar injury
Lee et al., 2021(Lee et al., 2021)	Normalization of spirometry in all patients at follow-up	Radiological improvement in all patients	–	Resolution of clinical symptoms
Carroll et al., 2020(Carroll et al., 2020)	Pulmonary function abnormalities in 7/11 patients (63.6%) during early follow-up	–	–	Symptoms improved more rapidly than pulmonary function

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Study	Respiratory Outcomes	Radiological Outcomes	Rehospitalization / Mortality	Other Outcomes
Ahmad et al., 2020(Ahmad et al., 2020)	Reduced DLCO (63% and 61% of predicted) in both patients; spirometry (FEV1, FVC, TLC) within normal limits	Complete resolution of ground-glass opacities at 2 months	–	DLCO reduction persisted despite full radiological resolution

Pulmonary Function Outcomes

Evidence from studies with follow-up durations of at least three months suggested that pulmonary recovery following EVALI is frequently incomplete despite substantial clinical improvement. Abdallah et al. reported improvement in spirometric indices, including FEV1 and FVC, among adolescents during follow-up, accompanied by reduced oxygen requirements and favorable responses to corticosteroid therapy. In contrast, longitudinal case-based investigations demonstrated persistent physiological abnormalities beyond apparent clinical recovery. Eddy et al. observed persistent airflow obstruction, abnormal ventilation distribution, and MRI ventilation defects up to eight months after severe EVALI, despite improvement in conventional imaging. Similarly, Wu et al. reported gradual improvement in FVC but delayed recovery of DLCO, indicating prolonged impairment of gas-transfer capacity. Nielsen et al. similarly documented persistently reduced lung function in a 19-year-old male who required ECMO support during the acute illness, with FEV1 ranging from 34% to 57% of predicted across serial pulmonary function tests extending to 1.5 years post-discharge, and a DLCO of 78% of predicted recorded at 4.5 months, despite progressive radiological improvement over the same period.

Findings from studies with shorter follow-up durations supported the presence of residual pulmonary dysfunction during early recovery. Wei et al. found persistent reductions in DLCO among most patients approximately one month after discharge, while Carroll et al. reported abnormal pulmonary function in 63.6% of adolescents during early follow-up. Aberegg et al. similarly documented abnormal spirometry findings in nearly half of patients who underwent pulmonary function testing. Ahmad et al. documented reduced DLCO in both patients assessed approximately two months after discharge, at 63% and 61% of predicted, respectively, with all other spirometric parameters, including FEV1, FVC, TLC, and FEV1/FVC ratio, remaining within normal limits. Together, these findings suggest that impairment in gas exchange and pulmonary physiology may persist beyond the acute illness phase and recover more slowly than clinical symptoms.

Radiological Outcomes

Radiological abnormalities generally improved over time but did not universally resolve. Triantafyllou et al. reported residual radiographic abnormalities in 6 of 18 patients (33%) with available follow-up imaging one year after diagnosis, including focal pulmonary scarring in two patients (11%). Long-term follow-up data from Zhang et al. demonstrated continued radiological improvement over three years, although residual scarring remained detectable in some individuals. Consistent findings were observed in individual longitudinal reports, with Eddy et al. documenting substantial radiographic improvement despite persistent physiological impairment, Wu et al. reporting minimal residual fibrotic changes on serial high-resolution computed tomography, and Nielsen et al. demonstrating progressive improvement on serial chest HRCT alongside persistently reduced spirometric values over 1.5 years of follow-up.

Studies evaluating earlier recovery periods also demonstrated incomplete radiological resolution. Aberegg et al. observed persistent opacities in approximately 40% of patients during early follow-up, whereas Lee et al. reported complete radiological normalization among adolescents. Ahmad et al. observed complete resolution of ground-glass opacities on follow-up computed tomography at approximately two months in both patients, despite persistent reductions in DLCO, further illustrating the dissociation between structural and functional recovery following EVALI. These findings collectively suggest that structural recovery generally parallels clinical improvement but may remain

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incomplete in a subset of patients, and that radiological normalization does not reliably indicate full restoration of pulmonary physiology.

Persistent Respiratory Symptoms

Persistent respiratory symptoms remained common among EVALI survivors. Triantafyllou et al. reported ongoing symptoms in approximately 45% of patients at one year, while Blagev et al. found patient-reported respiratory limitations in 48% of participants during prospective follow-up. Tannert Niang et al. similarly documented persistent respiratory symptoms and activity limitations extending up to 24 months after diagnosis. At the individual patient level, Nielsen et al. reported that the patient continued to experience functional limitations and reduced exercise tolerance across serial follow-up assessments extending to 1.5 years post-discharge, despite progressive radiological improvement, further illustrating that symptom burden may persist well beyond the acute illness phase in patients who sustained severe EVALI requiring intensive care and extracorporeal support.

Quality of Life Outcomes

Quality of life was prespecified as a synthesis domain in the PICOS framework; however, evidence addressing this domain directly was sparse and originated from a single registry cohort. Beyond respiratory manifestations, several studies identified important functional and neuropsychological sequelae. Blagev et al. reported cognitive impairment, depression, anxiety, and post-traumatic stress symptoms among substantial proportions of survivors (39%, 59%, and 62% of patients, respectively). Long-term matched comparison with vaping controls demonstrated that EVALI survivors experienced more frequent dyspnea, cognitive impairment, and limitations in activities of daily living than individuals who used vaping products but had never developed EVALI (cognitive impairment 46% vs 23%; activity limitations 17% vs 2%). These findings suggest that the long-term consequences of EVALI extend beyond pulmonary recovery alone.

Importantly, none of the other included cohorts administered a validated health-related quality-of-life instrument (e.g., the 36-Item Short Form Health Survey, EuroQol-5D, or St. George's Respiratory Questionnaire). The quality-of-life domain specified a priori in the PICOS framework was therefore addressed only indirectly, through symptom- and function-related items reported by a single cohort, representing a notable evidence gap and a priority for future EVALI follow-up research.

Healthcare Utilization and Mortality

Several studies reported continued healthcare utilization following hospital discharge. Triantafyllou et al. observed a rehospitalization rate of 24% and a one-year mortality rate of 4.9%. In the same patient registry followed for a longer duration, Zhang et al. reported a cumulative three-year mortality rate of 7.3% and emergency department utilization in 38% of patients. Although rehospitalization and mortality were not directly assessed in their interview-based design, Tannert Niang et al. found that 16 of 33 respondents (49%) reported a newly diagnosed health condition during follow-up, suggesting continued healthcare contact beyond the acute illness.
Collectively, these findings indicate that although many patients experience substantial clinical improvement after the acute episode, EVALI may be associated with persistent healthcare needs extending well beyond hospital discharge.

Continued Vaping Behavior

Several studies reported ongoing use of vaping products after recovery. Triantafyllou et al. and Zhang et al. documented continued vaping among survivors during follow-up, while Tannert Niang et al. reported that 15–29% of respondents continued vaping at each interview wave, and Blagev et al. reported that only 38% of participants had completely discontinued vaping. Nielsen et al. similarly noted that the patient resumed both cigarette and e-cigarette use following discharge despite strong

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medical advisement against doing so, and continued to do so at the time of reporting. These findings highlight the persistence of vaping behavior despite prior severe vaping-associated lung injury and may represent an important contributor to long-term morbidity.

DISCUSSION

This systematic review synthesized available evidence regarding long-term pulmonary outcomes following electronic cigarette or vaping product use-associated lung injury (EVALI). Across 14 reports representing 13 unique study cohorts, the findings suggest that although most patients experience substantial clinical and radiological improvement after the acute episode, recovery is frequently incomplete. Persistent abnormalities were observed across multiple domains, including pulmonary function, respiratory symptoms, healthcare utilization, cognitive health, and quality of life. Importantly, residual impairment was documented not only during the early recovery period but also up to three years after diagnosis, indicating that EVALI may have clinically relevant long-term consequences beyond the initial hospitalization (Ahmad et al., 2020; Butt et al., 2019; Triantafyllou et al., 2021; Wei et al., 2021; Zhang et al., 2024).

One of the most consistent findings across the included studies was the persistence of pulmonary function abnormalities despite apparent clinical recovery. Several cohorts demonstrated improvements in spirometric indices over time; however, abnormalities in gas transfer capacity, particularly reduced DLCO, frequently persisted during follow-up.(Blount et al., 2020; Carroll et al., 2020; Park et al., 2026; Wu et al., 2021) This pattern was evident across study designs and follow-up durations, from the early post-discharge reductions documented by Ahmad et al. in two EVALI survivors at two months, to the serial impairments extending to 1.5 years reported by Nielsen et al. in a patient who had required ECMO support during the acute illness (Ahmad et al., 2020; Ritzau Ishøj Nielsen et al., 2025). The selective and persistent impairment of DLCO in the setting of relatively preserved spirometric volumes warrants mechanistic consideration. DLCO is uniquely sensitive to injury at the alveolar-capillary membrane, reflecting the combined integrity of the alveolar surface area, the thickness and composition of the interstitial barrier, and the pulmonary capillary blood volume available for gas exchange. Vaping-associated injury, through vitamin E acetate-mediated disruption of pulmonary surfactant, lipoid pneumonia-like alveolar filling, and activation of pro-inflammatory and pro-fibrotic pathways, may produce microscopic injury to the alveolar-capillary interface that persists beyond the resolution of macroscopic radiological changes (Butt et al., 2019; Park et al., 2026). This is mechanistically distinct from obstructive or restrictive spirometric impairment, which reflects larger-airway or parenchymal volume changes visible on conventional imaging. As a result, DLCO may remain reduced even when chest CT has normalized and spirometric volumes have recovered to within normal limits, as observed consistently across the included evidence. These findings suggest that restoration of pulmonary physiology may lag behind symptomatic recovery and may reflect subclinical residual alveolar or microvascular injury not captured by routine clinical assessment. Similar observations have been reported in survivors of acute lung injury and acute respiratory distress syndrome (ARDS), where long-term impairment in diffusion capacity often persists despite normalization of spirometric parameters (Burnham et al., 2014; Herridge et al., 2011). The prolonged recovery of DLCO observed in EVALI survivors therefore supports the hypothesis that vaping-related lung injury may produce lasting abnormalities at the alveolar–capillary interface, with important implications for follow-up monitoring strategies.

The relationship between radiological and physiological recovery also warrants consideration. Most included studies reported progressive resolution of radiographic abnormalities over time, with substantial improvement in chest radiographs and computed tomography findings (Butt et al., 2019; Lee et al., 2021; Zhang et al., 2024). However, several studies documented persistent physiological abnormalities despite near-complete radiological recovery (Eddy et al., 2020; Wu et al., 2021). This discordance was particularly evident in the case series by Ahmad et al., in which DLCO remained reduced in both patients despite complete radiological normalization of ground-glass opacities at two

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months post-discharge, as well as in the longitudinal report by Nielsen et al., who demonstrated persistent spirometric impairment alongside progressive radiological improvement over 1.5 years (Ahmad et al., 2020; Ritzau Ishøj Nielsen et al., 2025). This discordance suggests that conventional imaging may underestimate residual pulmonary dysfunction following EVALI. Notably, Eddy et al. demonstrated persistent ventilation defects using hyperpolarized xenon-129 magnetic resonance imaging despite substantial radiographic improvement, highlighting the potential value of advanced functional imaging modalities in evaluating long-term recovery (Eddy et al., 2020). Similar discrepancies between structural and functional recovery have been described in other inflammatory lung disorders, emphasizing the need for comprehensive follow-up assessment beyond imaging alone (Cho et al., 2022).

Beyond pulmonary physiology, this review identified substantial evidence of persistent symptom burden and reduced quality of life among EVALI survivors. Respiratory symptoms, including dyspnea and exercise intolerance, remained common across multiple cohorts, while several studies reported ongoing cognitive impairment, depression, anxiety, and post-traumatic stress symptoms (Ahmad et al., 2020; Triantafyllou et al., 2021; Wei et al., 2021). These findings are particularly noteworthy because EVALI predominantly affects adolescents and young adults who generally have few chronic comorbidities (Center for Disease Control and Prevention, 2020; Krishnasamy et al., 2020). The persistence of neurocognitive and psychological symptoms may reflect a combination of severe acute illness, intensive care exposure, and the broader psychosocial consequences associated with vaping-related disease. Similar multidimensional sequelae have been reported among survivors of critical illness and ARDS, further supporting the need for multidisciplinary follow-up strategies in this population (Herridge et al., 2011; Needham et al., 2012).

Long-term healthcare utilization remained substantial among a subset of survivors. Rehospitalization, emergency department visits, and mortality continued to be reported months to years after the initial diagnosis (Butt et al., 2019; Zhang et al., 2024). Although mortality rates remained relatively low, the persistence of healthcare utilization suggests that complete recovery cannot be assumed following hospital discharge. Continued vaping behavior was also frequently reported during follow-up, with several studies documenting ongoing use of vaping products despite a prior diagnosis of EVAL (Ahmad et al., 2020; Butt et al., 2019; Triantafyllou et al., 2021; Zhang et al., 2024). This finding may have important implications for recurrent respiratory injury and could potentially contribute to persistent symptoms or delayed recovery.

The findings of this review have several specific clinical implications for the follow-up management of EVALI survivors. First, pulmonary function testing with particular emphasis on DLCO measurement should be performed routinely in all EVALI survivors at a minimum of two to three months after hospital discharge, and repeated at 12 months, regardless of symptomatic or radiological recovery. Given the consistent dissociation between structural and functional recovery observed across included studies, radiological normalization alone is insufficient to confirm complete pulmonary recovery. Second, persistent symptom burden, including dyspnea, exercise intolerance, and functional limitations, should be formally assessed at each follow-up visit using standardized instruments rather than relying on open-ended clinical inquiry, as patient-reported limitations may not be volunteered spontaneously. Third, the substantial prevalence of cognitive impairment, depression, anxiety, and post-traumatic stress symptoms identified in prospective cohort data indicates that neuropsychological screening should be integrated into routine post-EVALI follow-up, particularly for patients who required ICU admission or prolonged mechanical ventilation. Fourth, vaping cessation counseling and behavioral support should be initiated at the time of diagnosis and reinforced at every subsequent clinical contact, given the high rates of continued vaping behavior documented across multiple cohorts despite severe prior lung injury. Fifth, patients with evidence of persistent DLCO impairment beyond 12 months, residual radiological abnormalities such as focal scarring, or ongoing respiratory symptoms should be referred for specialist pulmonary assessment and consideration of pulmonary rehabilitation. Together, these recommendations support a structured, multidisciplinary follow-up approach for EVALI survivors that extends substantially beyond the period of acute clinical stabilization.

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Strengths and Limitations

This review has several strengths. To our knowledge, it is the first systematic review specifically focused on long-term pulmonary outcomes following EVALI and integrates evidence across multiple outcome domains, including pulmonary function, radiological findings, respiratory symptoms, healthcare utilization, mortality, and quality of life. The review also distinguished long-term outcomes (≥3 months) from early post-discharge recovery (<3 months), allowing a clearer interpretation of recovery trajectories and residual sequelae. Furthermore, companion reports derived from the same patient registry were carefully identified and synthesized at the cohort level to avoid double counting of participants. The inclusion of Nielsen et al. additionally extends the geographic scope of this review beyond the United States, providing evidence of EVALI and its long-term pulmonary sequelae in a European clinical context.

Several limitations should be acknowledged. First, the available evidence base was constrained by small sample sizes across most included studies and a predominance of lower-hierarchy observational designs, including case reports and case series. Although their inclusion was a deliberate methodological decision justified by the scarcity of higher-level evidence on long-term EVALI outcomes, case reports in the medical literature tend to disproportionately represent atypical or clinically severe presentations rather than the broader spectrum of recovery, which may have introduced publication bias and skewed findings toward more persistent and severe outcomes. Second, substantial heterogeneity existed across studies with respect to follow-up duration, outcome definitions, pulmonary function measurements, and reporting methods, precluding quantitative meta-analysis. Third, several studies lacked baseline pulmonary function data prior to EVALI, making it difficult to determine the extent to which observed abnormalities were attributable to EVALI itself versus pre-existing respiratory conditions or vaping-related effects. Fourth, ongoing vaping behavior during follow-up was inconsistently reported and may have influenced long-term outcomes. Fifth, the search strategy did not include Embase, a database that provides particularly comprehensive indexing of clinical case reports and European literature not fully captured by PubMed or ScienceDirect. Consequently, there is a risk of incomplete evidence retrieval, and additional studies with long-term follow-up data may exist but were not identified by the current search. Finally, because EVALI emerged relatively recently, long-term evidence beyond three years remains limited, and the true lifetime consequences of vaping-associated lung injury remain uncertain.

CONCLUSION

This systematic review of 14 reports shows that most EVALI survivors improve clinically and radiologically, but recovery remains incomplete in a subset, with persistently reduced gas-transfer capacity (DLCO), respiratory symptoms in 45–48% of survivors at 12 months, neuropsychological sequelae, and continued rehospitalization and mortality up to three years. Long-term multidisciplinary follow-up that includes DLCO assessment is therefore warranted, and larger prospective studies with standardized outcome measures are needed.

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Conflict of Interest

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Author Contribution

I Nyoman Dwi Suputra Diarsa conceived the study, developed the review protocol, conducted the literature search, performed study screening, data extraction, quality assessment, evidence synthesis, and drafted the manuscript. Desak Putu Candraningtyas contributed to study screening, data extraction, methodological quality assessment, interpretation of findings, and critical revision of the manuscript. Both authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

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