

Oscillometry-Defined Small Airway Dysfunction as a Predictor of Moderate-to-Severe Exacerbations in COPD: A Systematic Review and Meta-Analysis

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Abstract

Small airway dysfunction (SAD) is a pivotal feature of chronic obstructive pulmonary disease (COPD), yet spirometry has limited sensitivity for peripheral airway impairment. Oscillometry offers effort-independent assessment of respiratory mechanics during tidal breathing. We systematically reviewed longitudinal studies reporting the association between baseline oscillometry and subsequent moderate-to-severe acute exacerbations (AE) in COPD, and compared its predictive accuracy with spirometric indices. Effect estimates (OR, HR, IRR) were pooled using a random-effects model (DerSimonian–Laird). Eight studies (4,175 independent patients; follow-up 1–6 years) met inclusion criteria, five contributing to the meta-analysis. Patients with oscillometry-defined SAD had a 2.18-fold higher risk of moderate-to-severe AE (95% CI 1.49–3.20; $I^2 = 49.8\%$; $P < 0.001$). In four studies reporting both indices, oscillometry and FEV₁ showed comparable discrimination for AE (AUC 0.775 vs 0.777), whereas a combined model achieved superior discrimination (AUC 0.860). Patients with GOLD stage 1 COPD and abnormal oscillometry had exacerbation risk comparable to GOLD stage 2, indicating that oscillometry identifies at-risk patients missed by spirometry alone. Oscillometry-defined SAD independently predicts COPD exacerbations and provides incremental prognostic value over spirometry, supporting its integration into a precision-medicine approach. Further studies should validate oscillometric cut-offs for risk stratification.

Introduction

Chronic obstructive pulmonary disease (COPD) accounts for more than 3 million deaths worldwide each year [1,2], but its clinical burden extends far beyond mortality. Acute exacerbations accelerate lung function decline, impair quality of life, increase healthcare utilization, and are associated with a sustained excess cardiovascular risk beyond the acute event itself [3]. Identifying patients at increased risk of future exacerbations therefore remains a major challenge in routine clinical practice. For decades, forced expiratory volume in one second (FEV₁) has been central to the diagnosis and physiological characterization of COPD [4,5]. However, spirometry has important limitations. It requires a maximal forced expiratory manoeuvre, may remain relatively preserved despite substantial peripheral airway abnormalities, and can fail to identify patients with clinically relevant small airway dysfunction (SAD) before more advanced airflow obstruction becomes apparent [6]. Thus, FEV₁ may provide an incomplete representation of the early and heterogeneous pathophysiological changes occurring in COPD.

Small airways, conventionally defined as bronchioles with an internal diameter < 2 mm, represent a major site of airflow limitation in COPD [7]. Pathological and imaging studies have shown that terminal bronchiolar narrowing, obstruction, and loss may precede overt spirometric abnormalities [8]. Computed tomography studies further demonstrate airway remodelling and gas trapping even in patients with mild airflow obstruction [9]. These observations underpin the concept of the small airways as the lung's “silent zone”, in which substantial structural and functional abnormalities may accumulate before they are adequately captured by conventional spirometry.

Oscillometry has been introduced as an alternative technique to assess lung function, with particular application to obstructive airways disease [10]. Encompassing both impulse oscillometry (IOS) and the forced oscillation technique (FOT), the method imposes sound waves at multiple frequencies during tidal breathing and captures resistance (R) and reactance (X) of the respiratory system. The frequency-dependent resistance (R5–R20) reflects peripheral airway resistance; reactance at 5 Hz (X5), the area of reactance (AX), and resonant frequency (Fres) add complementary information on lung elastance and ventilation heterogeneity [11]. Importantly, these measurements are obtained during quiet tidal breathing, without requiring a forced expiratory manoeuvre, and may detect abnormalities not captured by conventional spirometry [12,13]. This potential has gained increasing recognition, including in the GOLD 2026 report, which discusses oscillometry-defined SAD in tobacco-exposed individuals with preserved spirometry [14].

Emerging longitudinal evidence suggests that oscillometric abnormalities may also have prognostic relevance in COPD, with associations reported for exacerbations, subsequent lung function decline, and mortality [15–17]. However, this evidence remains fragmented. To our knowledge, no systematic review and meta-analysis has quantitatively synthesized the relationship between oscillometry-defined SAD and future COPD exacerbations or directly examined its prognostic performance relative to conventional spirometric indices. This distinction is clinically important: if oscillometry identifies exacerbation-prone patients who are insufficiently characterized by FEV₁, it could provide complementary information for risk stratification and support a more individualized, treatable-traits approach to COPD management [18]. We therefore conducted a systematic review and meta-analysis with three objectives: (1) to quantify the association between oscillometry-defined SAD and the risk of moderate-to-severe COPD exacerbations; (2) to compare the prognostic performance of oscillometric parameters with FEV₁ for the same outcome; and (3) to identify and summarize the oscillometric thresholds associated with increased exacerbation risk across the available literature.

Results

Study selection

The initial literature search generated 57 potentially eligible articles from the aforementioned databases, plus 4 records identified additionally by manual search. A total of 3 duplicates were identified and removed. After excluding 50 articles, 8 articles were included in this review according to the prespecified inclusion and exclusion criteria, and 5 contributed to the quantitative meta-analysis. A flow chart showing the study selection is presented in Fig. 1.

Characteristics of included studies

The eight included studies [15–17,21–25] comprised 4,175 unique patients with COPD from five countries (China, Sweden, Japan, South Korea, and Taiwan) and were published between 2022 and 2025

(Table 1). To avoid double counting, the overlapping ECOPD sub-cohort reported by Lu et al. (2025a; n = 529) was excluded from the cumulative sample size. Five studies had a prospective cohort design and three were retrospective analyses, with follow-up ranging from 1 to 6 years. The largest study enrolled 2,572 patients [24], while the smallest followed 66 patients [21]. Oscillometry parameters assessed included R5–R20 (6 studies), Fres (5 studies), X5 (4 studies), AX (3 studies), and composite IOS severity indices (1 study). SAD was defined using z-score thresholds in three studies [15,16,25], fixed absolute cut-offs in three studies [21,22,24], and composite scoring in two studies [22,23].

Table 1
Characteristics of included studies.

Study	Ref.	Country	Design	N	Follow-up	IOS parameters	SAD definition
Lu 2025a (ECOPD)	15	China	Prospective	529	3 yr	Fres	Fres > ULN
Lu 2025b (ECOPD)	25	China	Prospective	833	2 yr	X5, AX, Fres	z-score > 1.645
Färdig 2025	16	Sweden	Prospective	150	1 + 3 yr	R5, X5, ΔX	z-score > 1.645
Zhang 2024	17	Japan	Prospective	114	4 + 6 yr	X5	Tertile decline
Zhang 2022	23	Japan	Prospective	134	5 yr	Fres (insp.)	Continuous + group
Huang 2025	21	China	Retrospective	66	1 yr	R5–R20, Fres	R5–R20 > 0.09
Park 2024	22	S. Korea	Retrospective	306	~ 2 yr	IOSsi	IOSsi ≥ 4
Tseng 2025	24	Taiwan	Retrospective	2,572	6 yr	AX	AX > 0.44

IOS, impulse oscillometry; SAD, small airway dysfunction; ULN, upper limit of normal; ΔX, change in reactance; IOSsi, IOS severity index.

Primary meta-analysis: oscillometry-defined SAD and exacerbation risk

Five studies provided extractable effect estimates for the association between oscillometry-defined SAD and moderate-to-severe AE. The pooled effect estimate, calculated using a random-effects model, was 2.18 (95% CI 1.49–3.20; $P < 0.001$), indicating that patients with oscillometry-defined SAD had an approximately 2.2-fold increased risk of experiencing moderate-to-severe exacerbations compared with those without SAD (Fig. 2). Heterogeneity was moderate ($I^2 = 49.8\%$, $\tau^2 = 0.0871$, $Q = 7.97$, $df = 4$, $P =$

0.093; 95% prediction interval 0.82–5.82). The effect estimates ranged from an IRR of 1.52 (95% CI 1.24–1.87) in the largest prospective cohort (Lu et al. [15], ECOPD, n = 529) to an HR of 5.23 (95% CI 1.43–19.1) for the composite IOS severity index in a Korean cohort [22]. All five individual study estimates were statistically significant and favoured an increased risk of exacerbation in patients with SAD.

In a sensitivity analysis restricted to the three prospective cohorts (Lu et al. 2025a, Färdig et al., and Zhang 2022), the pooled estimate was 1.77 (95% CI 1.29–2.44; $I^2 = 30.9\%$); excluding the potentially overlapping ECOPD cohort (Lu et al. 2025a) left four studies and yielded 2.64 (95% CI 1.81–3.86; $I^2 = 0.0\%$). Both analyses remained statistically significant and directionally consistent with the primary estimate. Subgroup analysis by oscillometry parameter type showed consistent associations for both resistance-based indices (R5–R20, R5) and reactance-based indices (X5, AX, Fres), although the limited number of studies in each subgroup precluded formal statistical comparison between parameter types.

Head-to-head comparison of oscillometry and FEV₁

Four studies evaluated oscillometry and FEV₁ as predictors of exacerbation within the same cohort, allowing a direct comparison of their prognostic performance (Fig. 3). In the study by Huang et al. [21], which provided the most detailed head-to-head analysis, R5–R20 and FEV₁ % predicted showed virtually identical discrimination for future COPD exacerbations when considered individually (AUC 0.775 vs 0.777). Importantly, a combined model incorporating R5–R20, FEV₁ % predicted, and body mass index achieved substantially greater discrimination (AUC 0.860, 95% CI 0.753–0.933), supporting the incremental value of oscillometry when added to spirometry. In the TIE study [16], an abnormal R5 z-score (> 1.645) was associated with future exacerbations at 1 year (OR 3.09, 95% CI 1.26–7.57). Severe airflow obstruction, defined as FEV₁ $< 50\%$ predicted, was also associated with increased risk, although FEV₁ and oscillometry were not directly compared within the same exacerbation-prediction model. Park et al. [22] provided complementary evidence that oscillometry may refine risk stratification beyond spirometric staging: patients with GOLD stage 1 COPD and an IOS severity index ≥ 4 had a time to first moderate-to-severe exacerbation comparable to that of patients with GOLD stage 2 disease. This suggests that oscillometry can identify a clinically relevant high-risk subgroup that may not be apparent from FEV₁-based staging alone.

Oscillometry cut-offs and SAD definitions

Considerable heterogeneity existed in the definitions and cut-offs used to classify SAD across studies (Table 2, Fig. 4). Three studies employed z-score-based thresholds aligned with the ERS recommendation (z-score > 1.645 for resistance parameters or < -1.645 for reactance), while three used fixed absolute cut-offs (R5–R20 > 0.09 kPa·L⁻¹·s, AX > 0.44). One study used a composite IOS severity index, and one assessed longitudinal X5 decline. Despite this heterogeneity, all definitions identified patient subgroups with significantly increased exacerbation risk, with effect estimates ranging from 1.52

(Fres > ULN) to 5.23 (the composite IOS severity index). The z-score-based definitions, recommended by the current ERS technical standards for oscillometry, were associated with effect sizes of 2.77–3.09 for AE at 1–3 years.

Table 2
Association between oscillometry-defined small airway dysfunction and COPD exacerbations according to the operational definition used in individual studies.

Cut-off / SAD definition	IOS parameter	Study [ref]	N	Effect (95% CI)	Metric
Fres > ULN (z > 1.645)	Fres	Lu 2025a [15]	529	1.52 (1.24–1.87)	IRR
R5 z > 1.645	R5	Färdig 2025 [16]	150	3.09 (1.26–7.57)	OR
X5 z < - 1.645	X5	Färdig 2025 [16]	150	2.81 (NR)	OR
R5–R20 > 0.09 kPa·L ⁻¹ ·s	R5–R20	Huang 2025 [21]	66	2.85 (1.40–5.80)	OR
IOSsi ≥ 4	Composite	Park 2024 [22]	306	5.23 (1.43–19.1)	HR

Fres, resonant frequency; R5, resistance at 5 Hz; R5–R20, frequency dependence of resistance between 5 and 20 Hz; X5, reactance at 5 Hz; IOSsi, IOS severity index; ULN, upper limit of normal; NR, not reported; IRR, incidence rate ratio; OR, odds ratio; HR, hazard ratio; CI, confidence interval.

Risk of bias assessment

Risk of bias assessment using the Newcastle–Ottawa Scale is presented in Fig. 5. The five prospective cohort studies (Lu 2025a, Lu 2025b, Färdig 2025, Zhang 2024, Zhang 2022) were rated as good quality (7–8 of 9 stars), with low risk of bias across selection and outcome domains. The three retrospective studies (Huang 2025, Park 2024, Tseng 2025) were rated as fair quality (5–6 stars), with some concerns regarding representativeness of the exposed cohort and adequacy of follow-up. The Kyoto cohort studies by Zhang et al. received some concerns for comparability due to the exclusively male enrolment. Overall, the quality of evidence was considered adequate for the primary analysis.

Discussion

To our knowledge, this is the first systematic review and meta-analysis to quantify the prognostic value of oscillometry-defined small airway dysfunction (SAD) for exacerbations in COPD. The pooled estimate was clinically meaningful and statistically robust: patients with oscillometric SAD had a 2.18-fold higher risk of moderate-to-severe exacerbations (95% CI 1.49–3.20). Importantly, available comparative data suggest that oscillometry provides prognostic information comparable to FEV₁, while assessing a distinct component of COPD pathophysiology; when combined, the two measures may offer greater predictive value than either alone. The magnitude of this association is noteworthy. An approximately two-fold increase in exacerbation risk is comparable to that associated with established clinical predictors, including a history of previous exacerbations, and appears greater than the prognostic effect generally attributed to elevated blood eosinophil counts alone [26]. The consistency of the association

across cohorts from China, Sweden, Japan, South Korea, and Taiwan, and across different oscillometric parameters (including R5–R20, X5, Fres, and composite indices) further strengthens the signal. The moderate between-study heterogeneity ($I^2 = 49.8\%$) is plausible given differences in SAD definitions, oscillometry devices, study populations, and follow-up duration, and supports the use of a random-effects model.

The head-to-head comparison with FEV_1 is particularly informative. In the study by Huang et al., R5–R20 and FEV_1 % predicted showed almost identical discrimination for subsequent exacerbations (AUC 0.775 and 0.777, respectively). However, a combined model incorporating R5–R20, FEV_1 , and BMI achieved substantially greater discrimination (AUC 0.860). This finding supports a complementary rather than redundant role for oscillometry. Whereas FEV_1 reflects the integrated mechanical consequences of airflow limitation during forced expiration, oscillometry characterizes respiratory-system resistance and reactance during quiet breathing and is particularly sensitive to abnormalities arising in the peripheral airways. Thus, the two techniques interrogate different physiological dimensions of COPD, providing a rationale for their combined use in risk stratification.

One finding deserves particular emphasis. Park et al. [22] showed that patients with GOLD grade 1 airflow obstruction ($FEV_1 \geq 80\%$ predicted) but an IOS severity index ≥ 4 had a time to first exacerbation comparable to that of patients with GOLD grade 2 disease. In other words, oscillometry identified increased risk among patients who would otherwise appear relatively preserved on spirometry. A similar pattern emerged from the ECOPD cohort: among patients with mild-to-moderate COPD without conventional treatable traits, abnormal Fres remained associated with a higher exacerbation rate (IRR 1.52), whereas this excess risk was not observed in those without oscillometric abnormalities. Collectively, these findings suggest that oscillometry may identify a clinically relevant, otherwise occult high-risk phenotype within the mild, spirometrically reassuring GOLD 1–2 population (Fig. 6).

These findings emerge at a time when the treatable-traits paradigm is increasingly shaping COPD management. Toumpanakis et al. [12] recently proposed oscillometry-defined SAD as a potentially treatable trait, while the ATLANTIS study established the prognostic relevance of IOS-defined SAD for exacerbations in asthma [27,28]. Peng et al. [29] subsequently pooled evidence on the diagnostic performance of oscillometry in COPD but did not address longitudinal outcomes; the ATLANTIS toolbox study [30] validated a multidimensional strategy for SAD detection combining oscillometry and spirometry; and Jang et al. [31] reviewed the broader clinical applicability of IOS. Our study extends this literature into the prognostic domain, providing the first quantitative synthesis of the association between oscillometry-defined SAD and future COPD exacerbations. Further support for this concept comes from the study by Abdo et al. [14], which showed that approximately 26% of tobacco-exposed individuals with preserved spirometry have oscillometry-defined SAD and that this phenotype is associated with structural abnormalities, impaired respiratory physiology, and cardiovascular consequences. Collectively, these observations support the view that oscillometry may identify clinically meaningful disease not captured by conventional spirometry alone.

An important unresolved issue is the definition of the optimal oscillometric threshold for SAD. Considerable heterogeneity was evident across the included studies. Z-score-based thresholds (> 1.645 or < -1.645 , depending on the parameter), as recommended by the ERS Delphi consensus, were adopted in three of the strongest prospective cohorts and offer the advantage of accounting for age, sex, and height. In contrast, fixed thresholds—such as $R5-R20 > 0.07-0.09 \text{ kPa}\cdot\text{L}^{-1}\cdot\text{s}$ and $AX > 0.44 \text{ kPa/L}$ —are easier to implement clinically but may be less generalisable across populations and devices. Notably, the composite IOS severity index yielded the largest observed effect estimate (HR 5.23), although this finding requires independent external validation. At present, no single oscillometric threshold has been prospectively validated against clinically meaningful outcomes in a large, multicentre cohort. Establishing reproducible, outcome-anchored cut-offs therefore represents one of the most important priorities for the field and a necessary step before oscillometry can be incorporated more systematically into COPD risk stratification.

This study has several limitations. First, the evidence base remains relatively small, with eight studies included in the qualitative synthesis and five contributing to the meta-analysis, reflecting the still-emerging literature on oscillometry-defined SAD in COPD. The limited number of studies also precluded a meaningful assessment of publication bias using funnel plots or Egger's test. Second, ORs, HRs, and IRRs were pooled under the assumption that they provide approximately comparable estimates for relatively uncommon outcomes, an accepted approach that nevertheless introduces some methodological imprecision [20]. Third, heterogeneity in SAD definitions, oscillometric parameters, and measurement techniques (IOS vs FOT) limits direct comparability across studies and precludes identification of a single clinically applicable threshold. Two analyses derived from the ECOPD cohort may have included partially overlapping participants despite differences in eligibility criteria and follow-up duration; however, sensitivity analysis excluding one of these studies yielded a similar pooled estimate, supporting the robustness of the main findings. In addition, the Kyoto cohorts included only men, potentially limiting their generalizability. Finally, most available cohorts were conducted in Asian populations, and the extent to which these findings apply to more ethnically and geographically diverse COPD populations, particularly European and African cohorts, remains uncertain.

In conclusion, oscillometry-defined small airway dysfunction independently predicts moderate-to-severe COPD exacerbations, with a pooled approximately 2.2-fold increase in risk. As a standalone predictor, oscillometry performs similarly to FEV_1 , but the two measures appear to capture complementary aspects of airway dysfunction, and their combination improves discriminatory performance. Oscillometry may be particularly informative in patients with preserved FEV_1 , identifying individuals at increased exacerbation risk who might otherwise be considered low risk on the basis of spirometric staging alone. These findings support the incorporation of oscillometry into a precision-medicine approach to COPD and reinforce the concept of SAD as a potentially treatable trait. Prospective multicentre studies are now needed to establish clinically actionable oscillometric thresholds, determine whether oscillometry-guided treatment improves outcomes, and confirm generalizability across ethnically and geographically diverse populations.

Methods

Study design and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [19]. The protocol was developed a priori and registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD420261479304).

Search strategy

We searched PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane CENTRAL, and Scopus from inception to March 2026 using a combination of MeSH terms and free-text keywords related to oscillometry, COPD, and exacerbation outcomes. The full PubMed search was: (“oscillometry”[MeSH] OR “forced oscillation technique” OR “impulse oscillometry”) AND (“pulmonary disease, chronic obstructive”[MeSH] OR “COPD”) AND (“exacerbation” OR “prognosis” OR “mortality” OR “lung function decline” OR “hazard ratio” OR “odds ratio” OR “predict*”). No language restrictions were applied. Reference lists of included studies and relevant reviews were hand-searched.

Study selection

Studies were included if they met the following criteria: (1) longitudinal cohort design (prospective or retrospective) with a minimum follow-up of 6 months; (2) individuals 18 years or older with COPD confirmed on post-bronchodilator spirometry (post-bronchodilator $FEV_1/FVC < 0.70$ or below the lower limit of normal); (3) baseline assessment of oscillometry parameters ($R5$, $R20$, $R5-R20$, $X5$, AX , $Fres$, or composite oscillometry scores); (4) reporting of moderate-to-severe acute exacerbations as an outcome, defined as events requiring systemic corticosteroids, antibiotics, emergency department visits, or hospitalisation; and (5) reporting of effect estimates (hazard ratio, odds ratio, incidence rate ratio, or relative risk) with 95% confidence intervals, or sufficient data to calculate these. Cross-sectional studies reporting associations with previous-year exacerbations were included in the qualitative synthesis but excluded from the primary meta-analysis. Case reports, editorials, conference abstracts, and studies in exclusively asthmatic populations without a COPD subgroup were excluded.

Data extraction

Data were extracted using a standardised form and included study characteristics, population demographics, oscillometry parameters assessed, SAD definitions and cut-offs, exacerbation definitions, effect estimates with 95% CI, and FEV_1 effect estimates from the same multivariable model where available.

Risk of bias assessment

Risk of bias was assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies, evaluating selection, comparability, and outcome domains. Studies were rated as good (7–9 stars), fair (4–6 stars),

or poor (0–3 stars) quality.

Statistical analysis

Effect estimates (OR, HR, IRR) with 95% CI were pooled using a random-effects model (DerSimonian–Laird method) on the natural-logarithm scale. Given the low event rates in most studies and follow-up durations exceeding one year, we treated OR, HR, and IRR as approximately equivalent effect measures in the primary analysis, consistent with accepted practice for rare outcomes in meta-analyses of observational studies [20]. Heterogeneity was quantified using the I^2 statistic and Cochran's Q test, with I^2 values of 25%, 50%, and 75% considered low, moderate, and high, respectively; a 95% prediction interval was also computed. All tests were two-sided with an alpha level of 0.05, and exact P values are reported. Pre-specified sensitivity analyses included (a) restriction to prospective cohort studies, (b) exclusion of potentially overlapping cohorts, and (c) analysis by oscillometry parameter subgroup (resistance-based vs reactance-based). For the head-to-head comparison with FEV₁, we extracted paired effect estimates from studies reporting both oscillometry and spirometric predictors in the same multivariable model and compared their discriminative accuracy using the area under the receiver operating characteristic curve (AUC) where available. All analyses were performed in R (metafor package, version 4.4).

Ethics declaration

This systematic review and meta-analysis was based on aggregate data from previously published studies; no ethics approval or informed consent was required. All included studies had obtained the relevant ethical approvals as reported in their original publications.

Use of artificial intelligence

An AI assistant (Claude, Anthropic) was used to support bibliographic search and manuscript formatting. All scientific content, data extraction, statistical interpretation, and conclusions were performed and verified by the authors, who take full responsibility for the accuracy and integrity of the work.

Data availability

All data supporting the findings of this review are derived from published studies and are available in the referenced articles. The extracted dataset and analysis code are available from the corresponding author upon reasonable request.

Declarations

Competing interests

The authors declare no competing interests.

Author Contribution

P.V.M. conceived the study, designed the protocol and registered it prospectively. P.V.M. and L.C. developed and executed the search strategy. Title/abstract and full-text screening were performed independently and in duplicate by L.C. and S.I., with disagreements resolved by discussion and, where necessary, adjudicated by P.V.M. Data extraction was carried out independently and in duplicate by M.S. and A.C. using a piloted extraction form; risk of bias was assessed independently by the same two reviewers. L.C. performed the statistical analysis, including the random-effects meta-analysis, assessment of heterogeneity, publication bias and sensitivity analyses, and prepared the figures. P.V.M. and L.C. interpreted the findings and wrote the first draft. S.B., R.S., V.O. and A.R. provided critical revision for important intellectual content and clinical interpretation. R.S. and A.R. supervised the project. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Data Availability

All data supporting the findings of this review are derived from previously published studies and are available in the referenced articles. The extracted dataset and the analysis code generated during the current study are available from the corresponding author upon reasonable request.

References

1. 1. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir. Med.* **8**, 585–596 (2020).
2. 2. Wedzicha, J. A. & Seemungal, T. A. COPD exacerbations: defining their cause and prevention. *Lancet* **370**, 786–796 (2007).
3. 3. Hurst, J. R. & Gale, C. P. MACE in COPD: addressing cardiopulmonary risk. *Lancet Respir. Med.* **12**, 345–348 (2024).
4. 4. Agustí, A. et al. Global Initiative for Chronic Obstructive Lung Disease 2023 report: GOLD executive summary. *Eur. Respir. J.* **61**, 2300239 (2023).
5. 5. Singh, D., Long, G., Cançado, J. E. D. & Higham, A. Small airway disease in chronic obstructive pulmonary disease: insights and implications for the clinician. *Curr. Opin. Pulm. Med.* **26**, 162–168 (2020).

6. 6. Aaron, S. D. et al. Early diagnosis and treatment of COPD and asthma – a randomized, controlled trial. *N. Engl. J. Med.* **390**, 2061–2073 (2024).
7. 7. Hogg, J. C. et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N. Engl. J. Med.* **350**, 2645–2653 (2004).
8. 8. McDonough, J. E. et al. Small-airway obstruction and emphysema in chronic obstructive pulmonary disease. *N. Engl. J. Med.* **365**, 1567–1575 (2011).
9. 9. Koo, H. K. et al. Small airways disease in mild and moderate chronic obstructive pulmonary disease: a cross-sectional study. *Lancet Respir. Med.* **6**, 591–602 (2018).
10. 10. King, G. G. et al. Technical standards for respiratory oscillometry. *Eur. Respir. J.* **55**, 1900753 (2020).
11. 11. Lipworth, B. J. & Jabbal, S. What can we learn about COPD from impulse oscillometry? *Respir. Med.* **139**, 106–109 (2018).
12. 12. Toumpanakis, D., Kim, Y. & Usmani, O. S. Small airways disease in patients with COPD: a question-and-answer approach for everyday clinical practice. *Chest* **169**, 641–651 (2026).
13. 13. Zhou, R., Wang, H., Zhang, Y., Mai, J. & Yang, L. Small airway disease as a key factor in COPD: new perspectives and insights. *Front. Med.* **12**, 1648612 (2025).
14. 14. Abdo, M. et al. Oscillometry-defined small airway dysfunction in tobacco-exposed adults with impaired or preserved airflow. *Am. J. Respir. Crit. Care Med.* **211**, 1652–1661 (2025).
15. 15. Lu, L. et al. Impulse oscillometry-defined airway abnormalities as a treatable trait for mild-to-moderate COPD: a prospective cohort study with 3-year follow-up. *ERJ Open Res.* **11**, 00428–2025 (2025).
16. 16. Färdig, M. et al. Peripheral airway function and disease burden in COPD. *ERJ Open Res.* **11**, 01078–2024 (2025).
17. 17. Zhang, Y. et al. Longitudinal changes in respiratory reactance in patients with COPD: associations with longitudinal change in air-trapping, exacerbations, and mortality. *Respir. Physiol. Neurobiol.* **322**, 104216 (2024).
18. 18. Agusti, A. et al. Treatable traits: toward precision medicine of chronic airway diseases. *Eur. Respir. J.* **47**, 410–419 (2016).
19. 19. Page, M. J. et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* **372**, n71 (2021).
20. 20. Higgins, J. P. T. et al. (eds). *Cochrane Handbook for Systematic Reviews of Interventions Version 6.5*. (Cochrane, 2024).
21. 21. Huang, Y. et al. Role of impulse oscillometry in chronic obstructive pulmonary disease and asthma–chronic obstructive pulmonary disease overlap. *Clin. Transl. Allergy* **15**, e70057 (2025).
22. 22. Park, H. et al. Diagnosis and evaluation of small airway disease and COPD using impulse oscillometry. *Sci. Rep.* **14**, 28030 (2024).

23. 23. Zhang, Y. et al. Physiological impairments on respiratory oscillometry and future exacerbations in chronic obstructive pulmonary disease patients without a history of frequent exacerbations. *COPD* **19**, 149–157 (2022).
24. 24. Tseng, C. H. et al. Increased risk of acute exacerbation in obstructive airway disease: the impact of metabolic dysfunction-associated steatotic liver disease and small airway dysfunction. *BMJ Open Respir. Res.* **12**, e003352 (2025).
25. 25. Lu, L. et al. Associations of small airway dysfunction assessed by impulse oscillometry with lung function decline and exacerbations in participants with chronic obstructive pulmonary disease: a prospective cohort study in China. *Respir. Med.* **241**, 108075 (2025).
26. 26. Hurst, J. R. et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N. Engl. J. Med.* **363**, 1128–1138 (2010).
27. 27. Kraft, M. et al. The role of small airway dysfunction in asthma control and exacerbations: a longitudinal, observational analysis using data from the ATLANTIS study. *Lancet Respir. Med.* **10**, 661–668 (2022).
28. 28. Galant, S. P. et al. Assessment of the role of small airway dysfunction in relation to exacerbation risk in patients with well controlled asthma (ATLANTIS): an observational study. *Lancet Respir. Med.* **13**, 990–1000 (2025).
29. 29. Peng, J. et al. Clinical value of impulse oscillometry in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respiration* **104**, 100–109 (2025).
30. 30. Siddiqui, S. et al. Detecting small airways dysfunction in asthma: rationale, findings, and future of ATLANTIS. *J. Allergy Clin. Immunol. Pract.* **14**, 56–66 (2026).
31. 31. Jang, J. G., Joo, H. & Lee, H. Small airway dysfunction in chronic obstructive pulmonary disease pathology: assessment and clinical implications. *Tuberc. Respir. Dis.* **89**, 133–142 (2026).

Figures

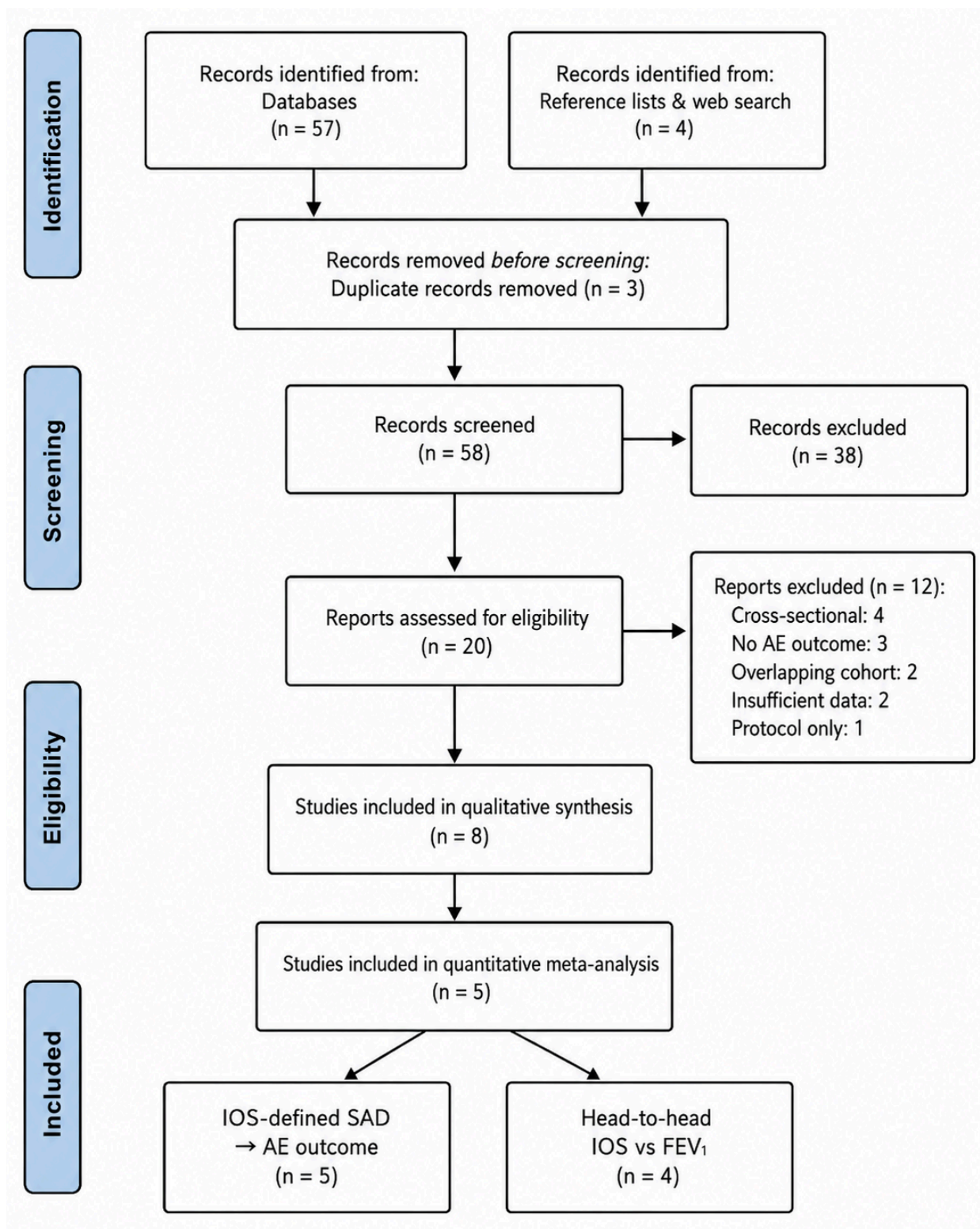


Figure 1

PRISMA 2020 flow diagram of study selection.

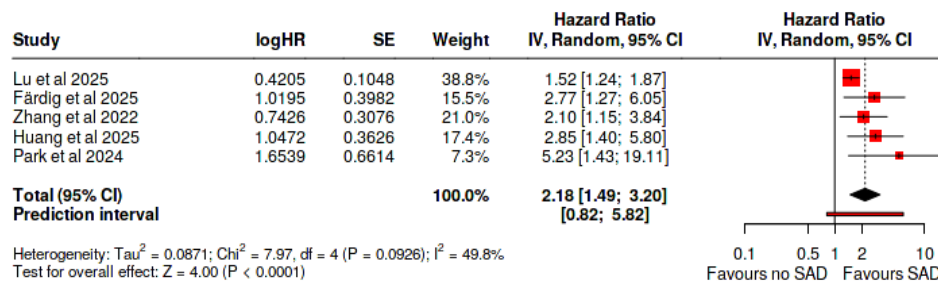


Figure 2

Risk of moderate-to-severe exacerbation according to oscillometry-defined small airway dysfunction. Forest plot of five independent COPD cohorts. Effect estimates are presented with 95% confidence intervals; the pooled estimate was calculated using a DerSimonian–Laird random-effects model. SAD, small airway dysfunction; OR, odds ratio; HR, hazard ratio; IRR, incidence rate ratio; CI, confidence interval.

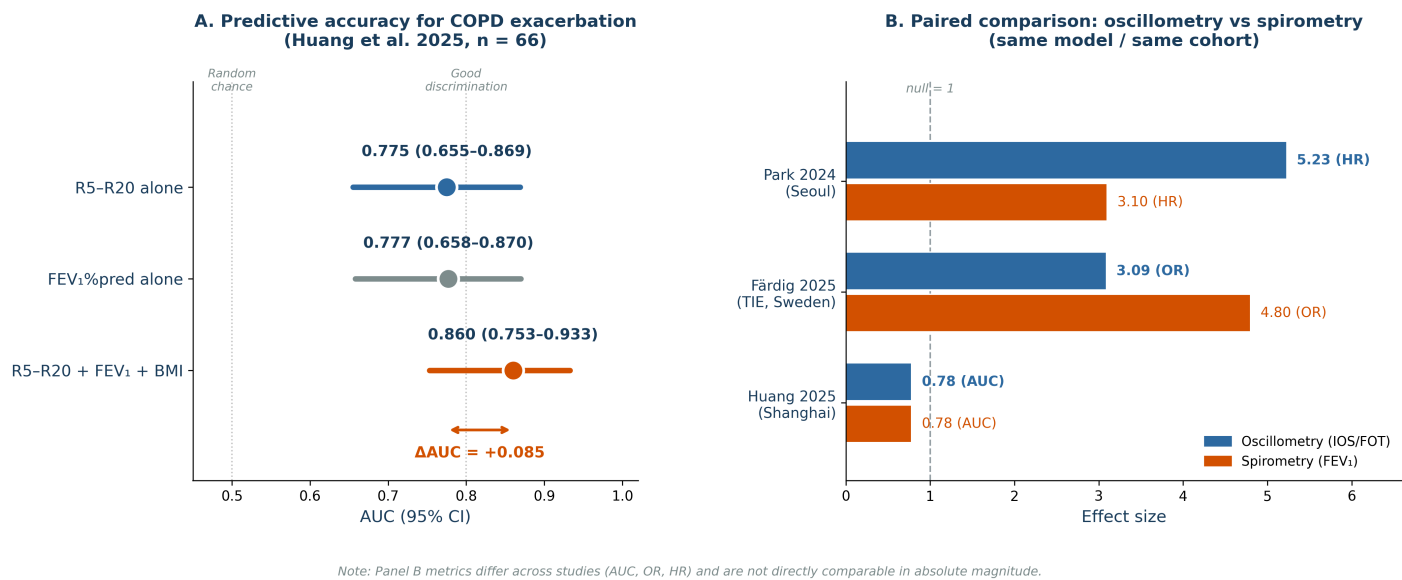


Figure 3

Head-to-head comparison of oscillometry vs spirometric indices. (a) AUC comparison from Huang et al. (COPD, n = 66). (b) Paired effect sizes from studies reporting both IOS and FEV₁ predictors in the same cohort. Effect-size metrics differ across studies (AUC, OR, HR) and are not directly comparable in absolute magnitude.

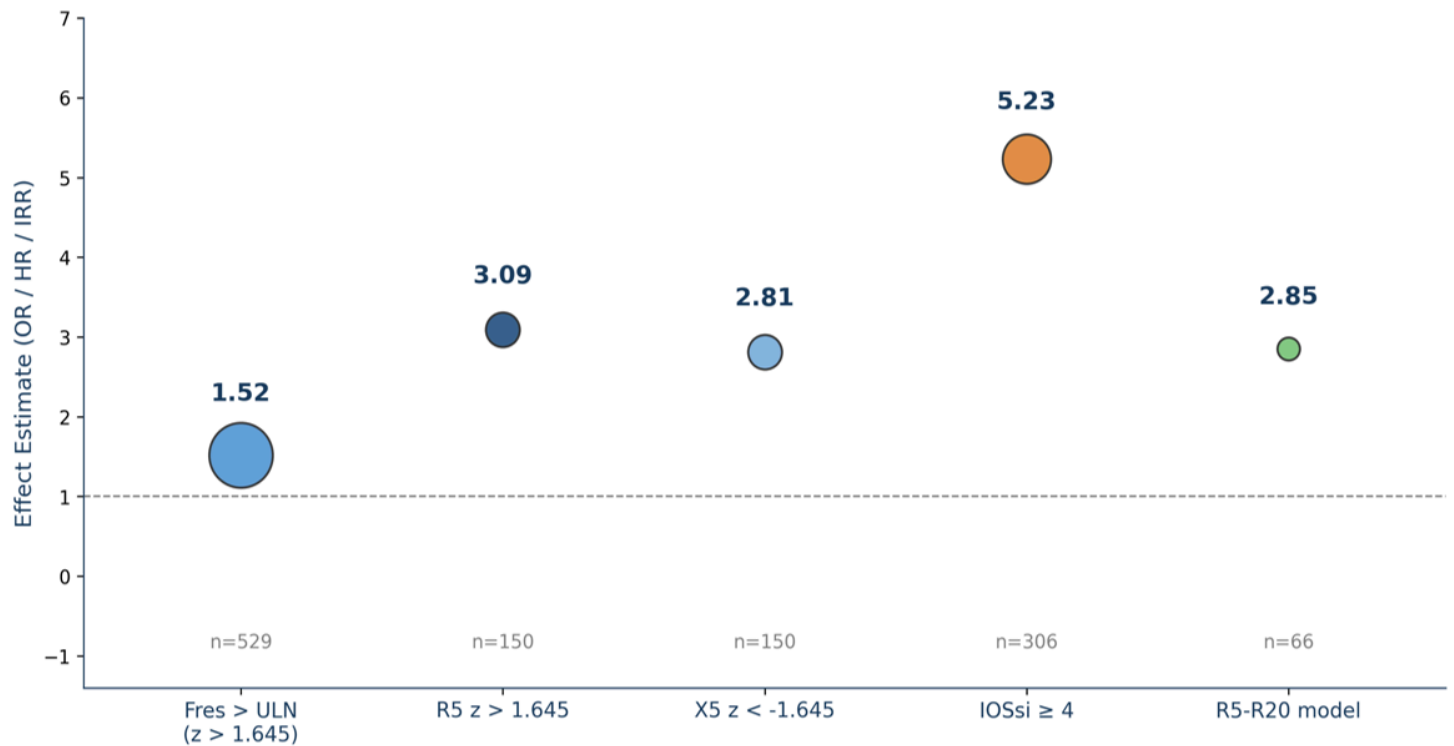


Figure 4

Oscillometry thresholds and associated risk of COPD exacerbations across included studies. Bubble size is proportional to the study sample size; the dashed horizontal line denotes the null effect (effect estimate = 1.0). Effect measures are reported as odds ratios, hazard ratios, or incidence rate ratios according to the original study and should be interpreted as complementary rather than directly interchangeable estimates.

	Risk of bias							Overall
	D1	D2	D3	D4	D5	D6	D7	
Study Lu 2025a (ECOPD, 3 yr)	+	+	+	+	+	+	+	+
Lu 2025b (ECOPD, 2 yr)	+	+	+	+	+	+	-	+
Färdig 2025	+	+	+	+	+	+	+	+
Zhang 2024	+	+	+	-	+	+	-	+
Zhang 2022	+	+	+	-	+	+	-	+
Huang 2025	-	-	+	+	+	-	-	-
Park 2024	-	-	+	+	+	+	-	-
Tseng 2025	-	-	+	+	+	+	-	-

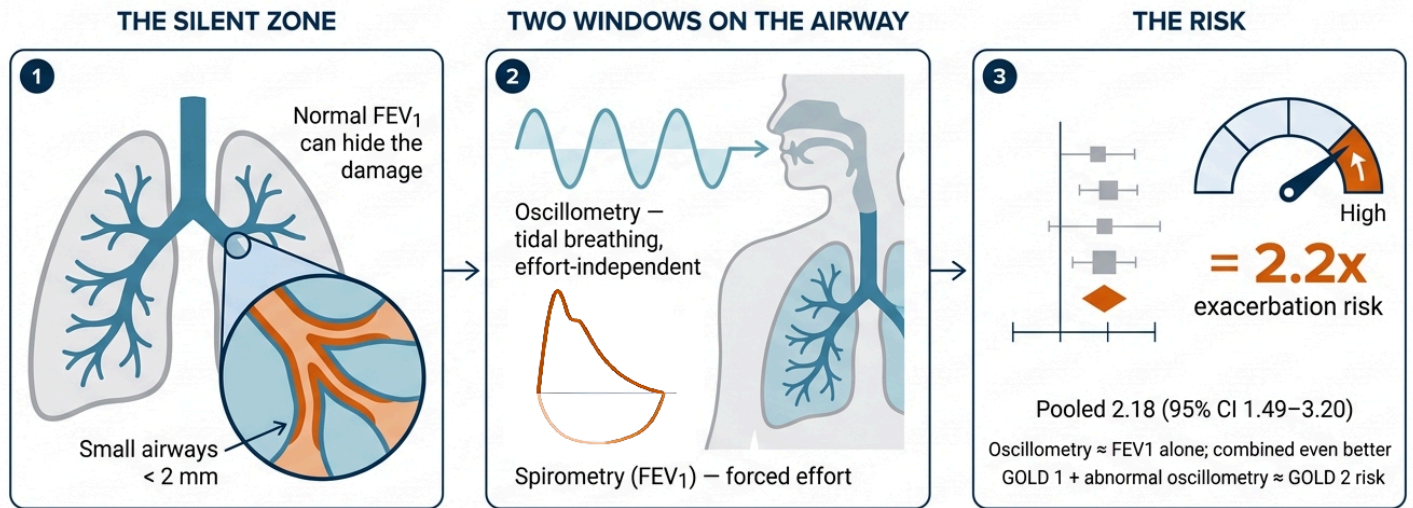
D1: Representativeness of exposed cohort
 D2: Selection of non-exposed cohort
 D3: Ascertainment of exposure
 D4: Comparability (design / analysis)
 D5: Assessment of outcome
 D6: Follow-up long enough
 D7: Adequacy of follow-up

Judgement
 - Unclear
 + Low

Figure 5

Risk of bias assessment using the Newcastle–Ottawa Scale for the included cohort studies.

Oscillometry-Defined Small Airway Dysfunction Predicts COPD Exacerbations



Systematic review & meta-analysis · 8 cohort studies (5 pooled) · 5 countries

Figure 6

Schematic illustration of oscillometry-defined small airway dysfunction in COPD. Oscillometry probes peripheral airways during tidal breathing; abnormal oscillometry with preserved FEV₁ marks a higher-risk phenotype (pooled ≈ 2.2-fold exacerbation risk). Conceptual illustration; not derived from study data.