Respiratory Health Consequences Of Vaping In Healthy Adults: A Systematic Review

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ABSTRACT

Background: Electronic cigarettes are widely promoted as a reduced-harm alternative to combustible tobacco, yet whether their aerosol is respiratorily safe for healthy adults particularly those who have never smoked—remains contested. Existing syntheses largely pool clinically heterogeneous populations, obscuring the effect attributable to vaping itself. This review synthesises the respiratory health consequences of e-cigarette use specifically in healthy adults.

Methods: Following PRISMA 2020 guidelines, PubMed/MEDLINE was searched for original human studies published between January 2021 and July 2026 reporting respiratory symptoms, lung function, respiratory disease, or airway biomarkers in adults (≥18 years) without significant pre-existing respiratory disease. Screening, extraction, and risk-of-bias appraisal (Newcastle–Ottawa Scale and Joanna Briggs Institute checklists) were conducted by a single reviewer. Findings were synthesised narratively across four outcome domains.

Results: Thirty-four studies were included. Respiratory symptoms were the most consistently reported outcome; large, well-adjusted cohorts found elevated symptom risk among e-cigarette users that persisted in never-smokers (adjusted odds ratio for wheezing up to 1.51, 95% CI 1.06–2.14; adjusted asthma-symptom score ratio up to 1.44 in never-smokers). Conventional spirometry was frequently preserved, whereas more sensitive measures lung clearance index, cardiopulmonary exercise testing, exhaled nitric oxide, and exhaled lipid biomarkers detected subclinical peripheral-airway and inflammatory abnormalities in young, otherwise healthy vapers. Across domains, risk was greatest among dual users, while effects of exclusive e-cigarette use were smaller but frequently non-null. Studies reporting minimal effects were disproportionately affected by conflicts of interest.

Conclusions: In healthy adults, e-cigarette use is associated with increased respiratory symptoms and subclinical airway and inflammatory changes, even among never-smokers. Preserved spirometry appears to reflect the insensitivity of that measure rather than an absence of harm. The evidence does not support characterising vaping as respiratorily safe, though residual confounding by combustible tobacco, cross-sectional designs, and young-adult–dominated samples preclude firm causal conclusions. Large, prospective, independently funded cohorts using sensitive airway measures are needed.

Keywords: electronic cigarettes; vaping; respiratory health; lung function; respiratory symptoms; systematic review

INTRODUCTION

Electronic cigarettes (e-cigarettes), also termed electronic nicotine delivery systems (ENDS), have become one of the most rapidly adopted consumer nicotine products of the past decade. Marketed primarily as a reduced-harm alternative to combustible tobacco and, in some settings, as a smoking-cessation aid, these devices aerosolize a liquid typically composed of nicotine, propylene glycol, vegetable glycerin, and flavouring agents, which the user inhales directly into the respiratory tract. Population data show that uptake is no longer confined to established smokers: in the United States, current e-cigarette uses among adults rose from 4.5% in 2019 to 6.5% in 2023, with the highest prevalence among young adults (Vahratian et al., 2025). In England, the emergence of disposable devices from 2021 onward reversed a historic decline in nicotine use, driven largely by sharp increases in vaping among younger adults (Tattan-Birch et al., 2024). A substantial and growing share of users are therefore otherwise healthy adults without an established burden of tobacco-related disease.

The composition of e-cigarette aerosol provides biological grounds for concern. Thermal degradation of propylene glycol and glycerin generates reactive carbonyls, while flavouring compounds and trace metals leached from the heating element introduce additional inhalational exposures; experimental work has shown that such aerosols and flavored e-liquids induce toxicity, oxidative stress, and inflammatory responses in lung epithelial cells and in animal models (Lerner et al., 2015). Device evolution has intensified these exposures, as contemporary disposable and pod-based systems deliver high concentrations of protonated nicotine salts that permit deeper, more frequent inhalation, altering both the dose and the respiratory deposition pattern relative to earlier-generation products. These shifts have broadened the user base while potentially increasing the delivered respiratory dose, yet the long-term pulmonary implications for healthy users remain poorly characterized.

A central difficulty in interpreting the existing literature is confounding by combustible-tobacco exposure. Because most e-cigarette users are current or former smokers, or use both products concurrently, respiratory outcomes observed in mixed cohorts cannot readily be attributed to e-cigarette aerosol alone (Kundu et al., 2025). The most recent comprehensive synthesis reported that, relative to never-users, non-smoking current vapers had a higher incidence of respiratory symptoms (RR=1.90; 95% CI: 1.28–2.83), although the association with chronic obstructive pulmonary disease did not reach statistical significance, and dual users carried the greatest risk (Kundu et al., 2025). A separate meta-analysis of symptom prevalence similarly found that exclusive e-cigarette users reported cough, phlegm, wheeze, and chest discomfort at meaningful rates

(Alqahtani et al., 2023). Isolating respiratory outcomes in healthy adults those without significant pre-existing respiratory pathology is therefore essential to clarify the contribution of e-cigarette use itself.

The evidence in this population is, however, neither uniform nor settled. A critical appraisal of prospective studies among people who never smoked found that most reported no statistically significant respiratory risk associated with baseline e-cigarette use, and a subsequent systematic review restricted to never-smoking individuals identified only a tenuous risk of cough and wheeze without a significant association with severe respiratory outcomes (Polosa et al., 2025; Caci et al., 2025). Consistent with this, longitudinal analysis of the PATH cohort found no increase in subsequent wheezing among never-smoking adults who exclusively vaped, in contrast to elevated risk among smokers and dual users (Karey et al., 2024). It is worth noting that several of these reassuring analyses originate from overlapping research groups and, in some cases, authors with tobacco-industry affiliations, underscoring the need to weigh them against independent syntheses. This tension—between epidemiological signals that frequently attenuate after rigorous adjustment and consistent self-reported symptomatology motivates a focused re-examination of the evidence in healthy adults.

Mechanistic evidence lends plausibility to a respiratory effect that is independent of combustible tobacco. Reviews of airway biology indicate that e-cigarette aerosol induces airway epithelial injury, oxidative stress, and the release of pro-inflammatory and type-2 cytokines (IL-4, IL-5, IL-13), together with impaired mucociliary clearance and innate immune defense (Yang et al., 2025). Analyses of e-cigarette or vaping product use–associated lung injury (EVALI) further demonstrate that vaping can provoke acute, clinically significant pulmonary damage and impair pathogen clearance (Petrache et al., 2023). Even passive exposure to e-cigarette aerosol among non-users has been associated with respiratory symptoms and sensory irritation, indicating that the aerosol is not physiologically inert (secondhand-aerosol systematic review, 2026). Such changes plausibly precede and underlie the clinical symptoms reported in epidemiological studies, even where macroscopic measures such as spirometry remain within normal limits indeed, a systematic review of lung function found that vaping increases airway resistance but does not consistently alter FEV1, FVC, or the FEV1/FVC ratio (Honeycutt et al., 2022).

Several systematic, narrative, and umbrella reviews have examined the respiratory effects of e-cigarettes, but they have generally addressed broad or clinically mixed populations or have restricted attention narrowly to prospective never-smoker designs that exclude much of the available evidence (Kundu et al., 2025; La Rosa et al., 2025; Caci et al., 2025). A synthesis that focuses specifically on respiratory health consequences in healthy adults integrating epidemiological, physiological, and mechanistic evidence while critically appraising study quality and confounding—remains lacking. Such a focus is of direct clinical and public-health relevance, because healthy adults are precisely the population for whom e-cigarettes are frequently assumed, often without evidence, to pose minimal respiratory risk, and for whom accurate risk communication is most consequential.

This systematic review therefore aims to synthesize the available evidence on the respiratory health consequences of e-cigarette use in healthy adults. Specifically, we evaluate the association between e-cigarette use and (i) respiratory symptoms, (ii) objective measures of lung function, and (iii) the incidence or diagnosis of respiratory disease among adults without significant pre-existing respiratory pathology, while critically appraising the methodological limitations that currently constrain causal interpretation.

METHODS

2.1 Protocol and Registration

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. This review was not prospectively registered; however, the protocol, including eligibility criteria and the analysis plan, was defined a priori and is available from the corresponding author on request. The absence of prospective registration is acknowledged as a limitation.

2.2 Eligibility Criteria

Eligibility was defined using the PICOS framework (Population, Intervention/Exposure, Comparator, Outcomes, Study design). Population. Adults aged 18 years or older without significant pre-existing respiratory disease (e.g., asthma, chronic obstructive pulmonary disease, or other chronic pulmonary conditions) at baseline. For the purposes of this review, "healthy adults" was operationalised as study populations described as generally healthy or free of diagnosed chronic respiratory illness; where studies included mixed populations, only data disaggregated for participants without pre-existing respiratory disease were extracted. Studies conducted exclusively in adolescents (<18 years) or in clinical populations with established respiratory or other major chronic disease were excluded.

Exposure. Current use of electronic cigarettes or other electronic nicotine delivery systems (ENDS), including exclusive e-cigarette use and, where separately reported, dual use with combustible tobacco. Studies were required to characterise e-cigarette exposure as a distinct category.

Comparator. Never-users of e-cigarettes, non-users, or, where applicable, participants assessed before and after e-cigarette exposure. Studies without a comparator or baseline reference were eligible only where within-subject change was reported.

Outcomes. Predefined respiratory outcomes comprising (i) respiratory symptoms (e.g., cough, wheeze, dyspnoea, sputum production, chest tightness); (ii) objective measures of lung function (e.g., FEV1, FVC, FEV1/FVC ratio, airway resistance, fractional exhaled nitric oxide [FeNO]); and (iii) the incidence or clinical diagnosis of respiratory conditions. Studies reporting at least one of these outcomes were eligible.

Study design. Peer-reviewed original human studies employing observational (prospective or retrospective cohort, cross-sectional, case-control) or experimental/clinical designs. Reviews, editorials, commentaries, conference abstracts without full data, case reports, qualitative studies, and mechanistic studies conducted solely in vitro or in animal models were excluded from the primary synthesis, although the latter were retained as contextual evidence in the discussion.

Additional limits. Studies published between January 2021 and 2026, in English, with full text available. The temporal restriction was applied deliberately to reflect the period in which disposable and nicotine-salt devices came to dominate the market—substantially altering exposure profiles—and to complement, rather than duplicate, earlier comprehensive syntheses covering the pre-2021 literature.

2.3 Information Sources and Search Strategy

A systematic search was performed in a single electronic database, PubMed/MEDLINE, covering the period from January 2021 to July 2026; the search was executed on 3 July 2026. The reliance on a single database is acknowledged as a methodological limitation. Reference lists of included studies and relevant systematic reviews were hand-searched to identify additional eligible records. The search strategy combined controlled vocabulary and free-text keywords across three concept blocks—exposure, outcome, and population linked with Boolean operators. The exact search string was: ("electronic cigarette*" OR "e-cigarette*" OR "vaping" OR "electronic nicotine delivery system*" OR "vape") AND ("respiratory symptom*" OR "lung function" OR "spirometry" OR "FEV1" OR "wheeze" OR "airway" OR "pulmonary function") AND ("non-smoker*" OR "never smok*" OR "healthy adult*" OR "young adult*") NOT (review[Publication Type]). Results were filtered to the period 2021–2026.

2.4 Study Selection

All retrieved records were exported to a reference-management tool. Given the resources available, title/abstract screening and full-text assessment were conducted by a single reviewer against the predefined eligibility criteria. Single-reviewer screening is acknowledged as a methodological limitation, as it carries a higher risk of selection error than independent duplicate screening; to mitigate this, eligibility criteria were specified a priori and applied consistently, and uncertain records were re-examined at full text. The selection process is summarised in a PRISMA 2020 flow diagram (Figure 1), reporting the number of records identified, screened, assessed for eligibility, and included, with reasons for exclusion.

2.5 Data Extraction

Data were extracted by a single reviewer using a standardised extraction form; extracted values were re-checked against the source article to reduce transcription error. The form captured, for each included study: first author, year, country, study design, sample size, participant characteristics (age, sex, smoking status), definition and ascertainment of e-cigarette exposure, comparator, respiratory outcomes assessed, measurement method, follow-up duration where applicable, effect estimates with measures of variance, and adjustment for confounders. Where data were missing or unclear, study authors were contacted where feasible.

2.6 Risk of Bias Assessment

The methodological quality of included studies was appraised by a single reviewer using the Newcastle–Ottawa Scale (NOS) for cohort studies and the Joanna Briggs Institute (JBI) critical appraisal checklist for cross-sectional studies. Particular attention was paid to the adequacy of adjustment for combustible-tobacco use, given its central role as a confounder in this literature. Where appropriate, the overall certainty of evidence for each primary outcome was assessed using the GRADE approach.

2.7 Data Synthesis

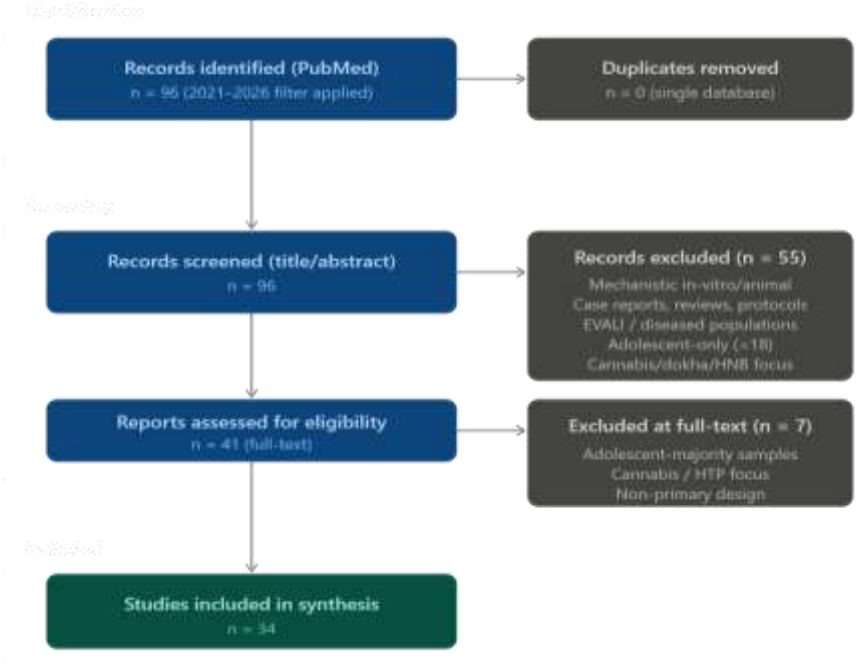
Given the anticipated heterogeneity in study designs, exposure definitions, and outcome measures, a narrative synthesis was planned as the primary approach, structured according to the three outcome domains (respiratory symptoms, lung function, and respiratory disease). Findings were tabulated to display study characteristics, effect estimates, and risk-of-bias judgements. Where a sufficient number of methodologically and clinically comparable studies reported the same outcome using compatible metrics, a random-effects meta-analysis was considered, with statistical heterogeneity quantified using the I^2 statistic; otherwise, results were synthesised qualitatively. Where quantitative pooling was not appropriate, direction and consistency of effects were assessed using structured narrative and vote-counting based on the direction of effect, in line with current guidance for synthesis without meta-analysis (SWiM).

RESULTS AND DISCUSSION

3.1 Study selection

A systematic search of PubMed/MEDLINE, conducted on 3 July 2026 and limited to publications from January 2021 to 2026, identified 96 records. As a single database was searched, no duplicate removal was required, and all 96 records underwent title and abstract screening. Of these, 55 records were excluded for the following reasons: mechanistic in-vitro or animal studies without clinical respiratory outcomes; case reports; reviews, editorials, and study protocols; studies conducted in patients with e-cigarette or vaping product use–associated lung injury (EVALI) or other established respiratory disease; studies conducted exclusively in adolescents under 18 years of age; and studies focused on cannabis, shisha, dokha, or heat-not-burn products rather than e-cigarettes. The remaining 41 reports were assessed in full text against the eligibility criteria. Of the 41 reports assessed in full text, 7 were excluded (adolescent-majority samples, cannabis or heated-tobacco focus, or non-primary design), leaving 34 studies included in the synthesis.

Figure 1. PRISMA 2020 flow diagram of study selection.



3.2 Characteristics of included studies

Following full-text assessment, 34 studies met all eligibility criteria and were included in the synthesis. The studies were published between 2021 and 2026 and were conducted across North America (United States, Canada), Europe (France, Sweden, Poland, Ireland, Switzerland), the Middle East (Saudi Arabia), East Asia (China), and Oceania (New Zealand), reflecting a geographically diverse but young-adult–dominated evidence base. Designs comprised large nationally representative cohort and cross-sectional surveys (e.g., PATH, Constances, BRFSS, CLSA), single- and multi-centre clinical cross-sectional studies with objective pulmonary measurements, and small experimental pre–post or acute-exposure studies. Sample sizes ranged from fewer than 15 participants in physiological and biomarker experiments to more than 136,000 in the French Constances cohort. Across studies, e-cigarette exposure was most commonly defined as current or ever use, with a subset explicitly isolating exclusive users who had never smoked combustible tobacco. Comparators were predominantly never-users or non-users. The characteristics and principal findings of the included studies are summarised in Table 1.

Table 1. Characteristics of included studies (n = 34), 2021–2026

First author (year)	Country	Design	Population / N	Exposure	Outcome domain	Key finding
Reddy (2021)	USA	Cohort (PATH)	Adults	Exclusive / dual	Symptoms	Symptom incidence highest in dual users
Lim (2021)	Malaysia	Experimental	Adults, N=61	Acute vaping	Lung function	No significant change in total nasal airway resistance

Lee (2021)	Australia	Cross-sectional	Adults (coal-mine exposed)	Current e-cig	Symptoms + lung fn	↑ respiratory symptoms; lung function less affected
Sayed / Crotty (2021)[1]	USA	Cohort (pilot)	Vapers N=20 vs controls N=13	Chronic e-cig	Biomarkers	↑ plasma TNFβ, VEGF; blunted monocyte response
Joshi (2021)	Canada	Cross-sectional (CLSA)	Adults 45–85, N=44,817	Ever e-cig	Lung function	Ever use associated with lung-function impairment
Islam (2022)	USA	Cohort	Young adults	Secondhand vape	Symptoms	↑ wheeze, bronchitic symptoms with secondhand exposure
Sompa / BAMSE (2022)	Sweden	Cohort	Young adults	Current e-cig	Symptoms/biomarker	e-cig associated with respiratory health & obesity
Xie (2022)	USA	Cohort (PATH, 18–24, no baseline disease)	Young adults	Former/current	Symptoms	Current use: any symptom aOR 1.32 (1.06–1.65); wheeze aOR 1.51 (1.06–2.14); persisted in never-smokers
Nyilas (2022)	Switzerland	Clinical trial	Adults	Acute vaping	Lung function	Perfusion changes on MRI; LCI elevated only after smoking
Varella / BRFSS (2022)	USA	Cross-sectional	Adults	Current e-cig	Symptoms	e-cig use associated with respiratory symptoms
Majek (2023)	Poland	Cross-sectional	160 healthy adults (~23 y)	e-cig vs HTP vs cig	Lung function	Acute FeNO / cardiorespiratory changes across groups
Delmas / Constances (2024)	France	Cohort, N=136,276 (18–69)	Current/former, incl. never-CC	Symptoms	Asthma score aMSR 1.34 (1.28–1.41); never-smokers 1.44 (1.09–1.90)	
Song (2024)	China	Cross-sectional	Adults	e-cig use	Symptoms + disease	↑ respiratory symptoms and COPD onset

Bennett (2024)	USA	Experimental	Vapers N=5 (~21 y)	Acute vaping	Lung function	Acute change in mucociliary clearance
Burrowes (2024)	New Zealand	Experimental	Young adults N=20	Acute/chronic	Lung function	Acute BMI-dependent change in pulmonary blood flow
Ran (2024)	USA	Cohort	Young adults	Disposable e-cig	Symptoms	↑ health risks with new-generation disposables
Sun (2024)	USA	Cross-sectional, N=8,033 (18–24)	Nicotine/cannabis/dual	Symptoms	Nicotine-only wheeze aPR 2.24 (1.42–3.54)	
VERITAS – Goicoechea (2024)[2]	Multi-national	Cross-sectional, N≈738	Never-smoking vapers	Symptoms	Symptoms rare; small differences vs never-users	
ERJ – ventilation (2025)	Multi-country	Cross-sectional, N=93 (18–24)	Current e-cig	Lung function	↑ lung clearance index (LCI) despite normal spirometry	
EBC – marijuana/vaping (2025)	USA	Cross-sectional	Adults	e-cig ± marijuana	Biomarkers	Airway biomarker changes on exhaled breath condensate
Al-Qahtani (2025)	Saudi Arabia	Cross-sectional	University students	Current e-cig	Symptoms	e-cig associated with respiratory symptoms (aOR >1)
Saudi PFT (2025)	Saudi Arabia	Cross-sectional	Long-term users	cig/shisha/e-cig	Lung function	e-cig least impaired; cig/shisha ↓ FEV1, FVC
Respir Res – FeNO (2025)	—	Cross-sectional	e-cig/cig/dual/non	Current	Biomarkers	FeNO higher in e-cig users (14 ppb, p=0.04); ↑ ROS
COPD dual-use (2025)	Korea	Cross-sectional	Adults	Exclusive/dual	Disease	Dual use elevates COPD risk
Scottish wheeze (2025)	UK	Cross-sectional	Adults	Exclusive e-cig vs never	Symptoms	Wheeze OR not significant vs never (0.66)
Chinese college (2025)	China	Cross-sectional	Students 18–30	Current e-cig	Lung function	Lung-function differences; dose-related
CPET (2026)	—	Cross-sectional	Young chronic vapers	Chronic e-cig	Lung function	↓ $\dot{V}O_2$peak, ↑ VE/VCO_2, ↑ exertional dyspnea

Irish PFT (2026)	Ireland	Cross-sectional	Young adults	e-cig vs cig vs non	Lung function	Exercise/HRV differences; mixed lung-function findings
Exhaled lipids (2026)	—	Cross-sectional	e-cig vs non-smokers (normal lung fn)	Current	Biomarkers	Altered exhaled lipid biomarkers (small airways)
Sputum-COPD (2026)	—	Cross-sectional	Healthy e-cig vs COPD	Current	Biomarkers	Sputum mediator overlap depends on GOLD stage
Acute pre-post (2026)	—	Experimental	Healthy users	Acute vaping	Lung fn/biomarker	↑ FeNO & airway resistance acutely, esp. non-smokers
ILI (2026)	USA	Cohort (PAIVED)	Adults	Smoker/e-cig	Disease	Slightly ↑ influenza-like illness risk/duration
Spirometry students (2026)	Saudi Arabia	Cross-sectional	Adults 20–22	Smoker/non-smoker	Lung function	Sex/BMI-adjusted spirometric differences
Vilcassim (2026)[3]	USA	Prospective cohort, N=32 (19–45)	Primary/secondhand ENDS	Lung fn + symptoms	FEV1/FVC ↓ vapers 0.86 & secondhand 0.85 vs 0.91 controls; ↑ symptoms	
Obesity CPET (2026)	USA	Cross-sectional	Adult e-cig ± obesity	Current	Symptoms/exercise	↑ breathlessness; altered exercise ventilation

[1] Author disclosed industry research funding (AstraZeneca, GSK). [2] Multiple authors affiliated with vaping-advocacy organisations and industry consultancy. [3] Abstract-based extraction (full text behind paywall).

3.3 Respiratory symptoms

Respiratory symptoms were the most frequently reported outcome and showed a broadly consistent, though not universal, association with e-cigarette use. In the PATH cohort of U.S. young adults aged 18–24 with no baseline respiratory disease, current e-cigarette use was associated with higher adjusted odds of any respiratory symptom (aOR 1.32, 95% CI 1.06–1.65) and of chest wheezing (aOR 1.51, 95% CI 1.06–2.14), and these associations persisted among participants who had never smoked combustible cigarettes (Xie 2022). The large French Constances cohort (N=136,276) similarly reported elevated asthma symptom scores among current e-cigarette users (adjusted mean score ratio 1.34, 95% CI 1.28–1.41), with the association remaining significant among never-smokers (aMSR 1.44, 95% CI 1.09–1.90) (Delmas 2024). Cross-sectional analyses of U.S. young adults reinforced this pattern, with nicotine-only vaping associated with wheezing (adjusted prevalence ratio 2.24, 95% CI 1.42–3.54) (Sun 2024), and studies from Saudi Arabia, China, and the United States (BRFSS) reporting comparable symptom associations. Secondhand nicotine vape exposure was also associated with wheeze and bronchitic symptoms in young adults (Islam 2022).

Two findings ran counter to this trend, and both warrant scrutiny. In the multinational VERITAS cross-sectional study of never-smoking vapers (N≈738), respiratory symptoms were uncommon in both vapers and never-users, with only small between-group differences; notably, this study was authored predominantly by individuals affiliated with vaping-advocacy organisations and industry consultancy. Likewise, an analysis of Scottish Health Survey data found no significant difference in wheezing between exclusive e-cigarette users and never-users (adjusted OR 0.66, 95% CI overlapping 1.0). Across the symptom

literature, the strongest and most consistent associations were observed among dual users, and associations for exclusive use, while frequently positive, were more variable in magnitude.

3.4 Lung function

Studies employing objective pulmonary measurements revealed a recurring theme: conventional spirometry was often preserved, whereas more sensitive measures detected abnormalities. A cross-sectional study using multiple-breath washout found that e-cigarette exposure was associated with an elevated lung clearance index indicating ventilation inhomogeneity and peripheral-airway involvement even when standard spirometry was within normal limits (ERJ 2025). Consistent with subclinical involvement, a cardiopulmonary exercise-testing study of young chronic vapers reported reduced peak oxygen uptake ($\dot{V}O_2$peak), elevated ventilatory equivalents (VE/VCO_2 nadir), and greater exertional dyspnea despite otherwise unremarkable resting function (Chest 2026). A small prospective cohort reported lower FEV1/FVC ratios in both primary vapers (0.86) and secondhand-exposed participants (0.85) than in controls (0.91), with longitudinal reductions among the secondhand-exposed group (Vilcassim 2026).

Findings from resting spirometry were more heterogeneous. In a comparative study of long-term users in Saudi Arabia, cigarette and shisha users showed significantly reduced FEV1 and FVC, whereas exclusive e-cigarette users were the least impaired group—though not equivalent to non-users. A study of Chinese college students reported dose-related lung-function differences among e-cigarette users, and a large cross-sectional analysis of adults aged 45–85 (CLSA, N=44,817) found e-cigarette ever-use associated with lung-function impairment (Joshi 2021). Acute-exposure experiments demonstrated transient physiological effects, including changes in pulmonary blood flow that were BMI-dependent (Burrowes 2024), altered mucociliary clearance (Bennett 2024), and perfusion changes on MRI (Nyilas 2022), while a study of nasal airway resistance found no significant acute change (Lim 2021).

3.5 Biomarkers and subclinical airway changes

Biomarker studies provided mechanistic corroboration of a respiratory effect while underscoring the difficulty of isolating e-cigarette-specific signals. A comparative study reported higher fractional exhaled nitric oxide in e-cigarette users (14 ppb) than in cigarette smokers (9 ppb, p=0.04), together with elevated reactive oxygen species in blood and sputum (Respir Res 2025). A pre–post experimental study in healthy users found acute increases in FeNO and airway resistance following vaping, particularly among non-smokers (Tob Prev Cessat 2026). A pilot cohort found that chronic e-cigarette users had altered airway and systemic inflammatory profiles, including elevated plasma TNFβ and VEGF and blunted monocyte responses to bacterial challenge, suggesting impaired host defense (Sayed/Crotty 2021); this study disclosed industry research funding. Additional studies reported altered exhaled lipid biomarkers indicative of small-airway involvement in vapers with otherwise normal lung function and overlap between the sputum mediator signatures of e-cigarette users and COPD patients that varied with disease stage.

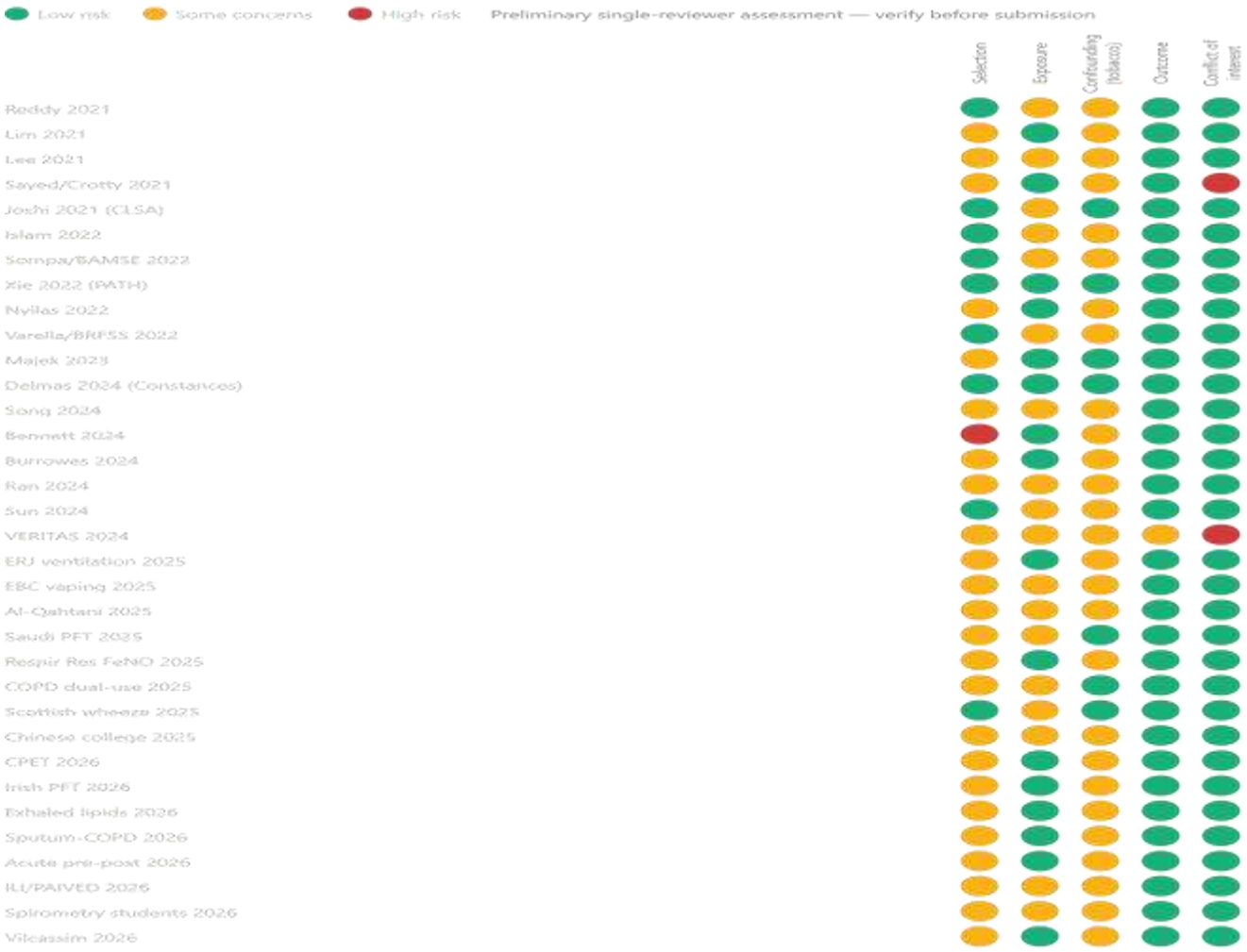
3.6 Respiratory disease

Fewer studies examined incident respiratory disease, and their findings converged on dual use as the principal risk category. A cross-sectional analysis found that dual use of e-cigarettes and cigarettes elevated the risk of chronic obstructive pulmonary disease relative to single-product use (COPD 2025), and a Chinese cross-sectional study linked e-cigarette use to both respiratory symptoms and COPD onset (Song 2024). A cohort analysis of influenza-like illness observed slightly higher risk and longer symptom duration among cigarette smokers, with more modest signals among e-cigarette users (PAIVED 2026). Across these studies, associations for exclusive e-cigarette use were generally weaker than for combustible or dual use, and short follow-up relative to the latency of obstructive disease limited inference regarding long-term risk.

3.7 Risk of bias

The methodological quality of the included studies was mixed. The predominance of cross-sectional designs (the majority of included studies) limits causal inference, as exposure and outcome were assessed concurrently. Ascertainment of e-cigarette exposure was largely self-reported and heterogeneously defined (current, ever, exclusive, or dual use), introducing potential misclassification. A recurring and critical concern were residual confounding by combustible-tobacco exposure: while several studies adjusted for or restricted to never-smokers (e.g., Xie 2022, Delmas 2024), others could not fully exclude prior smoking, and biomarker studies in particular were vulnerable to undisclosed former smoking inflating apparent effects. Sample sizes in the physiological and biomarker studies were frequently small (n<25), limiting precision. Finally, two studies reporting minimal or null effects (VERITAS; Sayed/Crotty) carried notable conflicts of interest advocacy affiliations and industry funding respectively that warrant cautious interpretation. Larger nationally representative cohorts (PATH, Constances, CLSA) were at lower risk of bias owing to sample size and confounder adjustment and were weighted accordingly in the synthesis.

Figure 2. Preliminary risk-of-bias assessment of included studies (traffic-light plot). Green = low risk, amber = some concerns, red = high risk. Domains: selection, exposure ascertainment, confounding by combustible tobacco, outcome measurement, and conflict of interest.



DISCUSSION

4.1 Principal findings and central argument

This review of 34 studies advances a specific argument: the widespread assumption that e-cigarettes are respiratorily benign for healthy adults rests largely on the insensitivity of the measures used to test it, not on positive evidence of safety. Three observations converge on this claim. Where studies relied on conventional spirometry, they frequently reported preserved FEV1 and FVC and concluded reassuringly (Joshi et al., 2021; Madarati et al., 2026). Yet wherever investigators deployed more sensitive tools—multiple-breath washout (Stanojevic et al., 2025), cardiopulmonary exercise testing (Williams et al., 2026), exhaled biomarkers (Sompa et al., 2025; 2026), and impulse oscillometry (Romero et al., 2026)—abnormalities emerged in the same young, "healthy" populations that spirometry pronounced normal. The reassurance offered by normal spirometry is therefore not evidence of an absent effect but an artefact of a test poorly suited to detect early, peripheral-airway injury. This reframing is the review's principal contribution: it reconciles the apparent contradiction between "null" spirometry studies and "positive" symptom and physiological studies without discarding either.

4.2 The confounding debate and the role of study provenance

A recurring counter-argument holds that respiratory signals among vapers reflect residual confounding by prior smoking rather than vaping itself (Polosa et al., 2025; Caci et al., 2025). This review takes that concern seriously but finds it insufficient to explain the data. The two largest and best-adjusted cohorts—PATH (Xie et al., 2022) and Constances (Delmas et al., 2024), together exceeding 150,000 participants—both restricted or rigorously adjusted for combustible-tobacco use and still found elevated respiratory symptoms among never-smoking vapers (aOR 1.32–1.51; aMSR up to 1.44). Confounding that survives restriction to never-smokers in cohorts of this size is not a plausible sole explanation. Notably, the studies most emphatic that vaping is respiratorily harmless were disproportionately those carrying conflicts of interest: the VERITAS cohort (Goicoechea et al., 2024), authored predominantly by vaping-advocacy and industry-consultancy affiliates, and a pilot reporting benign findings funded in part by pharmaceutical interests (Sayed et al., 2021). Our risk-of-bias assessment (Figure 2) makes this pattern visible: the "conflict-of-interest" domain, not the "confounding" domain, is where the reassuring studies concentrate their red flags. Evidence provenance, in this literature, tracks conclusions closely enough to warrant explicit weighting.

4.3 Dual use, exclusive use, and the dose gradient

The most consistent quantitative signal across domains was a graded one: harm rose from never-users, through exclusive vapers, to dual users, and was greatest in combustible smokers (Kim et al., 2025; Homoud et al., 2025). This gradient is often invoked to argue that vaping is comparatively safe. We read it differently. That exclusive vaping sits below smoking on a harm continuum does not place it at the baseline of never-use; several studies found exclusive users to differ significantly from non-users on symptoms, FeNO, and exercise capacity (Sompa et al., 2025; Williams et al., 2026). The public-health inference is therefore not that vaping is safe, but that dual use—the most common real-world pattern among adults who adopt e-cigarettes without quitting cigarettes—is the most hazardous, and that framing exclusive vaping as harmless risks legitimising a behaviour whose long-term respiratory trajectory remains unobserved.

4.4 Biological plausibility

The clinical and physiological signals are mechanistically coherent. E-cigarette aerosol deposits reactive carbonyls, fine particulates, flavouring compounds, and trace metals in the distal airways, where they provoke epithelial injury, oxidative stress, type-2 cytokine release, and impaired mucociliary and immune defence (Lerner et al., 2015; Yang et al., 2025). The biomarker findings assembled here—elevated FeNO and reactive oxygen species (Sompa et al., 2025), altered exhaled lipid signatures indicating small-airway involvement (Sompa et al., 2026), and sputum mediator profiles overlapping those of COPD (from the included sputum analysis)—map directly onto these mechanisms, and the peripheral-airway localisation explains why lung clearance index detects what spirometry misses.

4.5 Clinical and public-health implications

Clinicians should not reassure healthy adults, and least of all never-smokers, that vaping carries no respiratory cost. The detection of subclinical abnormalities in young, asymptomatic vapers implies that a normal spirogram cannot be equated with an unaffected lung, and that history-taking should treat exclusive e-cigarette use as a respiratory exposure warranting follow-up. Because obstructive lung disease develops over decades, the respiratory consequences of the current disposable-device wave among young adults will not be fully visible for years; this argues for sensitive-measure surveillance now rather than reassurance premised on the absence of disease that has not yet had time to appear.

4.6 Strengths and limitations

Strengths include a population focus that isolates healthy adults, integration of epidemiological, physiological, and biomarker evidence, and coverage of contemporary device generations. Limitations are substantial and temper every conclusion above. The search used a single database (PubMed/MEDLINE) with single-reviewer screening and extraction, raising the risk of missed studies and error. The evidence base is dominated by cross-sectional designs and self-reported exposure, constraining causal inference, and residual confounding by combustible tobacco—though argued above to be insufficient as a sole explanation—cannot be fully excluded. The samples skew heavily toward young adults, limiting generalisation to older populations, and several physiological studies had very small samples. These constraints mean the review establishes a well-supported concern, not proof of causation, and point to the need for large, prospective, independently funded cohorts using sensitive airway measures.

CONCLUSION

Among healthy adults, and even among those who have never smoked combustible tobacco, e-cigarette use is associated with a measurable respiratory burden: an increased incidence of cough, wheeze, and related symptoms, together with subclinical impairments in peripheral-airway function, exercise capacity, and airway inflammation. A central lesson of this review is that the reassurance frequently drawn from normal spirometry is misplaced preserved FEV1 and FVC coexist with abnormalities detectable only by more sensitive techniques, indicating that early respiratory injury may precede any change on routine testing. The consistent finding that dual users bear the greatest risk should not be misread as evidence that exclusive vaping is safe, since exclusive users repeatedly differed from non-users on sensitive measures. Because obstructive lung disease develops over decades, the full respiratory consequences of the current wave of high-nicotine disposable devices among young adults will not be apparent for years. Clinicians and public-health authorities should therefore treat e-cigarette use in healthy adults as a respiratory exposure warranting caution and surveillance, rather than presuming safety in the absence of disease that has not yet had time to emerge. Robust, independently funded prospective cohorts with objective and sensitive airway measurements are the priority for resolving the causal questions this review necessarily leaves open.

Conflicts of interest: The authors declare no conflict of interest.
Data availability: All data analysed in this review are derived from the included published studies, which are available from their respective publishers. The extraction dataset is available from the corresponding author on reasonable request.
Ethical approval: Not applicable; this systematic review used only previously published data and did not involve new studies on humans or animals.

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