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(copd OR "Pulmonary Disease, Chronic Obstructive"[Mesh])

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. 2025 Dec 16.

doi: 10.1186/s12931-025-03438-9. Online ahead of print.

Accuracy, comprehensiveness and understandability of AI-generated answers to questions from people with COPD: the AIR-COPD Study

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Collaborators, Affiliations Expand

- **PMID: 41402777**

- **DOI: 10.1186/s12931-025-03438-9**

No abstract available

Keywords: AI; Accuracy; Artificial intelligence; COPD; Comprehensiveness; Disease awareness; Reliability; Understandability.

Conflict of interest statement

Declarations: The AIR-COPD study was conducted in agreement with the current version of Declaration of Helsinki and the applicable regulations. Ethics approval and consent to participate: Not applicable. No interventions have been performed on patients for this research. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

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Thorax

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. 2025 Dec 15:thorax-2025-223282.

doi: 10.1136/thorax-2025-223282. Online ahead of print.

Disproportionate increase in COPD exacerbation risk for 3 months after discontinuing LAMA or ICS: insights from the FLAME trial

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- **PMID: 41402044**

- **DOI: 10.1136/thorax-2025-223282**

Abstract

Background: In real-world chronic obstructive pulmonary disease (COPD) care, poor adherence often leads to treatment discontinuations. Discontinuing inhaled corticosteroids (ICS) can trigger withdrawal effects transiently increasing exacerbation risk; but evidence for long-acting muscarinic antagonists (LAMA) withdrawal remains limited.

Methods: We performed a post hoc analysis of the 52-week, double-blind, Effect of Indacaterol Glycopyrronium versus Fluticasone Salmeterol on COPD Exacerbations trial that compared long-acting beta-2 agonist (LABA)+LAMA with LABA+ICS in

3362 patients with moderate-to-severe COPD and exacerbation history. Potential withdrawal effects after discontinuing LAMA or ICS were suggested by monthly exacerbation incidence plots during the first quarter of follow-up. Participants were stratified by their baseline use of these therapies, and outcomes were compared between the first and subsequent quarters among those who continued versus discontinued each treatment. Multivariable mixed-effects models assessed differences in exacerbation rates, with temporal variation in treatment effects interpreted as indicative of withdrawal effects.

Results: Discontinuing LAMA was associated with a marked, transient increase in moderate-to-severe exacerbations during the first versus subsequent quarters (p=0.001; rate ratio up to 2.2 (95% CI 1.2 to 4.1) in the subgroup least influenced by concomitant ICS use). This observation was not confirmed for severe exacerbations, likely due to low event count. In contrast, discontinuing ICS was associated with a significant early rise in severe exacerbations (p=0.023), though the difference for moderate-to-severe events did not reach statistical significance. Importantly, ICS withdrawal effects appeared consistent regardless of baseline blood eosinophil count.

Conclusion: Our findings suggest potent LAMA and ICS treatment withdrawal effects on exacerbations, highlighting the importance of treatment adherence and accounting for withdrawal effects in clinical trials.

Trial registration number: NCT01782326.

Keywords: COPD Exacerbations; COPD Pharmacology.

Conflict of interest statement

Competing interests: The authors declare no conflicts of interest directly related to this work. SB, VC-G, PS and J-USJ report no conflicts of interest. AGM reports honouraria for presenting from GSK, consulting fees from Sanofi, share options from ChestPal and non-financial support by Verona Pharma, not related to this work. NDB reports honouraria from AstraZeneca, GlaxoSmithKline, Sanofi, Orion, Chiesi, Teva and Boehringer Ingelheim and support for attending meetings from Chiesi, GlaxoSmithKline, AstraZeneca and Sanofi, not related to this work. JV reports consulting fees from GlaxoSmithKline, honouraria from AstraZeneca, Chiesi and GlaxoSmithKline, and participation on advisory board for GlaxoSmithKline, not related to this work. DS reports consulting fees from Adovate, Almirall, Anaveon, Apogee, Arcutis Biotherapeutics, Arrowhead, AstraZeneca, Belenos Biosciences, Bial, Celldex, Chiesi, Cipla, CONNECT Biopharm, Covis, DevPro Biopharma LCC, Elpen, Empirico, EpiEndo, Generate Biomedicines, GlaxoSmithKline, Glenmark, Jasper, Kinaset Therapeutics, KOLON, Kymera, Lupin, Melodia, Menarini, MicroA, OM Pharma, OrientEuroPharma, Recipharm, Revolo, RIGImmune, Roche, Roivant Sciences, Sanofi, Sitryx, Synairgen, Tetherex, UCB, Upstream, Verona Pharma, Winward, Zura Bio, Zymeworks, not related to this work.

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. 2025 Dec 16.

doi: 10.1007/s00063-025-01337-x. Online ahead of print.

[Core curriculum of intensive care and emergency medicine in internal medicine]

[Article in German]

DGIIN; DGIM; BDI; DGA; DGE; DGVS; DGG; DGHO; DGI; DGK; DGfN; DGP*; DGP**; DGRh; DGIIN und DGHO; Guido Michels [1], Stefan John [2], Hans-Jörg Busch [3], Matthias Baumgärtel [4], Klaus-Friedrich Bodmann [5], Stephan Braune [6], Michael Buerke [7], Kai-Uwe Eckardt [8], Philipp Enghard [8], Frank Erbguth [9], Georg Ertl [10], Wolf Andreas Fach [11], Valentin Fuhrmann [12], Frank Hanses [13], Hans Jürgen Heppner [14], Carsten Hermes [15], Uwe Janssens [16], Christian Jung [17], Christian Karagiannidis [18], Michael Kiehl [19], Stefan Kluge [20], Alexander Koch [21], Matthias Kochanek [22], Peter Korsten [23], Pia Lebiedz [24], Philipp M Lepper [25], Konstantin Mayer [26], Martin Merkel [27], Ursula Müller-Werdan [28], Martin Neukirchen [29], Michael Oppert [30], Alexander Pfeil [31], Reimer Riessen [32], Wolfgang Rottbauer [33], Christoph Sarrazin [34], Friedhelm Sayk [35], Sebastian Schellong [36], Alexandra Scherg [37], Daniel Sedding [38], Katrin Singler [39], Marcus Thieme [40], Carsten Willam [41], Sebastian Wolfrum [42], Karl Werdan [43]

Affiliations Expand

- PMID: 41400667

- DOI: 10.1007/s00063-025-01337-x

Abstract

in English, German

Internal medicine and its associated subspecialities represent an important cornerstone of intensive care and clinical emergency medicine. This curriculum-compiled by members of the German Society of Medical Intensive Care and Emergency Medicine (Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin), the German Society of Internal Medicine (Deutsche Gesellschaft für Innere Medizin) including subspeciality societies, the Professional Association of German Internists (Berufsverband Deutscher Internistinnen und Internisten, BDI) and the German Association for Palliative Medicine (Deutsche Gesellschaft für Palliativmedizin, DGP)-presents an overview of knowledge, skills (competence levels I-III), behaviors, and attitudes necessary for the highest treatment quality for the internal medicine aspects of intensive care and emergency medicine. It includes general aspects of intensive care and clinical emergency medicine (structure and process quality, emergency department: primary diagnostics and treatment as well as the indication for subsequent treatment, resuscitation room management, clinical syndromes in intensive care medicine, diagnostics and monitoring, general therapeutic measures, ethics, hygiene measures, and pharmacotherapy). Subsequently, specific aspects concerning angiology/vascular medicine, endocrinology, diabetology and metabolism, gastroenterology and hepatology, geriatric medicine, hematology and medical oncology, infectiology, cardiology, nephrology, palliative care, pneumology, rheumatology, and toxicology are addressed. Publications focusing on the content of advanced training are quoted to support this concept. The curriculum is written primarily for internists but may also show practicing intensivists and emergency physicians the broad spectrum of internal medicine diseases and comorbidities presented by patients admitted to the intensive care unit or the emergency department.

Keywords: German Medical Association; German Society of Internal Medicine; German Society of Medical Intensive Care and Emergency Medicine; Internal medicine training; Professional Association of German Internists.

Conflict of interest statement

Einhaltung ethischer Richtlinien. Interessenkonflikt: Dieses Manuskript wurde ohne finanzielle Unterstützung Dritter erstellt. Folgende Interessenkonflikte entsprechend ICMJE Disclosure Form (zurückliegende 36 Monate) wurden von den Autoren angegeben, aber nicht im Zusammenhang mit dem vorliegenden Manuskript gesehen. M. Baumgärtel: Honorare für Vorträge: Fa. Getinge, MSD, Novalung, Pfizer. Nichtmaterielle Interessenkonflikte – Funktionen in Fachgesellschaften: DGIIN (Mitglied des Wissenschaftlichen Beirats). K.-F. Bodmann: keine. S. Braune: Nichtmaterielle Interessenkonflikte – Funktionen in Fachgesellschaften: DGIIN (Stellvertretender Sektionssprecher Respiratorisches Versagen). M. Buerke: Honorare für Vorträge: Fa. AstraZeneca, Bayer Vital, Boehringer-Ingelheim, Daiichi-Sankyo, Novartis, Orion Pharma, Pfizer. Nichtmaterielle Interessenkonflikte – Funktionen in Fachgesellschaften: DGIIN (früherer Präsident, koordinierender Herausgeber der Zeitschrift Medizinische Klinik Intensivmedizin und Notfallmedizin; kooptiertes Vorstandsmitglied); DGK (Sprecher der AG 3 Kardiovaskuläre Intensiv- und Notfallmedizin). H.-J. Busch: Honorare für Vorträge: Fa. Zoll, Getinge und Braincool. Nichtmaterielle Interessenkonflikte – Funktionen in Fachgesellschaften: DGIIN (President-elect, Vorstandsmitglied, Sprecher der AG Reanimation und

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Multicenter Study

Int J Chron Obstruct Pulmon Dis

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. 2025 Dec 10:20:3993-4003.

doi: 10.2147/COPD.S554744. eCollection 2025.

Validation Study of Rome Criteria for Assessing COPD Exacerbation Severity and Predicting Clinical Outcomes: Turkish Thoracic Society COPD Assembly

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Affiliations Expand

- PMID: 41399649

- PMCID: PMC12702271

- DOI: 10.2147/COPD.S554744

Abstract

Objective: The Rome classification was introduced to assess the severity of acute exacerbation (AE) of chronic obstructive pulmonary disease (COPD) based on easily measurable variables. However, its validation for global use has not yet

reached a sufficient level. This study aims to evaluate the validity of the Rome criteria in determining the severity and prognosis of COPD AE in Turkey.

Methods: This multicenter study, conducted for the first time in Turkey and for the fourth time worldwide, included 750 patients diagnosed with AE-COPD who presented to emergency departments and outpatient clinics. According to the Rome criteria, patients were classified into three groups: mild, moderate, and severe AE-COPD.

Results: The study included 99 (13.2%) patients in the mild, 479 (63.9%) in the moderate, and 172 (22.9%) in the severe group. Emergency visits, hospitalizations, and ICU admissions in the past year were more frequent in the moderate and severe groups ($p < 0.001$ for all comparisons). Regarding outcomes of emergency or outpatient visits, most mild exacerbation cases were discharged ($p < 0.001$), while most moderate and severe exacerbations required hospitalization ($p < 0.001$). Compared to the moderate group, the severe exacerbation group had a higher risk of ICU admission ($p < 0.001$), NIV ($p < 0.001$), IMV ($p < 0.001$), in-hospital mortality ($p < 0.001$), and 30-day mortality ($p = 0.015$). No significant differences were found in 90-day mortality or 30 and 90-day readmission rates ($p = 0.258$, $p = 0.712$, $p = 0.681$, respectively). Survival analysis revealed no significant difference between the moderate and severe groups ($p = 0.764$).

Conclusion: The findings suggest that the Rome criteria can be successfully used to assess exacerbation severity in AE-COPD patients presenting to secondary and tertiary care hospitals in Turkey.

Keywords: COPD; exacerbation; mortality; prognosis; readmission.

Conflict of interest statement

The authors report no conflicts of interest in this work.

- 19 references
- 2 figures

Supplementary info

Publication types, MeSH termsExpand

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Comparative Study

J Comp Eff Res

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. 2026 Jan;15(1):e250111.

doi: 10.57264/cer-2025-0111. Epub 2025 Dec 15.

Cost-effectiveness modeling of mortality risk reduction comparing two fixed-dose combination triple therapies in moderate-to-very severe chronic obstructive pulmonary disease

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- PMID: 41392954

- DOI: 10.57264/cer-2025-0111

Free article

Abstract

Aim: Two fixed-dose combination triple therapies, budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF) 320/14.4/10 µg and fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) 100/62.5/25 µg, have been shown to reduce all-cause mortality in phase III trials. A recent matching-adjusted indirect comparison showed greater mortality reduction with BGF versus FF/UMEC/VI. However, the comparative cost-effectiveness of these treatments remains unknown. This study aimed to use a cost-effectiveness model to compare BGF with FF/UMEC/VI in patients with moderate-to-very severe chronic obstructive pulmonary disease (COPD) who are eligible for triple therapy from a UK third-party payer perspective. Materials & methods: A cohort-based semi-Markov model was used with the natural progression of COPD defined by four lung function levels. Input parameters included participant characteristics and clinical efficacy parameters derived from the ETHOS and KRONOS trials, the UK general population and published literature. Unit costs were obtained from the UK National Health System Schedule of Reference Costs (2021/2022), the Personal Social Services Research Unit (2022) and published literature. Outputs included an incremental cost-effectiveness ratio, costs, quality-adjusted life years and life years at time horizons of 1 and 5 years. Model inputs and assumptions were subject to deterministic and probabilistic sensitivity and scenario analyses. Results: At both 1- and 5-year time horizons, BGF was less costly (-£7.24 and -£23.03 per patient) and more effective (0.002 and 0.21 quality-adjusted life years per patient) versus FF/UMEC/VI, respectively. Due to a reduced mortality rate, more patients remained on BGF treatment than on FF/UMEC/VI, which induced higher treatment-related costs; however, the latter was offset by decreased end-of-life costs, as BGF avoided

more deaths. Conclusion: BGF may improve health outcomes and reduce healthcare costs compared with FF/UMEC/VI in patients with moderate-to-very severe COPD in a UK setting.

Keywords: budesonide/glycopyrronium/formoterol fumarate dihydrate; chronic obstructive pulmonary disease; cost-effectiveness; cost-effectiveness model; mortality; single-inhaler triple therapy.

Plain language summary

What is this article about? Chronic obstructive pulmonary disease (COPD) is a serious lung disease that makes breathing difficult and worsens over time. COPD greatly impacts healthcare systems and a person's quality of life. This study examined two inhaler treatments for COPD: budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF) and fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI). We aimed to understand which treatment was more effective at lowering healthcare costs, improving quality of life and reducing death in a UK setting. What methodology/protocol is described? COPD guidelines recognize that BGF and FF/UMEC/VI lower the risk of death, but a comparison of costs is lacking. A cost-effectiveness model was developed using phase III clinical trials with BGF and a published matching-adjusted indirect treatment comparison study of BGF and FF/UMEC/VI. The model evaluated the total healthcare costs and health benefits of BGF and FF/UMEC/VI inhaler treatments over 1- and 5-year periods in COPD that worsened over time. What were the results? The model showed that BGF was less costly and more effective compared with FF/UMEC/VI because it reduced deaths, which led to lower end-of-life care costs, even when taking BGF for a longer period. Why is this important? This study suggests that BGF not only improves patient health outcomes but could also reduce healthcare costs within the duration of 1 to 5 years. The findings support the use of BGF as a cost-effective treatment for patients with COPD, which may lead to better management of this disease.

Supplementary info

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J Heart Lung Transplant

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. 2025 Dec 12:S1053-2498(25)02458-1.

doi: 10.1016/j.healun.2025.12.007. Online ahead of print.

Distinct Plasma Proteome in Severe Pulmonary Hypertension Associated with Chronic Lung Disease

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- PMID: 41391649

- DOI: 10.1016/j.healun.2025.12.007

Abstract

Background: The mechanisms underlying the development and severity of pulmonary hypertension (PH) in chronic lung diseases (CLD) remain incompletely understood. To identify relevant pathobiological pathways, we analyzed the protein expression profile in plasma of patients with chronic obstructive pulmonary disease (COPD) and fibrosing interstitial lung disease (ILD), stratified by the presence and severity of PH, and explored similarities with idiopathic pulmonary arterial hypertension (iPAH).

Methods: Plasma samples from 114 patients with CLD -36 without PH (17 COPD, 19 ILD), 33 with non-severe PH (18 COPD, 15 ILD) and 45 with severe PH (28 COPD, 17 ILD)- and 38 with iPAH were analyzed using liquid chromatography-tandem mass spectrometry. We examined differential protein expression across groups and associations with hemodynamic measurements. Functional enrichment and protein interaction analyses were used to identify relevant biological pathways. Predictive protein combinations were analyzed using stepwise logistic regression.

Results: Patients with COPD and ILD showed distinct proteomic profiles in relation to their hemodynamic status. In COPD, the presence and severity of PH were associated with dysregulation of extracellular matrix homeostasis and cell adhesion pathways, among others. Patients with ILD showed fewer differentially expressed proteins linked to PH, with the most conspicuous differences involving proteins related to immune and inflammatory response pathways. Patients with severe COPD- or ILD-associated PH displayed proteomic signatures distinct from those of iPAH.

Conclusions: The pathophysiological mechanisms underlying the development of PH differ between COPD and ILD, and the proteomic profile of severe PH in both conditions is distinct from that observed in iPAH.

Keywords: Disease; Interstitial Lung; Pulmonary Hypertension; chronic obstructive pulmonary disease; idiopathic pulmonary arterial hypertension; plasma proteomics.

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Respir Investig

. 2025 Dec 12;64(1):101353.

doi: 10.1016/j.resinv.2025.101353. Online ahead of print.

Identification of individuals with COPD using biometric voice and cough sound features

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Affiliations Expand

- PMID: 41389529
- DOI: 10.1016/j.resinv.2025.101353

Abstract

Background: Chronic obstructive pulmonary disease (COPD), a major global health burden linked to smoking, is frequently underdiagnosed due to low awareness and delayed symptom recognition. This study explored the feasibility of non-invasive voice and cough sound analysis for COPD identification.

Methods: In this prospective study, 55 participants (26 with COPD, 29 without) underwent pulmonary function testing and provided sociodemographic and clinical data. Speech and cough sounds were recorded three times per participant and processed using acoustic feature extraction, feature selection via the minimum redundancy maximum relevance algorithm, and logistic regression classification. Model performance was evaluated using four-fold cross-validation. Statistical analysis was conducted with JMP software ($p < 0.05$).

Results: The vowel sound/u/showed statistically significant discriminatory ability in the mixed-gender cohort, but sensitivity and specificity were both below 80 %, indicating limited diagnostic performance. When restricted to male participants,

both metrics exceeded 80 %, suggesting higher discriminatory power. Smartphone recordings yielded comparable accuracy to integrated circuit recorders. Adding COPD assessment test scores and smoking history did not improve classification.

Conclusions: Voice analysis may offer a non-invasive screening approach for COPD. However, this study was limited to male participants and a single disease target, restricting generalizability. Future research will expand to include related respiratory conditions such as bronchiectasis and assess performance across sexes and disease types.

Keywords: COPD screening; Machine learning; Non-invasive biomarker; Voice sound analysis.

Conflict of interest statement

Declaration of competing interest Takahiro Takazono received honoraria for lecture fee from Insmed, Asahikasei, Shionogi, Pfizer, and MSD, and research grants from GSK, Asahikasei, and Shionogi; Hiroshi Mukae received honoraria for lecture fee from Asahi Kasei Pharma Corporation, AstraZeneca K.K., Chugai Pharmaceutical Co., Ltd., Gilead Sciences Inc., GlaxoSmithKline K.K, Insmed Incorporated, Kyorin Pharmaceutical Co., Ltd., MSD Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Novartis Pharma K.K, Pfizer Inc., SHIONOGI Co., Ltd., and Taisho Pharma Co., Ltd., and research grants from FUJIFILM Toyama Chemical Co., Ltd, Kyorin Pharmaceutical Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Otsuka Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd., Taisho Pharma Co., Ltd., and SHIONOGI Co., Ltd. and Donations from Taiho Pharmaceutical Co., Ltd., and Taisho Pharma Co., Ltd.; the other authors have no conflict of interest.

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Respir Investig

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. 2025 Dec 12;64(1):101348.

doi: 10.1016/j.resinv.2025.101348. Online ahead of print.

High-intensity inspiratory muscle training and diaphragm thickness in severe COPD: a prospective pilot study

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Affiliations Expand

- PMID: 41389528

- DOI: 10.1016/j.resinv.2025.101348

Abstract

High-intensity inspiratory muscle training (IMT) has been reported to increase diaphragm thickness in healthy adults, but evidence in severe chronic obstructive pulmonary disease (COPD) remains scarce. This prospective pilot study evaluated the effects of high-intensity IMT on diaphragm thickness and functional outcomes in nine patients with severe COPD who had completed standard respiratory rehabilitation. Participants performed 30 breaths per day at 60 % of maximum inspiratory pressure for 12 weeks. Diaphragm thickness at maximum inspiration increased from 4.7 to 5.6 mm, maximum inspiratory pressure from 57.1 to 68.1 cmH_2O, 6-min walk distance from 318 to 366 m, and COPD Assessment Test scores from 19 to 12, both exceeding the minimal clinically important difference thresholds (all $p < 0.01$). These findings suggest that high-intensity IMT may be a feasible and beneficial adjunct for improving inspiratory function and symptoms in patients with severe COPD.

Keywords: COPD; Diaphragm thickness; Inspiratory muscle training; Pulmonary rehabilitation; Ultrasound.

Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest

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Thorax

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. 2025 Dec 12:thorax-2025-223967.

doi: 10.1136/thorax-2025-223967. Online ahead of print.

Measurement properties of the sit-to-stand test in community-dwelling people with chronic obstructive pulmonary disease: a COSMIN systematic review

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Affiliations Expand

- PMID: 41386962

- DOI: 10.1136/thorax-2025-223967

Abstract

Background: The sit-to-stand (STS) test can assess physical function in people with chronic obstructive pulmonary disease (COPD); however, there are multiple versions. No study has used current guidelines to assess the measurement properties of the STS tests in people with COPD.

Methods: We conducted a systematic review using current COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines. Full text peer-reviewed publications were included if they assessed the measurement properties (validity, reliability and/or responsiveness) of at least one STS test among community-dwelling people with COPD. We searched six databases and imported results into Covidence where title/abstract screening and full text selection was completed independently and in duplicate. Extraction was conducted independently and in duplicate using the COSMIN extraction file. We assessed study risk of bias (very good, adequate, doubtful or inadequate), measurement property quality (sufficient, indeterminate or insufficient) and overall certainty of evidence (high, moderate, low or very low) using the COSMIN recommended tools.

Results: We assessed 2577 titles/abstracts and 102 full texts for inclusion; 30 publications met eligibility. Seven unique STS tests were located with the most common being the 1 min STS test (n=14, 39%), 5-repetition STS test (n=10, 28%) and the 30 s STS test (n=8, 22%). Where assessed, reliability was sufficient for the 1 min, the 5-repetition and the 30 s STS tests. Only the 1 min STS test had high-quality evidence of sufficient construct validity, while the 30 s STS test was the sole test with at least moderate quality evidence of sufficient responsiveness.

Conclusions: The 1 min STS test has the most robust measurement properties for cross-sectional assessments while the 30 s STS test is more robust to assess change.

Keywords: Exercise; Pulmonary Disease, Chronic Obstructive; Pulmonary Rehabilitation.

Conflict of interest statement

Competing interests: None declared.

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Cite

10

Eur Respir J

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. 2025 Dec 11:2501435.

doi: 10.1183/13993003.01435-2025. Online ahead of print.

A multi-country cohort study evaluating the prevalence, risk factors, lung function and clinical outcomes of chronic bronchitis in low- and middle-income countries

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- PMID: 41381225

- DOI: 10.1183/13993003.01435-2025

Abstract

Background: Chronic bronchitis affects up to 40% of individuals with COPD and may serve as an early predictor of the disease and development of COPD. We investigated the prevalence, risk factors, and clinical outcomes associated with chronic bronchitis in three low- and middle-income countries (LMICs).

Methods: We conducted a population-based study of adults aged ≥40 years in Bhaktapur (Nepal), Lima (Peru), and Nakaseke (Uganda). Chronic bronchitis was defined as a productive cough several days per week for over four weeks. Multivariable log-binomial regression identified risk factors and outcomes associated with chronic bronchitis.

Results: Among 9664 participants (mean age 56.2 years, 51.0% male, 66.9% ever smokers), chronic bronchitis prevalence was 9.7%, with 31.5% of those also having

COPD. Significant risk factors included older age (adjusted RR=1.54 per 19.8 years, 95% CI 1.4-1.7), male sex (1.18, 1.05-1.34), prior tuberculosis (1.45, 1.14-1.83), prior asthma diagnosis (2.11, 1.84-2.42), pack-years of tobacco use (1.16 per 10 pack-years, 1.14-1.18), family history of chronic respiratory diseases (1.69, 1.50-1.91), second-hand smoke exposure (1.45, 1.28-1.64), lower socioeconomic status quartile (1.22,1.07-1.39), and indoor biomass exposure (1.45, 1.13-1.64). Participants with chronic bronchitis experienced more breathlessness, worse respiratory health (higher St. George's Respiratory Questionnaire scores), and higher hospitalization rates (all p<0.001).

Conclusions: Chronic bronchitis is common in LMIC settings and is associated with multiple modifiable risk factors, including second-hand smoke, biomass exposure, and prior respiratory disease. Addressing these factors may reduce disease burden and improve quality of life.

Cite

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J Appl Physiol (1985)

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. 2025 Dec 11.

doi: 10.1152/japplphysiol.00795.2025. Online ahead of print.

Dyspnea and Respiratory EMG in Patients with COPD: Results of the COPD Monitoring Study

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- PMID: 41379596

- DOI: 10.1152/japplphysiol.00795.2025

Free article

Abstract

Exertional dyspnea is the main symptom of COPD. Based on the positive relationship between the levels of dyspnea (Borg-score) and the electrical activity of respiratory muscles (electromyogram, EMG) during an incremental cardiopulmonary exercise test, it has been suggested that respiratory EMG can provide a physiological biomarker for dyspnea. This study aimed to characterize the relationship between dyspnea and EMG during exercises simulating daily activities. Surface EMG was measured at 2 locations on the chest of 28 COPD patients while they were performing constant-work rate cycling tests and walking/cycling exercises that were part of their rehabilitation program. Simultaneously, the level of dyspnea was assessed using the Borg-score at several timepoints throughout the exercise sessions, along with respiration rate (RR), heart rate (HR) and transcutaneous oxygen saturation (SpO_2). Patients completed each up to 10 such study visits during their 8-week stay at the rehabilitation center (CIRO, the Netherlands). In total, 1981 Borg-scores with associated EMG measurements were recorded during 263 study visits. A linear mixed model was used to assess the relation of the Borg-score with EMG while controlling for RR, HR, (type of) exercise, SpO_2, age and sex. Random effects for patient and visit were included to account for correlation in the measurements. EMG had a highly significant association with the Borg-score ($p<0.0001$). Respiratory EMG and Borg-score showed consistent positive correlations, of which the magnitude varied between patients. These results indicate that respiratory EMG can provide a physiological biomarker for dyspnea during activities of daily living in COPD patients.

Keywords: Biomarker; Borg-score; COPD; Electromyogram; Respiratory muscle.

Supplementary info

Grants and fundingExpand

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Chronic Obstr Pulm Dis

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. 2025 Dec 9.

doi: 10.15326/jcopdf.2025.0698. Online ahead of print.

Upper and Lower Limb Skeletal Muscle Mass Index as a Novel Evaluation Index in Patients with Chronic Obstructive Pulmonary Disease

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Affiliations Expand

- PMID: 41378828

- DOI: 10.15326/jcopdf.2025.0698

Free article

Abstract

Objectives: The objective of this study was to examine the relationships and usefulness of physical activity, physical performance, and physical function in patients with chronic obstructive pulmonary disease (COPD), focusing on two newly proposed skeletal muscle indices: the upper limb skeletal muscle mass index (USMI) and lower limb skeletal muscle mass index (LSMI).

Methods: Eighty stable patients with COPD who participated in outpatient pulmonary rehabilitation at Osaka Fukujuji Hospital were enrolled. The primary measurements were USMI, LSMI, and Skeletal Muscle Index (SMI). The explanatory measurements included physical activity, Incremental Shuttle Walking Distance (ISWD), quadriceps strength, handgrip strength, the Nagasaki University Respiratory Activities of Daily Living Questionnaire (NRADL), and pulmonary function. Pearson's correlation coefficient and stepwise multiple regression analysis were used for the statistical analyses.

Results: USMI showed no significant correlations with physical activity parameters or ISWD. In contrast, LSMI was significantly correlated with weekly exercise volume ($r = 0.42$, $p < 0.01$), daily exercise volume ($r = 0.42$, $p < 0.01$), time spent in activities ≥3 Metabolic Equivalents of Task (METs) ($r = 0.40$, $p < 0.01$), and ISWD ($r = 0.46$, $p < 0.01$). Multiple regression analysis identified ISWD as an independent factor for USMI, LSMI and SMI.

Conclusion: This study demonstrated that LSMI, similar to SMI, was associated with physical activity and exercise capacity in patients with COPD. These findings highlight the importance of evaluating, maintaining, and strengthening lower limb skeletal muscle mass and suggest that LSMI may serve as a useful clinical evaluation index.

Keywords: chronic obstructive pulmonary disease; lower limb skeletal muscle mass index; upper limb skeletal muscle mass index.

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Chronic Obstr Pulm Dis

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. 2025 Dec 9.

doi: 10.15326/jcopdf.2025.0689. Online ahead of print.

The Long-Term Effects of Cost-Related Nonadherence on COPD Outcomes and Progression in the COPDGene Study Cohort

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Affiliations Expand

- PMID: 41378823

- DOI: 10.15326/jcopdf.2025.0689

Free article

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease with a high prevalence and cost burden on the health care system. Overall, adherence to prescribed therapies is low and associated with worse outcomes.

Research question: Cost-related nonadherence (CRN) is a type of nonadherence that could be addressed through policy. We are evaluating the long-term association of CRN on COPD outcomes in a well-profiled cohort.

Study design and methods: We identified 2,521 participants with baseline COPD and having answered the social and economic questionnaire in the COPDGene cohort. Of these, 408 participants endorsed experiencing CRN. Multivariable regression models were utilized to assess the association of experiencing CRN and COPD outcomes including functional status, health status, and progression of disease.

Results: Experiencing CRN is associated with worse functional status by 6MWD, symptom burden by CAT Score and health status by SGRQ. Longitudinal analysis reveals an association of CRN with faster lung function decline and increased risk of COPD exacerbations.

Interpretation: Policy changes to address out-of-pocket medication costs may improve COPD outcomes and potentially lead to long-term cost savings.

Keywords: COPD; adherence; health outcomes; maintenance therapy.

Supplementary info

Grants and fundingExpand

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14

Sci Rep

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. 2025 Dec 11.

doi: 10.1038/s41598-025-31223-7. Online ahead of print.

Physical activity attenuates PD-1/PD-L1 expression and enhances CD4⁺ T-cell function in COPD patients

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Affiliations Expand

- PMID: 41372350

- DOI: 10.1038/s41598-025-31223-7

Free article

No abstract available

Keywords: COPD; Immune checkpoint; PD-1; PD-L1; Physical activity level; T-cells.

Conflict of interest statement

Competing interests: The authors declare no competing interests.

- 51 references

Supplementary info

Grants and fundingExpand

Cite

15

Eur Radiol

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. 2025 Dec 9.

doi: 10.1007/s00330-025-12188-7. Online ahead of print.

Quantitative CT of emphysema, wall thickness and mucus plugs in alpha-1-antitrypsin deficiency: relationship to clinical outcomes

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Affiliations Expand

- PMID: 41364209

- DOI: 10.1007/s00330-025-12188-7

Abstract

Objectives: Alpha-1-antitrypsin deficiency (AATD) is a rare genetic disorder leading to chronic obstructive pulmonary disease (COPD). Emphysema is the major structural damage visible on CT scans. However, there is little knowledge on the association between other structural abnormalities, such as bronchiectasis (BE), airway wall thickening (WT) or mucus plugs (MP), and clinical features.

Materials and methods: Retrospective study between 2008 and 2022 at one University Hospital of Bordeaux on all consecutive AATD patients. Bronchial and parenchymal alterations were evaluated with an (artificial intelligence) AI-driven Normalized Volume of Airway Abnormalities (NOVAA-CT) scoring system, including BE, WT, MP and emphysema quantifications. We evaluated correlations between forced expiratory volume in 1-s (FEV1%), dyspnea severity through the mMRC scale and the occurrence of at least one exacerbation in the year following CT scan.

Results: Fifty-two AATD patients were included (median FEV1: 47% (40-65)). CT features of BE, WT and MP were present in 100%, 94.2% and 59% of the study population, respectively, with a lower versus upper lung predominance ($p < 0.05$).

WT ($p < 0.001$) and BE ($p = 0.04$) correlated with FEV1% but not mMRC ($p \geq 0.09$). Conversely, MP did not correlate with FEV1% ($p = 0.08$) but with mMRC ($p = 0.01$). Emphysema strongly correlated with both FEV1% and mMRC ($p < 0.001$). In multivariate analysis, after adjustment for age, genotype and tobacco consumption, the best predictor of exacerbation was WT (OR = 1.12 [1.02-1.22]; $p = 0.01$).

Conclusion: This study demonstrates that AI-assisted identification of structural airway abnormalities is frequent in AATD patients and carries distinct clinical significance. Among them, WT was the most robust predictor of exacerbations.

Key points: Question Emphysema is the major structural damage in alpha-1-antitrypsin deficiency (AATD). Clinical associations of bronchial abnormalities such as bronchiectasis (BE), mucus plugs (MP) and wall thickness (WT) are lacking. Findings Quantitative CT of BE and WT correlated with PFT ($p \leq 0.05$), while MP correlated with dyspnea scale ($p = 0.01$). The best predictor of exacerbation was WT (OR = 1.12 [1.02-1.24]). Clinical relevance AI-assisted identification of bronchial abnormalities is frequent in AATD patients in addition to emphysema alone and carries distinct clinical significance. These findings highlight the importance of comprehensive CT-based evaluations to better characterize disease phenotype and guide clinical management in AATD.

Keywords: Alpha-1-antitrypsin deficiency; Artificial intelligence; CT scan; Chronic obstructive pulmonary disease; Exacerbation.

Conflict of interest statement

Compliance with ethical standards. Guarantor: The scientific guarantor of this publication is Gael Dournes. Conflict of interest: The authors of this manuscript declare relationships with the following companies: Patrick Berger: GSK, AstraZeneca, Sanofi, Chiesi. Maeva Zysman: GSK, AstraZeneca, Menarini, Novartis, CSL Behring, Chiesi, Pfizer. Gael Dournes: Sanofi, AstraZeneca, Vertex Pharmaceuticals. The other authors do not have relationship of interest with the manuscript content. Statistics and biometry: One of the authors (Patrick Berger) has significant statistical expertise. No complex statistical methods were necessary for this paper. Informed consent: Written informed consent was waived by the Institutional Review Board. Ethical approval: Institutional Review Board approval was obtained. Study subjects or cohorts overlap: None. Methodology: Retrospective Observational Performed at one institution

- 37 references

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Expert Rev Respir Med

. 2025 Dec 11:1-9.

doi: 10.1080/17476348.2025.2596919. Online ahead of print.

Understanding the relationship between eosinophils and chronic obstructive pulmonary disease. A new dawn?

Clare Tiedeman [1], Ian Pavord [1]

Affiliations Expand

- PMID: 41359670

- DOI: 10.1080/17476348.2025.2596919

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a leading cause of global morbidity and mortality. It is a complex and heterogeneous condition defined by the presence of an incompletely reversible airflow obstruction.

Area covered: Airway inflammation and remodeling are central to the pathogenesis of this airflow limitation, and eosinophilic or type 2 inflammation has emerged as a measurable and treatable therapeutic target in those patients in whom it is identified. This review addresses the role of type 2 inflammation in COPD pathogenesis as well as current and future therapeutic options.

Expert opinion: The last 15 years has seen the emergence of a precision medicine, type-2 biomarker directed approach to the use of inhaled corticosteroids in COPD, resulting in better targeting of treatment and an increased benefit/risk ratio. We have also seen the approval of first biological therapy against type 2 inflammation in COPD. There is increasing interest in biomarker directed early intervention to prevent progression or even the development of COPD.

Keywords: COPD; biologic treatments; eosinophils; lung function decline; treatable traits.

. 2025 Dec 13:thorax-2025-223457.

doi: 10.1136/thorax-2025-223457. Online ahead of print.

Multidisciplinary, non-pharmacological breathlessness intervention service for patients with moderately severe to severe COPD: a randomised controlled trial

Tracy A Smith [1 2], Mary M Roberts [3 2 4 5], Tim Luckett [5], Jin-Gun Cho [3 2 4], Ester Klimkeit [3], Heather Stephenson [3], Nicola McCaffrey [6], Adrienne Kirby [7], John R Wheatley [3 2 4]

Affiliations Expand

- PMID: 41309286

- DOI: 10.1136/thorax-2025-223457

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is an often-progressive respiratory disease associated with disabling breathlessness. Breathlessness intervention services (BIS), which coach patients to self-manage breathlessness using non-pharmacological strategies, are effective in a variety of populations, including those with cancer and serious respiratory disease. This study aimed to compare the impact of the Westmead Breathlessness Service in people with moderate to severe COPD.

Methods: We analysed 113 participants randomised (1:1) with moderate/severe COPD (forced expiratory volume in 1 s (FEV_1)/forced vital capacity <0.70 and FEV_1 ≤60% predicted) and disabling breathlessness (modified Medical Research Council (mMRC) Breathlessness Score ≥2) to either an 8-week intervention involving breathing techniques, handheld fan use, exercise, energy conservation, dietetic advice (n=54) or 8-week wait-list control group (n=59). The primary outcome was change in Chronic Respiratory Questionnaire (CRQ) Mastery of breathlessness subscale. Secondary outcomes included change in other CRQ subscales (Fatigue, Emotion and Dyspnoea), exertional breathlessness intensity/unpleasantness (0-10 Numerical Rating Scale Score), anxiety and depression. Difference in change over 8 weeks between groups was compared using ANCOVA; p<0.05 statistically significant.

Findings: Participants were aged 70.9 (±8.5) years, 50% female, mean FEV_1 =0.8 L (±0.3 L; 34% predicted), mMRC Breathlessness Score 3 (IQR 3-4). CRQ-Mastery improved following intervention compared with control (between-group difference 0.5 units; 95% CI 0.2 to 0.8; p=0.0262) using modified intention-to-treat analysis. Better CRQ-Dyspnoea and CRQ-Fatigue were seen in the intervention group (between-group difference-CRQ-Dyspnoea 0.4 units; CI 0.1 to 0.7; p=0.005, and CRQ-Fatigue 0.4 units; CI 0.1 to 0.7; p=0.014). Exertional breathlessness intensity

(difference -0.8 units; CI -1.4 to -0.2; p=0.013) and breathlessness unpleasantness (difference -1.2 units; CI -1.7 to -0.6; p=0.001) also improved.

Interpretation: An 8-week BIS improved CRQ-Mastery, Dyspnoea and Fatigue, exertional breathlessness intensity and unpleasantness in people with severe COPD.

Keywords: COPD Exacerbations; Palliative Care; Perception of Asthma/Breathlessness.

Conflict of interest statement

Competing interests: None declared.

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Thorax

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. 2025 Dec 15;81(1):61-70.

doi: 10.1136/thorax-2024-222795.

Time to diagnosis and long-term outcomes for adults presenting with breathlessness

Urvee Karsanji [1], Claire A Lawson [2], Emily Petherick [3], Kamlesh Khunti [4], Gillian Doe [1], Jennifer K Quint [5], Alex Bottle [5], Michael C Steiner [1], Rachael A Evans [6]

Affiliations Expand

- PMID: 41285477

- DOI: 10.1136/thorax-2024-222795

Abstract

Background: The impact of delays to diagnosis for individuals presenting with chronic breathlessness is unknown. We investigated the time to diagnosis after

presenting with chronic breathlessness and associations with future unplanned hospitalisation and mortality.

Methods: A retrospective cohort study using the UK Clinical Practice Research Datalink involving adults with a first recorded code for breathlessness and no pre-existing cardiorespiratory disease. Adjusted Cox regression was used to investigate the associations with unplanned hospitalisation and mortality during all follow-up and within 2 years after the first code of breathlessness between those with and without a diagnosis, and using landmark analysis for time to diagnosis.

Results: 66 909/101 369 (66%) of adults with a first recorded code for breathlessness received an explanatory diagnosis during a median 5 years of follow-up. 43 394 (43%) of adults received an explanatory diagnosis within 2 years and had a higher risk (HR (95% CI)) of unplanned hospitalisation (1.25, 1.19 to 1.31) and mortality (1.84, 1.42 to 2.38) in the subsequent 2 years compared with adults without a diagnosis. In those with a recorded diagnosis, waiting ≥6 months was associated with increased mortality (6-24 months: 3.33 (2.13 to 5.20); ≥24 months: 13.30 (8.98 to 19.80)).

Conclusion: We describe better outcomes in adults coded for breathlessness without subsequent explanatory diagnoses. In adults with an explanatory diagnosis, waiting ≥6 months for a diagnosis was associated with reduced survival. Diagnostic pathways for chronic breathlessness need to differentiate between these two groups and achieve earlier diagnosis in those at higher risk.

Keywords: Asthma; Bronchiectasis; COPD epidemiology; Clinical Epidemiology; Interstitial Fibrosis; Symptom Assessment.

Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure. KK is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC).

- Cited by 1 article

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Review

Physiol Int

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. 2025 Oct 27;112(4):428-444.

doi: 10.1556/2060.2025.00704. Print 2025 Dec 11.

Cardiopulmonary exercise testing in chronic obstructive pulmonary disease

Diana Poparcea [1], Alexandru Corlateanu [1], Alexandr Ceasovschih [2 3], Janos T Varga [4]

Affiliations Expand

- **PMID: 41143924**

- **DOI: 10.1556/2060.2025.00704**

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a common lung disease causing airflow obstruction and breathing problems. Despite the current advances in the treatment of COPD, exercise intolerance remains a challenge, impacting quality of life and increased morbidity. Cardiopulmonary exercise testing (CPET) is a non-invasive test with concomitant gas exchange analysis that provides a thorough assessment of exercise physiology, involving the integrative respiratory, cardiovascular, muscle and metabolic responses to exercise, and, thus providing insights into exercise limitation mechanisms. This review hypothesizes that CPET offers prognostic value in COPD and can be used to evaluate the response to several therapeutic interventions.

Aim: To investigate the clinical usefulness of CPET in assessing exercise tolerance, disease progression and therapeutic outcomes in COPD patients.

Methods: This this systematic literature review was conducted to analyse studies published between 2020 and 2024 on the role of CPET in COPD management. Studies were reviewed focusing on CPET's prognostic value, its correlation with disease severity, and its impact on therapeutic strategies. The quality of the selected studies was assessed by using PRISMA guidelines.

Results: As a result, CPET-integrated monitoring supports as a valuable tool for evaluating exercise intolerance in COPD, with parameters such as peak oxygen uptake ($\dot{V}O_2$ peak), ventilatory efficiency ($\dot{V}E/\dot{V}CO_2$ slope), and dynamic hyperinflation correlating with disease severity and prognosis. According to studies a $\dot{V}O_2$ peak value below 15 mL kg-1 min-1 is associated with increased mortality risk and hospitalizations. Undoubtedly, CPET-derived thresholds for ventilatory and cardiovascular limitations remain an invaluable tool for COPD diagnosis and

management, and contribute to optimizing rehabilitation strategies and pharmacological interventions.

Conclusion: CPET provides important information about the pathophysiology of exercise intolerance in COPD, helping with personalized treatment planning and risk stratification. CPET should be integrated into COPD management guidelines.

Keywords: cardiopulmonary exercise testing; chronic obstructive pulmonary disease; oxygen uptake; pulmonary rehabilitation.

Supplementary info

Publication types, MeSH termsExpand

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Multicenter Study

Am J Cardiol

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. 2025 Dec 15:257:101-109.

doi: 10.1016/j.amjcard.2025.08.020. Epub 2025 Aug 16.

Clinical Characteristics and Prognosis of Acute Heart Failure in Patients with Chronic Obstructive Pulmonary Disease

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Affiliations Expand

- PMID: 40819680

- DOI: 10.1016/j.amjcard.2025.08.020

Abstract

This study describes clinical profiles of acute heart failure (AHF) patients from the Heart Failure Registry of Patient Outcomes (HERO) study and evaluates the prognostic impact of chronic obstructive pulmonary disease (COPD). HERO

enrolled 5,620 hospitalized AHF patients (November 2017 to 2018); 4,428 were followed. Primary endpoint: composite all-cause death or heart failure (HF) readmission. Secondary endpoints included all-cause death, HF readmission, and cardiovascular death. Patients were stratified by COPD status. Clinical characteristics were compared. Adjusted multivariate Cox regression estimated hazard ratios (HRs) with 95% confidence intervals (CIs) for COPD's impact on outcomes. Kaplan-Meier analysis (log-rank test) compared time-to-event data; sensitivity analyses were performed. Of 4,428 patients, 405 (9.2%) had COPD. COPD patients were older, more often male, had lower education, higher smoking rates, and received care predominantly in secondary hospitals. They had lower body mass index (BMI), higher heart rate, elevated hemoglobin (Hb), higher New York Heart Association (NYHA) class IV prevalence, but lower N-terminal pro-B-type natriuretic peptide (NT-proBNP). Hypertension, diabetes, and coronary artery disease were less frequent; hyponatremia was more common. Use of renin-angiotensin-aldosterone system (RAAS) inhibitors, β-blockers, statins, and diuretics was significantly lower in the COPD group. After adjustment, COPD independently predicted higher risks for the composite endpoint (HR = 1.38, 95% CI: 1.17 to 1.62, p <0.001), HF readmission (HR = 1.26, 95% CI: 1.02 to 1.55, p = 0.047), cardiovascular death (HR = 1.38, 95% CI: 1.09 to 1.74, p = 0.008), and all-cause death (HR = 1.40, 95% CI: 1.15 to 1.72, p = 0.001). Survival curves showed early and widening separation, indicating worse COPD outcomes. COPD independently increases adverse outcome risk in AHF patients. These individuals often present with poorer baseline health, leading to unfavorable prognosis. Integrated multidisciplinary care and individualized treatment are crucial to improve survival.

Keywords: acute heart failure; chronic obstructive pulmonary disease; comorbidity; prognosis.

Conflict of interest statement

Declaration of competing interest The authors declare that they have known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary info

Publication types, MeSH termsExpand

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21

Thorax

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. 2025 Dec 15;81(1):51-60.

doi: 10.1136/thorax-2024-222871.

Air pollution, genetic susceptibility and risk of progression from asthma to COPD

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Affiliations Expand

- PMID: 40691049

- DOI: 10.1136/thorax-2024-222871

Abstract

Background: In the UK, an estimated 15% of asthma patients have concurrent chronic obstructive pulmonary disease (COPD), yet the underlying causes and mechanisms remain largely unexplored. This study aimed to investigate the roles of both ambient air pollution and genetic susceptibility in the progression from asthma to COPD.

Methods: 46 832 participants with asthma were recruited from the UK Biobank during the baseline period (2006-2010). Particulate matter with a diameter of 2.5 µm ($PM_{2.5}$) and nitrogen dioxide (NO_2) were estimated at baseline address using land-use regression models. Air pollution score reflected joint exposure to air pollution. Polygenic risk score was calculated using novel genetic signals identified for coexistence of asthma+COPD. Cox proportional hazards regression analysis was employed to quantify the risks of both ambient air pollution and genetic scores on incident COPD among asthmatics, adjusting for covariates.

Results: Over a median follow-up of 10.84 years, 3759 participants with asthma at baseline developed COPD. For an IQR increase in $PM_{2.5}$ and NO_2, the HR for developing COPD was 1.07 (95% CI: 1.02 to 1.11) and 1.10 (95% CI: 1.04 to 1.15), respectively. Adverse effects could be observed at concentrations as low as 8 µg/m^3 for $PM_{2.5}$ and 12 µg/m^3 for NO_2. A significant multiplicative interaction was identified between ambient air pollution and genetic susceptibility. Individuals with the highest genetic risk score exhibited the greatest risk, with an HR of 1.13 (95% CI: 1.05 to 1.22) per IQR increase in air pollution score ($P_{interaction}$ <0.05).

Conclusions: Ambient air pollution is strongly associated with progression from asthma to comorbidity COPD, particularly among individuals with high genetic risk.

Keywords: Asthma Epidemiology; Asthma Genetics; COPD epidemiology; Clinical Epidemiology.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

MeSH terms, Substances

"Multimorbidity"[Mesh Terms] OR Multimorbidity[Text Word]

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J Pediatr

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. 2025 Dec 12:114948.

doi: 10.1016/j.jpeds.2025.114948. Online ahead of print.

Neonatal Multimorbidity is a Poor Predictor of Health and Developmental Outcomes after Preterm Birth

Jonathan S Litt [1], Mandy B Belfort [2], Erika M Edwards [3], Henning Tiemeier [4]

Affiliations Expand

- PMID: 41391543

- DOI: 10.1016/j.jpeds.2025.114948

Abstract

Objective: To test and compare the capability of three multimorbidity-based models to predict outcomes in early childhood among infants born with extremely low birth weight (<1000g, ELBW).

Study design: Participants included 8,332 surviving ELBW infants born 2010-2020 in North America who contributed follow-up data at 24-months corrected age to the Vermont Oxford Network. Neonatal morbidities included: bronchopulmonary dysplasia (BPD), grade 3-4 intraventricular hemorrhage (IVH), periventricular leukomalacia, stage 3-4 retinopathy of prematurity (ROP), late infection, necrotizing enterocolitis, and spontaneous intestinal perforation. Outcomes included: 1) developmental delay (Bayley score <70 in ≥1 domain), 2) rehospitalization, and 3) therapeutic service use. We compared three gestational age-adjusted risk models with the following predictors: 1) morbidity count, 2) count of three morbidities (BPD, IVH, ROP), and 3) multimorbidity-based latent classes.

Results: Thirty five percent of the study sample had ≥2 neonatal morbidities. Most (64%) received ≥2 therapeutic services, 36% were re-hospitalized, and 19% had developmental delay at 24-months. Morbidity counts and multimorbidity-based latent classes were associated with increased risk for poor 24-month outcomes compared with no morbidity. However, the predictive ability of all three models was modest (area under the receiver operating curve=0.66).

Conclusions: Neonatal multimorbidity is common among ELBW infants and associated with later health and developmental outcomes. However, diagnosis-based multimorbidity risk models have poor prognostic ability. More robust characterization of multimorbidity symptom severity, physiologic impact, and environmental correlates may improve the clinical utility of future risk models.

Keywords: multimorbidity; neurodevelopment; prematurity; risk prediction.

Conflict of interest statement

Declaration of interests ☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. ☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jonathan S Litt reports financial support was provided by National Institute of Child Health and Human Development. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

2

Review

Ageing Res Rev

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. 2025 Dec 11:114:102991.

doi: 10.1016/j.arr.2025.102991. Online ahead of print.

Stage-specific risk factors of cardiometabolic multimorbidity: A systematic review and meta-analysis from incidence to mortality

Lin Yang [1], Zirui Zhang [1], Jie Zhang [1], Jingyou Miao [2], Hui Zhang [2], Yihui Du [3], Lilu Ding [4]

Affiliations Expand

- PMID: 41390099

- DOI: 10.1016/j.arr.2025.102991

Abstract

Background: Cardiometabolic multimorbidity (CMM)-the co-occurrence of diabetes, cardiovascular disease, and related conditions-is a growing global health burden. Identifying risk factors across its developmental trajectory is critical for targeted prevention.

Methods: We conducted a systematic review and meta-analysis to quantify risk factors for the incidence and progression of CMM across five transitions: health → first cardiometabolic disease (FCMD), FCMD→CMM, CMM→death, FCMD→death, and health→death. For incidence, we used conventional random-effects meta-analysis to estimate pooled odds ratios (ORs). For disease progression, we applied Bayesian multi-state meta-analysis to estimate pooled hazard ratios (HRs). Subgroup analyses were performed to assess heterogeneity.

Results: Nine modifiable risk factors were identified for CMM incidence. Metabolic factors (overweight: OR=1.82, obesity: OR=3.13, hypertension: OR=2.05) and socioeconomic determinants (low income: OR=1.24, living alone: OR=1.58) showed the strongest associations. Depression (OR=1.70) and behavioral factors (smoking, physical inactivity, alcohol use) further increased risk. Trajectory analyses revealed stage-specific drivers: overweight/obesity drove transitions from healthy to FCMD (OR=1.69) and FCMD to CMM (OR=1.36), while smoking showed escalating effects across stages (health→FCMD: OR=1.22; FCMD→CMM: OR=1.37; CMM→death: OR=1.83). Alcohol use and physical inactivity increased mortality risk (13-28 %). Heterogeneity primarily stemmed from outcome measurement methods (i.e., objective vs. self-reported) and CMM composition.

Conclusion: CMM prevention requires stage-specific prioritization: early weight management, hypertension control and depression intervention to mitigate incidence; smoking cessation to curb progression; and intensified lifestyle interventions targeting smoking and alcohol cessation in established CMM. This evidence underscores the need for dynamic, trajectory-informed interventions to reduce the CMM burden.

Keywords: Cardiometabolic multimorbidity; Disease trajectory; Risk factors; Stage-specific prevention; Systematic review and meta-analysis.

Conflict of interest statement

Declaration of Competing Interest All authors declare that they have no competing interests. This statement is submitted as part of the manuscript titled: “Stage-

Specific Risk Factors of Cardiometabolic Multimorbidity: A Systematic Review and Meta-Analysis from Incidence to Mortality."

Supplementary info

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3

BMC Health Serv Res

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. 2025 Dec 12.

doi: 10.1186/s12913-025-13817-z. Online ahead of print.

Multimorbidity measurement strategies for predicting hospital visits

Bernardo Neves [1 2 3], José M Moreira [# 4], Simão Gonçalves [# 4], Jorge Cerejo [# 4], Inês Mota [# 4], Nuno A Silva [# 4], Francisca Leite [# 4], Mário J Silva [# 5]

Affiliations Expand

- **PMID: 41388459**

- **DOI: 10.1186/s12913-025-13817-z**

Free article

No abstract available

Keywords: Comorbidity; Electronic health records (EHRs); Extreme gradient boosting (XGBoost); Hospital utilization; Logistic regression; Multimorbidity; Predictive modeling; Risk prediction.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: This study was approved by the Institutional Review Board of Hospital da Luz Lisboa (HLL), under approval number CES/03/2021/ME. The research involved secondary analysis of fully anonymized data obtained through automated processes, with no human interaction. Therefore, the requirement for informed consent was waived by the IRB.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Consent for publication: Not applicable Competing interests: The authors declare no competing interests.

- 37 references

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4

Review

Aging Clin Exp Res

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. 2025 Dec 10.

doi: 10.1007/s40520-025-03279-y. Online ahead of print.

The evolution toward integrated community health care for older people in Italy

A Marengoni [1 2], A Zucchelli [3 4], A Padovani [3], E Belli [5], L Cajazzo [6], E Burato [6]

Affiliations Expand

- PMID: 41369843

- DOI: 10.1007/s40520-025-03279-y

Abstract

The progressive aging of the Italian population and the increasing prevalence of multimorbidity and frailty call for a reorganization of health and social care services. In this paper we aim to critically examine Ministerial Decree 77/2022, within Mission 6 of the National Recovery and Resilience Plan, which establishes new models and standards for community-based care and offers an unique opportunity to deliver care that is closer to people's homes, fostering a holistic approach that combines clinical expertise, social support, and technological innovation. The reform places Community Houses and Health Districts at the core of integration between hospitals, general practitioners, and social services. The care of frail older adults relies on population stratification through validated tools, such as the Primary Care Frailty Index (PC-FI), and on the development of individualized care plans that

integrate multidisciplinary interventions. Although general practitioners remain central in the health care system, geriatricians may play a pivotal role in multidimensional assessment, pharmacological management, health promotion, and the coordination of care teams. Telemedicine and digital tools support continuity of care and ensure traceability of clinical processes. Indicators of accessibility, equity, appropriateness, acceptability, and effectiveness are proposed, including the use of Patient-Reported Outcome and Experience Measures proposed for the evaluation of its impact. The reform's success will depend on overcoming methodological and operational barriers, reducing regional disparities, and ensuring that clinical expertise, social support, and technological innovation deliver measurable benefits for frail older adults.

Keywords: Community care; Community house; Frailty; Geriatrician; Older persons; Primary care physician.

Conflict of interest statement

Declarations. Competing interests: The authors declare no competing interests.

- 20 references

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5

J Gen Intern Med

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. 2025 Dec 9.

doi: 10.1007/s11606-025-09941-5. Online ahead of print.

Understanding the Causes of Nonadherence to Chronic Medications Among Patients With Cancer and Multimorbidity: A Qualitative Study

Deborah R Kaye [1 2 3 4 5], Roshni Varma [6], Sophia Roud [7], Laura Fish [8 9], Devika Shenoy [6], Heather E Parnell [8 10], Leah L Zullig [4 5 11], Peter A Ubel [12], Caroline E Sloan [13 14 15 16]

Affiliations Expand

- **PMID: 41364401**

- **DOI: 10.1007/s11606-025-09941-5**

Abstract

Background: When patients with multimorbidity (≥ 2 chronic diseases) are diagnosed with cancer, their adherence to non-cancer medications declines. Nonadherence in this patient population has been linked to an increased risk of disease progression, hospitalization, and death. However, the reasons for declines in adherence are not well understood.

Objective: To qualitatively explore barriers and facilitators of chronic medication adherence among patients with multimorbidity and active cancer.

Design: Semi-structured interviews conducted in March-November 2023.

Participants: Adults aged ≥ 50 years with 2+ chronic conditions and cancer diagnosed within the past year and under active treatment at one large academic health system. We used purposive sampling to include balanced numbers of advanced (stage 3-4) and non-advanced (stage 1-2) cancers, and perceived change in chronic medication adherence after cancer diagnosis (same/better vs. worse).

Approach: We asked participants to describe medication adherence barriers and facilitators, and experiences balancing cancer and non-cancer symptoms, medications, and medical appointments. We analyzed transcripts using applied thematic analysis.

Key results: We interviewed 20 participants. The majority were female (14/20), had breast cancer (8/20) or lung cancer (6/20), and took 3+ medications (12/20). Half had stage 3-4 disease. Three themes emerged. First, participants felt forced to prioritize among their diseases, medications, and appointments. Many focused their energy on their cancer, putting management of their chronic diseases on pause. Second, participants' trust in caregivers, medical teams, and their own self-confidence influenced their motivation to adhere to medications. Third, adherence was logistically difficult and depended on drug side effects, drug-disease interactions, drug-drug interactions, and conflicting recommendations from cancer and non-cancer care teams.

Conclusions: Patients with cancer and multimorbidity must manage the demands of their cancer and non-cancer treatments simultaneously and navigate relationships with multiple healthcare professionals whose recommendations may conflict. Interventions are needed to address barriers to adherence in this population.

Keywords: cancer; medication adherence; multimorbidity; nonadherence.

Conflict of interest statement

Declarations:. Human Ethics and Consent to Participate Declarations:: This study was approved by the Duke Health Institutional Review Board (Pro00111621), and all participants provided informed consent to participate in the study. Conflict of interest:: DRK received consulting fees from Janssen Pharmaceuticals. LLZ reports consulting fees from Eisai. CES and DRK are 2024-2025 Health and Aging Policy Fellows and American Political Science Association Fellows. All other co-authors report no conflicts.

- **48 references**

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Aging Male

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. 2025 Dec 11;28(1):2581661.

doi: 10.1080/13685538.2025.2581661. Epub 2025 Nov 12.

Higher charlson comorbidity index is associated with increased risk of erectile dysfunction: evidence from NHANES data

Xiaobao Chen [1], Junwei Lin [1], Binhong Liu [1], Lingjun Liu [1], Wei Jiang [1], Ruoyun Xie [1]

Affiliations Expand

- **PMID: 41222099**

- **DOI: 10.1080/13685538.2025.2581661**

Free article

Abstract

Background: The Charlson Comorbidity Index (CCI) quantifies multimorbidity, but its link to erectile dysfunction (ED) remains underexplored.

Methods: Using data from the National Health and Nutrition Examination Survey (NHANES), our study investigated the association between CCI and ED. Our analysis involved weighted multivariate regression, subgroup analyses, restricted cubic spline (RCS) analyses, and propensity score matching (PSM) analyses.

Results: Among the 2295 adults included in this study, 863 (37.6%) were diagnosed with ED. Weighted multivariate regression analyses revealed a significant positive association between the CCI and the risk of ED. Each additional point on the CCI was associated with a 32% higher risk of ED (OR 1.32, 95% CI 1.18-1.47). Furthermore, when participants were categorized into two groups based on CCI scores (CCI = 0 and CCI ≥ 1), the risk of ED was notably higher for those with CCI ≥ 1, showing a 122% increased risk compared to those with CCI = 0 (OR 2.22, 95% CI 1.62-3.05). Sensitivity analyses, including subgroup analyses and PSM, consistently supported the strong positive correlation between the CCI and ED.

Conclusion: Our study indicates that a higher CCI is positively correlated with an increased risk of ED, suggesting that lower CCI scores are associated with lower risk of ED.

Keywords: Charlson comorbidity index; National Health and Nutrition Examination Survey; cross-sectional study; erectile dysfunction.

Supplementary info

MeSH termsExpand

Full text links

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J Affect Disord

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. 2025 Dec 15:391:119958.

doi: 10.1016/j.jad.2025.119958. Epub 2025 Jul 17.

Association between multimorbidity trajectories and subsequent cognitive decline: evidence from two nationwide longitudinal cohorts

Linlin Wang [1], Yiling Lou [1], Qingqing Jiang [2], Hengchang Wang [1], Shen Huang [1], Yulin Xie [1], Furong Wang [2], Shiyi Cao [3]

Affiliations Expand

- **PMID: 40683537**
- **DOI: 10.1016/j.jad.2025.119958**

Abstract

Background: The number of chronic diseases in a patient may change over time, but how multimorbidity developmental trajectories affect subsequent cognitive decline remains unknown.

Methods: Data were drawn from eight waves (2004-2018) of the English Longitudinal Study of Ageing (ELSA) and the Health and Retirement Study (HRS), involving 5300 and 4357 participants, respectively. Group-based trajectory modeling was used to identify multimorbidity trajectories over six years (2004-2010) according to ten chronic diseases. We performed linear mixed-effects models to investigate the association between multimorbidity trajectories and subsequent cognitive decline in global cognition and three cognitive domains, including memory, executive function, and orientation.

Results: Three multimorbidity trajectories (low-stable, moderate-increasing, and rapid-increasing) were identified in two cohorts. Compared to the low-stable trajectory group, the moderate-increasing trajectory group exhibited faster declines in memory [pooled β = -0.027 standard deviation (SD)/year, 95 % confidence interval (CI): -0.044 to -0.011], orientation (pooled β = -0.036 SD/year, 95 % CI: -0.066 to -0.006), and global cognition (pooled β = -0.043 SD/year, 95 % CI: -0.084 to -0.002). Furthermore, the rapid-increasing trajectory group was associated with steeper declines in memory (pooled β = -0.049 SD/year, 95 % CI: -0.084 to -0.015), executive function (pooled β = -0.044 SD/year, 95 % CI: -0.065 to -0.022), orientation (pooled β = -0.077 SD/year, 95 % CI: -0.116 to -0.037), and global cognition (pooled β = -0.138 SD/year, 95 % CI: -0.211 to -0.065).

Limitations: Limited by the structure of questionnaire, some of the information was derived by self-report, which may lead to recalling bias.

Conclusions: Both moderately and rapidly increased multimorbidity are associated with accelerated cognitive decline among older people. Multimorbidity surveillance and management might help to delay the decline rate of cognition.

Keywords: Cognitive decline; Cognitive function; ELSA; HRS; Multimorbidity trajectories; Older people.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- **Cited by 1 article**

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Evid Based Nurs

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. 2025 Dec 15;29(1):13.

doi: 10.1136/ebnurs-2024-104111.

Multimorbidity is highly prevalent in adults with severe mental illness

James Hill [1], Emma Hill [2]

Affiliations Expand

- PMID: 39025660

- DOI: 10.1136/ebnurs-2024-104111

No abstract available

Conflict of interest statement

Competing interests: None declared.

Full text links

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"asthma"[MeSH Terms] OR asthma[Text Word]

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J Asthma Allergy

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. 2025 Dec 10:18:1713-1725.

doi: 10.2147/JAA.S551901. eCollection 2025.

Clinical Impact of Mepolizumab on Airway Mucus Plugs in Patients with Severe Asthma

Yu Hara [1], Naoya Tanabe [2], Satoshi Marumo [3 4], Kota Murohashi [1], Yusuke Hayashi [2], Mayu Nagata [4], Takuji Asada [5], Satoshi Nagaoka [1], Nobuaki Kobayashi [1], Toyohiro Hirai [2], Takeshi Kaneko [1]

Affiliations Expand

- PMID: 41399491

- PMCID: PMC12702269

- DOI: 10.2147/JAA.S551901

Abstract

Purpose: Airway mucus plugs are driven by eosinophilic inflammation and considered an important treatable trait in severe asthma. However, whether mepolizumab, an antibody that suppresses the interleukin-5 pathway and eosinophilic inflammation, can remove mucus plugs remains unclear. The purpose of this study is to evaluate whether mepolizumab treatment could reduce the extent of mucus plugs on computed tomography (CT), and whether changes in mucus plugs were associated with changes in symptoms and pulmonary function following the treatment.

Patients and methods: This retrospective study included consecutive patients with severe asthma who underwent an asthma control test (ACT), spirometry, and chest CT before and after treatment with mepolizumab at three Japanese hospitals. The mucus plug score (MPS) and total airway count (TAC) were quantified by CT.

Results: Thirty-one (15 male) patients were included in this analysis. Their baseline (pre-mepolizumab) median age, ACT, CT-measured MPS, and TAC were 67 years, 19 points, 7 points, and 232, respectively. Baseline MPS was significantly correlated with forced expiratory volume in one second (FEV1) and TAC (R= -0.39 and R= -0.71, respectively). After treatment with mepolizumab (median 466 days later), median ACT and MPS were 23 points and 1 point, respectively, significantly improved from baseline (both $P<0.001$). Changes in MPS were significantly correlated with changes in ACT and FEV1 (R= - 0.47 and R= - 0.68, respectively). Furthermore, a higher baseline MPS was significantly associated with greater changes in ACT and FEV1 (R= 0.41 and R= 0.47, respectively).

Conclusion: In this study, mepolizumab treatment coincided with a decrease in MPS, although a direct causal relationship could not be established. Nevertheless, the observed associations between higher baseline MPS and ACT improvement suggest the potential utility of MPS as a biomarker for biological treatment.

Keywords: asthma control test; computed tomography; eosinophilic inflammation; mucus plug score; total airway count.

Conflict of interest statement

TN and HT were supported by grants from FUJIFILM Co., Ltd., and Daiichi Sankyo Company, Ltd outside this study. HY and MS have received honoraria for speakers from AstraZeneca, GlaxoSmithKline and Sanofi. KT has received honoraria for speaker from GlaxoSmithKline. HT have received fees for lectures from Nippon Boehringer Ingelheim, fees for lectures from AstraZeneca, outside the submitted work. The other authors report no conflicts of interest in this work.

- **41 references**
- **6 figures**

Full text links

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J Allergy Clin Immunol

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. 2025 Dec 13:S0091-6749(25)02175-X.

doi: 10.1016/j.jaci.2025.11.014. Online ahead of print.

High airway TSLP in asthma associates with type 2 inflammation, mucus plugging and airway remodeling

Kritika Khanna [1], Monica Tang [2], Nathan D Jackson [3], Mats W Johansson [4], Eugene R Bleecker [5], Mario Castro [6], Suzy A Comhair [7], Loren C Denlinger [4], Serpil C Erzurum [7], Annette T Hastie [8], Wendy Moore [8], Elliot Israel [9], Bruce D Levy [9], Nizar N Jarjour [4], David T Mauger [10], Brenda R Phillips [10], Kaharu Sumino [11], Sally E Wenzel [12], Prescott G Woodruff [1], Max A Seibold [13], John V Fahy [14]; National Heart, Lung, and Blood Institute Severe Asthma Research Program-3

Affiliations Expand

- **PMID: 41397482**

- **DOI: 10.1016/j.jaci.2025.11.014**

Abstract

Background: Inhibition of thymic stromal lymphopoietin (TSLP) improves asthma control but the relationships between airway TSLP levels and clinical and immunologic features of asthma are unclear.

Objective: To determine associations between airway TSLP, disease control, and airway remodeling in asthma.

Methods: We measured TSLP protein in sputum from mild-moderate asthma patients (University of California San Francisco cohort, n=137), moderate-severe patients (Severe Asthma Research Program-3 cohort, n=397), and healthy controls (n=95). We explored how sputum TSLP levels relate to measures of lung function and exacerbations, airway inflammation, and lung image-based measures of mucus plugging and airway remodeling.

Results: The upper 95th centile value for sputum TSLP concentration in health was 1.6 pg/mL, and 16% of the UCSF cohort and 33.5% of the SARP cohort had TSLP concentrations above this value. High sputum TSLP levels occurred most often in severe asthma patients showing clinical traits typical of type 2 inflammation. There was considerable overlap between subgroups who were high for TSLP and high for eosinophilic inflammation. High sputum TSLP levels were associated with a strong sputum cell gene expression profile for type 2 immune responses and a weak expression for type 1 responses. High sputum TSLP levels were also associated with high sputum MUC5AC expression, and high scores for mucus plugging, air trapping and other measures of airway remodeling on CT lung scans.

Conclusion: High levels of airway TSLP in asthma are associated with more severe asthma, predominantly type 2 airway immune responses, and with mucus plugging, air trapping and airway remodeling.

Clinical implication: High airway TSLP levels occur in severe asthma patients with a type 2-high endotype despite treatment with corticosteroids, providing rationale for treatment with anti-TSLP or other type 2 directed biologics.

Capsule summary: A subset of asthma patients with severe disease has high airway TSLP levels despite high-dose inhaled corticosteroids, and these patients have predominant airway type 2 immune responses, increased mucus plugging, air trapping, and airway remodeling.

Keywords: TSLP; mucus plugging; thymic stromal lymphopoietin; type 2 immune responses.

Int Forum Allergy Rhinol

. 2025 Dec 15.

doi: 10.1002/alr.70073. Online ahead of print.

The Global Airways in Practice: Long-term Effects of Mepolizumab With or Without FESS on Type 2 Inflammation in Patients With CRSwNP

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Affiliations Expand

- PMID: 41395863

- DOI: 10.1002/alr.70073

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a type 2 inflammatory disease often associated with asthma. The global airway hypothesis suggests bidirectional inflammatory interactions between upper and lower airways. Mepolizumab, an anti-IL-5 therapy, treats conditions systemically, while functional endoscopic sinus surgery (FESS) primarily addresses sinonasal disease and can improve asthma control. The combined effect on airway outcomes remains unclear. This study evaluated the global airway hypothesis with objective measures and targeted therapies.

Objective: To investigate the impact of mepolizumab, with or without FESS, on airway inflammation, lung function, and symptom burden in severe CRSwNP with or without asthma.

Methods: In this RCT, 58 patients received either mepolizumab alone or combined with FESS. Inflammation and symptom outcomes were analyzed in blood, nose, and bronchi at baseline, six, and 12 months. Patients were stratified by baseline inflammatory subgroup.

Results: Both groups showed improvements in FEV1% (MepoFESS: +3.4%, p = 0.010; Mepo Only: +3.5%, p = 0.015), FVC% (MepoFESS: +3.7%, p < 0.001; Mepo Only: +2.9%, p = 0.009), inflammation markers (FeNO, blood eosinophils, nasal polyp eosinophils), and all patient-reported outcomes. MepoFESS produced greater gains in nasal polyp score, nasal congestion, and overall symptom burden. Lung function and systemic inflammation improved similarly in both groups.

Conclusions: Mepolizumab improves upper and lower airway outcomes in CRSwNP. FESS adds localized benefits in sinonasal symptom control without further impact

on lower airway inflammation. Findings support a comprehensive approach targeting systemic and local type 2 inflammation in global airway disease.

Keywords: biologics treatment; chronic rhinosinusitis with nasal polyps; functional endoscopic sinus surgery; global airway hypothesis; type 2 inflammation.

- 26 references

Supplementary info

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J Asthma

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. 2025 Dec 13:1-19.

doi: 10.1080/02770903.2025.2603331. Online ahead of print.

Telemedicine Education for Caregivers and Asthma Control in Children: A Randomized Controlled Trial

Thang Hoang Le [1], Nghia Quang Bui [1], My Hoang Le [1], Duy-Truong Khac Le [1], Ly Cong Tran [1]

Affiliations Expand

- PMID: 41390740

- DOI: 10.1080/02770903.2025.2603331

Abstract

Background: Poorly controlled pediatric asthma increases morbidity, reduces quality of life, and raises healthcare use. Caregiver education on asthma and medication use is essential for control. In Vietnam, pediatric asthma services are

centralized at tertiary centers, limiting access for many families. Telemedicine may help bridge these gaps.

Objectives: To evaluate the effectiveness of telemedicine education on asthma control in children with uncontrolled asthma and its impact on caregiver knowledge, attitudes, and children's MDI technique.

Methods: We conducted a pragmatic randomized clinical trial among children aged 4-16 years with uncontrolled asthma. Participants were randomized 1:1, stratified by age and sex, to receive either a structured educational video call or a brief scheduling call. Changes in C-ACT/ACT scores, caregiver knowledge, caregiver attitudes, and children's MDI technique were compared between groups. A multivariable generalized linear model was used to identify factors associated with improvement in asthma control.

Results: Baseline characteristics were comparable between groups. At a median follow-up of 5 weeks (IQR 4-8), C-ACT scores were higher in the intervention than control group (median 25.0 vs 19.5, $P < 0.001$), with mean change exceeding the minimal clinically important difference. Caregiver knowledge and attitudes and children's MDI technique also improved more in the intervention group ($P < 0.001$ for all). In multivariable models, telemedicine education was independently associated with greater improvement in asthma control (β = 4.24, 95% CI: 2.64-5.85, $P < 0.001$).

Conclusion: Telemedicine-based education improved asthma control and caregiver-related outcomes and may serve as an effective supportive strategy where access to pediatric asthma services is limited.

Keywords: asthma control; caregivers; pediatrics; randomized controlled trials; telemedicine.

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Review

J Asthma

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. 2025 Dec 13:1-12.

doi: 10.1080/02770903.2025.2603325. Online ahead of print.

Asthma's clotting shadow: a meta-analysis unveiling a thrombotic ticking time bomb

Kaiwen Zheng [1], Yuling Zhao [2], Jiayi Li [2], Xing Chen [2]

Affiliations Expand

- PMID: 41388885

- DOI: 10.1080/02770903.2025.2603325

Abstract

Objective: To systematically evaluate the association between asthma and the risk of venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT).Data Sources: PubMed, Embase, Web of Science, and the Cochrane Library were searched for relevant studies published up to May 2025.Study Selection: Observational studies (cohort, case-control, and cross-sectional) reporting the association between asthma and VTE, PE, or DVT with available odds ratios (ORs) or hazard ratios and 95% confidence intervals (or data to calculate them) were included.

Results: The meta-analysis revealed a significant association between asthma and increased risk of VTE. Patients with asthma had a 2.41-fold higher odds of PE (OR = 2.41, 95% CI:1.77-3.27), 1.56-fold higher odds of DVT (OR = 1.56, 95% CI:1.49-1.63), and 1.61-fold higher odds of overall VTE (OR = 1.61, 95%:CI 1.45-1.77). Cohort studies showed the strongest association (OR = 4.21, 95% CI 2.56-6.92). Subgroup analysis by region indicated the highest risk in Asia (OR =3.19, 95% CI:2.06-4.96), followed by America (OR = 2.24, 95% CI:1.55-3.24) and Europe (OR = 1.64, 95% CI:1.49-1.81).

Conclusion: Asthma is significantly associated with an elevated risk of PE, DVT, and VTE, with particularly strong associations observed in cohort studies and Asian populations. These findings highlight the need for further research into underlying mechanisms and whether optimized asthma management can reduce thrombotic risk.

Keywords: asthma;deep vein thrombosis;venous thromboembolism;pulmonary embolism;risk factors; meta-analysis.

Allergy

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. 2025 Dec 13.

doi: 10.1111/all.70182. Online ahead of print.

EAACI Guidelines on the Importance of Green Space in Urban Environments for Allergy and Asthma Prevention

Tari Haahtela [1], Liam O'Mahony [2], Claudia Traidl-Hoffmann [3], Mubeccel Akdis [4], Ozlem Ceylan [5], Panagiotis Chaslaridis [6], Athanasios Damialis [7], Stefano Del Giacco [8], Antti Lauerma [1], Kari C Nadeau [9], Inês Paciência [10], Isabella Pali-Schöll [11 12], Oscar Palomares [13], Harald Renz [14 15 16], Jurgen Schwarze [17], Marilyn Urrutia-Pereira [18 19], Carina Venter [20], Donata Vercelli [21 22 23 24], Tonya Winders [25], Cezmi A Akdis [4], Marek Jutel [26 27], Ioana Agache [28]

Affiliations Expand

- **PMID: 41388798**

- **DOI: 10.1111/all.70182**

Abstract

The allergy and asthma epidemic in urban societies following World War II is mostly caused by changes in the environment, diet and lifestyle. Disconnection of urban populations from the wider environment has reduced the protective factors building up immunological resilience. The European Academy of Allergy and Clinical Immunology (EAACI) guidelines on greenness impact on allergy and asthma follow the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach and provide eight recommendations encouraging greenness exposure to support immune health. Controlled follow-up studies are still scarce, and the strength of evidence is generally low or moderate at best. For primary prevention of allergy and asthma, most of the evidence indicates beneficial effects. Exposure is also useful for secondary prevention. Asthma patients may feel better and need less medication by combining green space exposure with physical activity. During the high-pollen season, effective seasonal medication is necessary for patients with pollen allergy. In urban planning, implementing appropriate green infrastructure and easy access to green space promotes immune health and reduces risks of air pollution and heatwaves. These EAACI guidelines are the first recommendations highlighting the importance of urban green spaces on immune health and call for prioritising innovative research in this field.

Keywords: allergic rhinitis; asthma; atopic dermatitis; biodiversity; climate change; green space; greenness; guidelines; nature loss; nature-based solutions.

- 125 references

Supplementary info

Grants and fundingExpand

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Clin Exp Allergy

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. 2025 Dec 12.

doi: 10.1111/cea.70195. Online ahead of print.

Baseline Epigenetics as a Biomarker of Mepolizumab Response in Severe Asthma

Hongmei Zhang [1], Xin Jin [1], Hasan Arshad [2 3], Ramesh J Kurukulaaratchy [2 3]

Affiliations Expand

- PMID: 41387235

- DOI: 10.1111/cea.70195

No abstract available

Keywords: DNA methylation; biologic drugs; markers; prediction; severe asthma.

Update of

- Baseline epigenetics as a biomarker of mepolizumab response in severe asthma.

Zhang H, Jin X, Arshad H, Kurukulaaratchy RJ.medRxiv [Preprint]. 2025 Sep 4:2025.09.02.25334098. doi: 10.1101/2025.09.02.25334098.Update in: Clin Exp Allergy. 2025 Dec 12. doi: 10.1111/cea.70195.PMID: 40950472 Free PMC article. Preprint.

Supplementary info

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Acta Paediatr

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. 2025 Dec 12.

doi: 10.1111/apa.70416. Online ahead of print.

Release of Airway Alarmins IL-33 and TSLP in Paediatric Acute Severe Asthma: A Case-Control Study

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Affiliations Expand

- PMID: 41386689

- DOI: 10.1111/apa.70416

Abstract

Aim: Interleukin (IL)-33 and thymic stromal lymphopoietin (TSLP) released in the airways are believed to be associated with a greater risk of childhood-onset asthma. The aim of this study was to measure the release of IL-33 and TSLP into the airways of children and young people (CYP) during asthma attacks and compare these alarmin-cytokine levels with stable disease patients and non-asthmatic controls.

Methods: We conducted a prospective observational case-control feasibility study, where we measured the levels of IL-33 and TSLP using high sensitivity immunoassays in the airways of children and young people (CYP) during asthma attacks, stable disease patients and non-asthmatic control individuals.

Results: Median concentrations of sputum IL-33 and TSLP from acute asthmatics were 3.4 and 17.7 times higher, respectively, in acute asthmatics compared to stable asthmatic children. Sputum IL-33 and TSLP were not different in the stable asthma group compared to non-asthmatic controls.

Conclusion: IL-33 and TSLP were significantly elevated during acute severe asthma attacks and could potentially drive further airway inflammation and remodelling during asthma attacks in children. Results support further clinical evaluation of anti-TSLP and anti-IL-33 biologic therapeutics for preventing or reducing the frequency of asthma attacks in children.

Keywords: IL-33; TSLP; airway epithelium; alarmin; asthma; biomarker; exacerbation; paediatric; phenotyping.

- **25 references**

Supplementary info

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J Allergy Clin Immunol

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. 2025 Dec 10:S0091-6749(25)01180-7.

doi: 10.1016/j.jaci.2025.11.008. Online ahead of print.

Epinephrine and Emergency Medical Services Activation Recommendations During Acute Allergic Reactions in Community Settings: International Consensus Report

Timothy E Dribin [1], Hugh A Sampson [2], Aikaterini Anagnostou [3], Carlos A Camargo Jr [4], Adam T Fox [5], David B K Golden [6], Kenneth A Michelson [7], Marcus S Shaker [8], Julie Wang [2], Waleed Alqurashi [9], Amal H Assa'ad [10], David C Brousseau [11], Dianne E Campbell [12], Ronna L Campbell [13], Thomas B Casale [14], Derek K Chu [15], Ashley Lynn Devonshire [10], Motohiro Ebisawa [16], Matthew Greenhawt [17], David M Lang [18], Jay A Liebermann [19], Stephanie Leonard [20], Douglas P Mack [21], Antonella Muraro [22], Mark I Neuman [23], Kimberly A Risma [10], Graham Roberts [24], Nicholas Sargant [25], Scott H Sicherer [2], Jonathan M Spergel [26], Dana Wallace [27], Susan Waserman [28], Margitta Worm [29], Hannah R Bush [30], Barbara K Giambra [31], Lisa M Vaughn [32], Vincetta Kahmann [33], Brad Sobolewski [34], Yin Zhang [35], Stephanie Boyd [33], Sanaz Eftekhari [17], Hannah Jaffee [17], Melanie Carver [17], Rob Keefer [36], Lisa Douglas [36], Caroline Nickels [36], Ryan A Moore [37], David Schnadower [34]

Affiliations Expand

- **PMID: 41386477**

- **DOI: 10.1016/j.jaci.2025.11.008**

Abstract

Background: Limited research exists on when to use epinephrine (adrenaline) or activate emergency medical services (EMS) during acute allergic reactions in community settings. This contributes to suboptimal patient care, including both the underuse and overuse of epinephrine, as well as potentially unnecessary emergency department visits.

Objective: To develop consensus recommendations for administering epinephrine and activating EMS during acute allergic reactions.

Methods: From January 2024 to May 2025, we assembled a 34-member international panel of experts to develop clinical scenarios reflecting varying severity levels within and across organ systems, candidate modifiers that may lower the threshold for epinephrine administration (e.g., history of asthma), and candidate EMS activation recommendations. In Phase 1, the panel engaged in a modified Delphi process to reach consensus on these outputs. In Phase 2, we tested each consensus modifier by embedding it into scenarios where epinephrine was not recommended or lacked consensus, to assess potential impacts on treatment decisions.

Results: The expert panel developed 24 clinical scenarios, 9 candidate modifiers, and 12 candidate EMS activation recommendations. During the first phase, 21 statements reached consensus to recommend epinephrine, 2 reached consensus not to recommend it, and 1 did not reach a consensus. There were 5 consensus modifiers and 10 consensus EMS activation recommendations. In the second phase, 2 of the 15 clinical scenarios reached consensus to recommend epinephrine administration.

Conclusion: We developed consensus recommendations for administering epinephrine and activating EMS during acute allergic reactions in community settings. Integrating them into technology-based decision support tools may enhance reaction management, improve patient outcomes, optimize healthcare utilization, and empower patient and caregiver self-efficacy.

Clinical implications: We developed consensus recommendations for administering epinephrine (adrenaline) and activating emergency services during acute allergic reactions in the community. The care recommendations account for the range of severity and the dynamic nature of reactions. They can be integrated into patient-facing technologies to enhance reaction management and improve outcomes.

Keywords: acute allergic reactions; adrenaline; anaphylaxis; anaphylaxis action plans; emergency department; emergency medical services; epinephrine; epinephrine delivery devices.

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BMC Geriatr

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. 2025 Dec 11.

doi: 10.1186/s12877-025-06844-2. Online ahead of print.

Frailty in older adults with chronic obstructive pulmonary disease: preliminary findings of prevalence and care priorities

Mei Chen [#1], Ying Li [#1], Qiuyue Du [#1], Jing Yin [#1], Yan Xu [2], Fuchao Li [3,4]

Affiliations Expand

- PMID: 41382008

- DOI: 10.1186/s12877-025-06844-2

Free article

Abstract

Background: Frailty is prevalent among older adults and exerts a significant impact on their quality of life. The present study aims to analyze the current status of frailty in older adults with chronic obstructive pulmonary disease (COPD) as well as its influencing factors, thereby providing evidence-based support for clinical treatment and nursing practices.

Methods: Older patients with COPD admitted to our hospital from January 2024 to April 2025 were included in this study. Patients with concurrent asthma or interstitial lung disease (ILD) were excluded to minimize confounding. Clinical data were collected, and frailty was assessed within 24 h of admission (when patients were clinically stable). Correlation analysis and multivariate logistic regression analysis were conducted to identify the influencing factors of frailty in older patients with COPD.

Clinical trial number: not applicable.

Results: A total of 224 older adults with COPD were enrolled in the study, among whom 68 (30.36%) were robust (normal state), 84 (37.50%) were pre-frail, and 72

(32.14%) met the criteria for frailty. Correlation analysis showed that age(r = 0.602), GOLD stage(r = 0.596), and COPD duration(r = 0.558), serum interleukin-6(r = 0.534) and serum hemoglobin concentration(r=-0.579) were correlated with the frailty of older adults with COPD (all p < 0.05). Multivariate logistic regression analysis indicated that age (OR = 1.809, 95%CI: 1.233 ~ 2.195), GOLD stage (OR = 2.456, 95%CI: 1.977 ~ 2.850), and COPD duration (OR = 1.768, 95%CI: 1.104 ~ 1.993), serum interleukin-6 (OR = 1.454, 95%CI: 1.113 ~ 2.006) and serum hemoglobin concentration (OR = 0.675, 95%CI: 0.225 ~ 0.901) were the influencing factors of the frailty of older adults with COPD (all p < 0.05).

Conclusion: The prevalence of frailty is relatively high in older adults with COPD. Clinically, targeted interventions and nursing care should be carried out for factors that influence the frailty in older adults with COPD.

Keywords: COPD; Care; Clinical; Frailty; Nursing; Older adult.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: In this study, all methods were performed in accordance with the relevant guidelines and regulations. The study has been reviewed and approved by the Medical Research Ethics Committee of Suzhou Hospital, Affiliated Hospital of Medical School, Nanjing University (approval number: IRB2025064). And written informed consents had been obtained from all the included patients. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

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Eur Respir J

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. 2025 Dec 11:2501435.

doi: 10.1183/13993003.01435-2025. Online ahead of print.

A multi-country cohort study evaluating the prevalence, risk factors, lung function and clinical outcomes of chronic bronchitis in low- and middle-income countries

Nicole M Robertson [1 2 3], Arun K Sharma [4 3], Mingling Yang [1 2], Santa K Das [5], Trishul Siddharthan [2 6], Suzanne L Pollard [1], Natalie A Rykiel [1 2], Patricia Alupo [7], Oscar Flores-Flores [2 8], Bruce Kirenga [7], Ram K Chandyo [9], Shumonta A Quaderi [10], Laxman Shrestha [4], Robert A Wise [1], John R Hurst [10], William Checkley [11 2]; Global Excellence in COPD outcomes (GECo) Study Investigators

Affiliations Expand

- PMID: 41381225

- DOI: 10.1183/13993003.01435-2025

Abstract

Background: Chronic bronchitis affects up to 40% of individuals with COPD and may serve as an early predictor of the disease and development of COPD. We investigated the prevalence, risk factors, and clinical outcomes associated with chronic bronchitis in three low- and middle-income countries (LMICs).

Methods: We conducted a population-based study of adults aged ≥40 years in Bhaktapur (Nepal), Lima (Peru), and Nakaseke (Uganda). Chronic bronchitis was defined as a productive cough several days per week for over four weeks. Multivariable log-binomial regression identified risk factors and outcomes associated with chronic bronchitis.

Results: Among 9664 participants (mean age 56.2 years, 51.0% male, 66.9% ever smokers), chronic bronchitis prevalence was 9.7%, with 31.5% of those also having COPD. Significant risk factors included older age (adjusted RR=1.54 per 19.8 years, 95% CI 1.4-1.7), male sex (1.18, 1.05-1.34), prior tuberculosis (1.45, 1.14-1.83), prior asthma diagnosis (2.11, 1.84-2.42), pack-years of tobacco use (1.16 per 10 pack-years, 1.14-1.18), family history of chronic respiratory diseases (1.69, 1.50-1.91), second-hand smoke exposure (1.45, 1.28-1.64), lower socioeconomic status quartile (1.22,1.07-1.39), and indoor biomass exposure (1.45, 1.13-1.64). Participants with chronic bronchitis experienced more breathlessness, worse respiratory health (higher St. George's Respiratory Questionnaire scores), and higher hospitalization rates (all p<0.001).

Conclusions: Chronic bronchitis is common in LMIC settings and is associated with multiple modifiable risk factors, including second-hand smoke, biomass exposure, and prior respiratory disease. Addressing these factors may reduce disease burden and improve quality of life.

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J Investig Allergol Clin Immunol

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. 2025 Dec 11:0.

doi: 10.18176/jiaci.1136. Online ahead of print.

Effect of Dupilumab on Restoring Tolerance to Nonsteroidal Anti-Inflammatory Drugs in Patients With Aspirin-Exacerbated Respiratory Disease

Isamar De Agrela-Mendes [1], África Serrano-Sánchez [1], María D Moreno-Llorente [1], Valentín Lopez-Carrasco [1], Javier Domínguez-Ortega [1 2 3], Santiago Quirce [1 2 3], Leticia De Las Vecillas [1 2 3]

Affiliations Expand

- PMID: 41378720

- DOI: 10.18176/jiaci.1136

Free article

No abstract available

Keywords: Aspirin-exacerbated respiratory disease; Asthma; Dupilumab; Nonsteroidal anti-inflammatory drugs; Real life.

Full text links

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Cite

13

Review

Int Forum Allergy Rhinol

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. 2025 Dec 11.

doi: 10.1002/alr.70078. Online ahead of print.

The Role of Artificial Intelligence in Chronic Rhinosinusitis: A Scoping Review

Nicola M Pereira [1], Sarah J Wie [1], Karena Zhao [1], Michelle Demetres [2], Ashutosh Kacker [1]

Affiliations Expand

- PMID: 41376460

- DOI: 10.1002/alr.70078

Abstract

Background: In the modern medical landscape, artificial intelligence (AI) is becoming an increasingly common tool for the diagnosis and management of chronic pathologies. Chronic rhinosinusitis (CRS) comprises a significant part of the practice of otolaryngology and thus provides ample opportunity for AI optimization of diagnosis and management.

Objective: With increasing interest in AI, this scoping review aims to map the current landscape of AI applications in CRS, identifying trends, gaps, and future opportunities.

Methods: A comprehensive literature search was performed in the following databases from inception-April 2024: Ovid MEDLINE, Ovid EMBASE, Web of Science, and The Cochrane Library. Studies retrieved were then screened for eligibility. The inclusion criteria included studies whose methods included the use of any form of AI for the diagnosis or management of chronic rhinosinusitis. Any studies that were non-English language publications, publications older than 2003, studies analyzing acute rhinosinusitis, and studies involving pediatric populations were excluded. Discrepancies were resolved by consensus.

Results: 573 records were screened, with 49 studies included in the final review. The studies were qualitatively analyzed according to the type of AI used, study objectives, application of AI, training variables for AI in CRS, and AI accuracy reporting. Commonly used forms of AI included deep learning (36.7%), neural networks (24.5%), convolutional neural networks (10.2%), and random forest models (6.1%). The majority (55%) of studies were focused on applying AI to the diagnosis of CRS. The remaining studies used AI to predict prognostic outcomes in CRS (29%) and to assess patient response to treatment or inform patient treatment plans (12%). Some studies aimed to identify biomarkers or clinical variables for the diagnosis or prognosis of CRS (37%), while others used AI to subtype CRS (33%) or assess radiologic characteristics using AI (20%). CT imaging, tissue or blood eosinophil counts, clinical or demographic patient characteristics, histopathology characteristics, blood and tissue cytokines, and nasal endoscopy findings were all variables used to train the AI models. Classification metrics and regression metrics were used to assess AI model performance.

Conclusions: AI is a promising tool in the management of CRS, though it remains in its early stages. Current applications show significant progress in diagnosis, subtyping, and prognosticating in CRS, but there are few studies that analyze the utility of AI for surgical planning, economic evaluation, or interactive clinical tools. This review underscores the potential of AI for transforming an otolaryngologist's approach to CRS.

Keywords: asthma; chronic rhinosinusitis; rhinitis; rhinosinusitis; sinusitis.

- **55 references**

Supplementary info

Publication typesExpand

Full text links

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Cite

14

Environ Health

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. 2025 Dec 11;24(1):91.

doi: 10.1186/s12940-025-01245-9.

Wildfire smoke and pediatric asthma control in the Northeastern United States: a cross-sectional study

Anna K Maassel [1 2], Paige Brochu [3 4], Valerie S Harder [5 6], Taylor H Ricketts [3 4], Stephen J Teach [7 8], Keith J Robinson [6 9]

Affiliations Expand

- **PMID: 41372919**

- **PMCID: PMC12696890**

- **DOI: 10.1186/s12940-025-01245-9**

Abstract

Background: Poor air quality due to smoke from distant wildfires is a growing risk for the Northeastern United States, a region largely unaffected by these events until recently. Despite this emerging threat, few studies have examined the effect of wildfire smoke on respiratory health in this region. We investigated the association between wildfire smoke exposure and pediatric asthma control in Vermont and upstate New York.

Methods: We extracted data from the electronic health records of youth aged 3-21 years diagnosed with asthma within a single regional healthcare system and included three clinical measures of asthma control: Test for Respiratory and Asthma Control in Kids (3-4 years), Asthma Therapy Assessment Questionnaire (5-21 years), and the National Heart, Lung and Blood Institute (NHLBI) asthma control guidelines (3-21 years). We first compared asthma control in the smoke-affected summer of 2023 to the largely unaffected summers of 2022 and 2024 using regression models, controlling for pollen exposure. We then obtained airborne particulate matter ($PM_{2.5}$) values within ZIP codes and used regression models to investigate the association between asthma control and $PM_{2.5}$ during the smoke-affected summer of 2023.

Results: The study sample included 1,217 encounters (mean age 9.1 ± 4.4 years, 57% male). Asthma control was significantly worse in the severely smoke-affected summer of 2023 versus 2022 for two of the three clinical measures but was not different between 2023 and 2024 for any of the clinical measures. Within summer 2023, there were no significant associations between ZIP code-level $PM_{2.5}$ and asthma control for any of the three clinical measures.

Conclusions: Wildfire smoke exposure in the Northeast was associated with decreased asthma control in this pediatric population, though not consistently across years and all clinical measures. As climate change drives longer and more intense wildfire seasons, continued monitoring is needed to understand the impact on pediatric respiratory health in this historically low-exposed region.

Keywords: Asthma; Asthma control; Climate change; PM2.5; Particulate matter; Pediatrics; Planetary health; Wildfire.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: This study was approved by the University of Vermont's Institutional Review Board under study number 00003427. Clinical trial number: not applicable. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

- **58 references**
- **4 figures**

Supplementary info

MeSH terms, SubstancesExpand

Full text links

Cite

15

Pulm Ther

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. 2025 Dec 10.

doi: 10.1007/s41030-025-00336-9. Online ahead of print.

Home-Based FeNO Monitoring with the Vivatmo me Device Reveals Type 2 Inflammatory Patterns of Patients with Asthma at Different Treatment Steps: The FeNO@Home Study

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Affiliations Expand

- PMID: 41372581

- DOI: 10.1007/s41030-025-00336-9

Free article

Abstract

Introduction: Fractional exhaled nitric oxide (FeNO) is an important type 2 (T2) asthma biomarker. Home-based FeNO monitoring can provide longitudinal data better reflecting the variable nature of T2 inflammation versus single-point data. We sought to compare longitudinal mean FeNO and variability (CV) in relation to asthma control, and to compare detection rate of $T2_{FeNO}$ inflammation at diagnostic (≥ 40 ppb in GINA 1) and on-treatment (≥ 25 ppb in GINA 2-5) cutoffs during home versus clinic measurements.

Methods: This was an observational study with once-daily home-based FeNO (Vivatmo me) and symptom diary in patients with asthma of different GINA steps performed over 3 months. Clinic FeNO, forced expiratory volume in 1 s (FEV_1), and 5-item asthma control questionnaire (ACQ-5) scores were also collected at two visits (enrolment/study end).

Results: We enrolled 85 patients (n = 23 step 1, n = 37 steps 2-3, and n = 25 steps 4-5). Mean FeNO over 3 months was highest in uncontrolled steps 4-5 (p = 0.006), and FeNO variability in steps 2-3 (p = 0.046). Subjects with optimal control (ACQ < 0.75

both visits) had comparable mean FeNO values, but fewer patients with CV above the median vs. suboptimally controlled patients (39.1% vs. 54.1%; p = 0.03). In GINA 1, FeNO CV was lower in optimally controlled patients (p = 0.10). Mean FeNO was higher on symptomatic asthma days, particularly in step 1 (p = 0.002), with similar trends during loss of asthma control phases. Home FeNO increased the detection rate of $T2_{FeNO}$ inflammation at a diagnostic cutoff (≥ 40 ppb, step 1) from 8.7% (clinic FeNO) to 47.8% of subjects, and of on-treatment $T2_{FeNO}$ inflammation in GINA steps 2-3 and 4-5 from 58.3% to 83.3%, and 64% to 96%, respectively.

Conclusion: Home-based FeNO provides important information about airway inflammation, distinct and complementary to symptom control. Detection of $T2_{FeNO}$ inflammation is facilitated at all GINA steps at diagnostic and predictive/prognostic cutoffs, with important implications for management and diagnosis.

Trial registration: German Clinical Trial Register (DRKS) DRKS00029118, registered July 1, 2022.

Keywords: Asthma; Asthma control; Biomarker; Diagnosis; Digital companion; Exhaled nitric oxide; Home monitoring; Inflammation monitoring; Type 2 inflammation.

Conflict of interest statement

Declarations. Conflict of Interest: Kai M. Beeh has received personal and/or institutional compensation for clinical research, consulting, and/or lecturing fees from AstraZeneca, Bosch Healthcare Solutions, Chiesi, Clario, GSK, Novartis, Menarini/Berlin Chemie, Orion, Sanofi, and Sterna. Kai M. Beeh is an Editor-in-Chief of Pulmonary Therapy. Kai M. Beeh was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Tim Harrison is an employee of AstraZeneca, UK, and holds shares and share options in AstraZeneca. Enrico Heffler reports personal fees for: consulting activities from Sanofi, Regeneron, GSK, Novartis, AstraZeneca, Stallergenes-Greer, Chiesi, Almirall, Bosch, Lofarma; lecturing and educational activities from Sanofi, Regeneron, GSK, Novartis, AstraZeneca, Stallergenes-Greer, Chiesi, Almirall, Bosch, Lofarma; participation on data safety monitoring or advisory boards from Sanofi, Regeneron, GSK, Novartis, AstraZeneca, Stallergenes-Greer, Chiesi, Almirall, Bosch, Lofarma. Hartmut Timmermann reports fees for speaker, lecturing and consulting activities, and/or research grants from AstraZeneca, Almirall, Astellas Pharma, Bayer, Boehringer Ingelheim, Berlin-Chemie, Chiesi, GSK, Leti Pharma, Meda, Mundipharma, Novartis, Nycomed, Pfizer, Sanofi, Takeda, Teva. Stephan Weber is an employee of ACOMED Statistik. The institution received compensation for performing statistical analyses from Bosch Healthcare Solutions GmbH. Sandra Wegner is a full-time employee of Bosch Healthcare Solutions GmbH. Ethical Approval: The study was carried out in accordance with Good Clinical Practice guidelines under the provisions of the latest version of the Declaration of Helsinki (2013) and the protocol received approval from the State Chamber of Physicians of Hesse (Ethikkommission der Landesärztekammer Hessen) as the coordinating ethics committee of the German principle investigator, and ethics committees at Instituto Clinica Humanitas, Milano, Italy. The study was registered at the German Clinical Trial Register (Number DRKS00029118) on July 1,

2022. All patients provided written informed consent prior to any study-related activities.

- 58 references

Full text links

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Cite

16

Review

Eur Respir Rev

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. 2025 Dec 10;34(178):250024.

doi: 10.1183/16000617.0024-2025. Print 2025 Oct.

Persistent airway obstruction in severe eosinophilic asthma: targeting interleukin-5 and eosinophils

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Affiliations Expand

- PMID: 41371716

- PMCID: PMC12690368

- DOI: 10.1183/16000617.0024-2025

Abstract

A large proportion of patients (40-60%) with severe asthma present with persistent airway obstruction (PAO). Patients with severe eosinophilic asthma (SEA) and PAO appear to be an underrepresented group in clinical guidance, despite being associated with considerable healthcare and economic burden. High levels of eosinophils drive airway inflammation, obstruction and hyperresponsiveness, which are key characteristics of SEA and can increase the risk of PAO and subsequent irreversible worsening of lung function. Available clinical and real-world

data must examine the effectiveness of biologic treatment targeting SEA in PAO to identify any data gaps that might help further define such patients and optimise their management. However, clinical trials of SEA frequently exclude the enrolment of patients with PAO. Eosinophils are activated and recruited to airways in response to different cytokines, particularly interleukin-5 (IL-5), produced *via* a complex molecular and cellular cascade. A few studies evaluating the effectiveness of benralizumab and mepolizumab were able to identify cohorts of patients with SEA and PAO who had a significant response to these IL-5/Rα-targeted biologics. PAO in patients with SEA represents a distinct clinical entity, one which could be referred to as "persistent eosinophilic airway obstruction". Patients with persistent eosinophilic airway obstruction are likely to be responsive to targeted biologic treatment, although additional clinical studies and real-world data are needed to further assess treatment efficacy and safety in this population and provide guidance to clinical practice.

Conflict of interest statement

Conflict of interest: N.A. Hanania reports grants from GSK, AstraZeneca, Sanofi, Regeneron, Genentech and Chiesi, and participation on a data safety monitoring board or advisory board with GSK, AstraZeneca, Sanofi, Regeneron and Verona. F.J.F. Herth reports payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, Boehringer, Chiesi and GSK, and participation on a data safety monitoring board or advisory board with AstraZeneca, Boehringer, Chiesi and GSK.

- **96 references**
- **2 figures**

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

Cite

17

BMC Pulm Med

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. 2025 Dec 9.

doi: 10.1186/s12890-025-04045-6. Online ahead of print.

Can assessment of small airway dysfunction support the diagnosis or management of asthma exacerbations in children? A systematic review

Abdulrahman Alshehri [1 2], Mohammed Ibrahim Alshahrani [3], Elizabeth Sapey [4], Robert Stockley [3], Mohammed Almeshari [5]

Affiliations Expand

- PMID: 41366757

- DOI: 10.1186/s12890-025-04045-6

Free article

Abstract

Background: Asthma exacerbations are acute episodes associated with worsening symptoms and lung function decline. In children, diagnosis and monitoring rely largely on clinical judgment and measures of large airway function, which may overlook peripheral airway involvement. Tests of small airway function, such as forced expiratory flow between 25% and 75% of vital capacity (FEF25-75) and impulse oscillometry (IOS), may offer additional physiological insights. The aim of this systematic review is to evaluate the evidence supporting the use of small airway tests during pediatric asthma exacerbations.

Main body: The protocol was registered on PROSPERO, and this systematic review followed established methodology. Electronic databases searched included MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCOhost), and CENTRAL (Cochrane Library). The search strategy combined subject headings and keywords relating to asthma exacerbations and small airway function (e.g.,'asthma exacerbation', 'small airway dysfunction', 'impulse oscillometry'). Eligible studies included observational studies and randomised controlled trials assessing small airway tests during paediatric asthma exacerbations (aged <18 years). Risk of bias was assessed using appropriate validated tools according to study design. Thirty-five studies met inclusion criteria. Thirty-one studies reported FEF25-75; four studies reported IOS parameters, including one that also included multiple-breath washout (MBW). Most studies found that small airway indices were impaired during exacerbations and improved after treatment. In many cases, FEF25-75 and IOS parameters (R5-R20, AX) showed greater relative change than forced expiratory volume in one second (FEV1), and small airways dysfunction persisted longer despite clinical recovery. All IOS studies achieved high feasibility in acute settings. No study evaluated whether small airway tests could be used to direct clinical management.

Conclusion: Physiological tests of small airway function appear feasible during acute paediatric asthma exacerbations and may detect abnormalities not captured by FEV1. However, no included studies evaluated whether incorporating these indices altered management or improved outcomes. While these tests show promise for future diagnostic or monitoring use, further validation in larger cohorts is needed before routine implementation.

Systematic review registration: PROSPERO 2025 CRD42025623062. Available from:https://www.crd.york.ac.uk/PROSPERO/view/CRD42025623062.

Keywords: Asthma; Asthma exacerbation; Children; FEF25–75; Impulse oscillometry; Multiple-breath washout.; Paediatric asthma; Small airway dysfunction.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: Not applicable. Ethical approval was not required for this study as it involved the analysis of publicly available data from previously published studies. Consent for publication: Not applicable. No individual person's data is included in this manuscript. Competing interests: The authors declare no competing interests.

- **64 references**

Full text links

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Cite

18

Nat Rev Immunol

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. 2025 Dec 9.

doi: 10.1038/s41577-025-01257-z. Online ahead of print.

Parental allergy and early life infection combine to promote asthma in childhood

Yvonne Bordon [1]

Affiliations Expand

- **PMID: 41366093**

- **DOI: 10.1038/s41577-025-01257-z**

No abstract available

- **1 reference**

Full text links

Cite

19

Cochrane Database Syst Rev

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. 2025 Dec 9;12(12):CD016205.

doi: 10.1002/14651858.CD016205.

High-flow nasal cannula oxygen therapy for asthma exacerbation

Aiko Honda [1 2], Yoshitaka Watanabe [3], Yoshifusa Abe [2 4], Sojiro Kusumoto [5], Takeshi Hasegawa [2 6 7], Hisashi Noma [2 8], Erika Ota [2 9], Takanori Imai [1], Noyuri Yamaji [2 10], Edward Barroga [11]

Affiliations Expand

- PMID: 41363211

- PMCID: PMC12687409

- DOI: 10.1002/14651858.CD016205

Abstract

This is a protocol for a Cochrane Review (intervention). The objectives are as follows: To evaluate the clinical effectiveness and safety of high-flow nasal cannula (HFNC) oxygen therapy compared with conventional oxygen therapy for the management of asthma exacerbations in children and adults. We will also explore potential equity implications, including differences in access to and outcomes of HFNC oxygen therapy across diverse healthcare settings and populations.

Conflict of interest statement

AK has declared that they have no conflict of interest.

YW has declared that they have no conflict of interest.

YA has declared that they have no conflict of interest.

SK has declared that they have no conflict of interest.

TK has declared that they have no conflict of interest.

HN received research funding from GlaxoSmithKline for work unrelated to this review (contract period: 1 January 2023 to 31 August 2023).

EO has declared that they have no conflict of interest.

TI has declared that they have no conflict of interest.

NY has declared that they have no conflict of interest.

EB has declared that they have no conflict of interest.

- **36 references**

Supplementary info

MeSH termsExpand

Full text links

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Cite

20

Tuberc Respir Dis (Seoul)

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. 2025 Dec 9.

doi: 10.4046/trd.2025.0161. Online ahead of print.

Consensus of Korean Asthma Study Group on Definition of Clinical Remission in Severe Asthma: A Modified Delphi Study

Sun Hye Shin [1 2], Joon Young Choi [3], Junghee Yoon [2], Youlim Kim [4], Jong Geol Jang [5], Ji-Yong Moon [4], Chin Kook Rhee [6], Kyung Hoon Min [7], Yong Il Hwang [8], Yeon-Mok Oh [9], Seong Yong Lim [10]; Korean Asthma Study Group in the Korean Academy of Tuberculosis and Respiratory Disease (KATRD)

Affiliations Expand

- **PMID: 41362087**

- **DOI: 10.4046/trd.2025.0161**

Free article

Abstract

Background: Asthma remission has recently emerged as an aspirational treatment goal, yet its definition remains inconsistent across studies and expert groups. The absence of a standardized framework hampers its application in clinical practice and research, particularly in Korea where biologics use is rapidly increasing. This study aimed to establish a consensus definition of clinical remission in severe asthma among Korean experts.

Methods: A two-round modified Delphi survey, followed by a focused third round, was conducted among 28 board-certified pulmonologists from the Korean Academy of Tuberculosis and Respiratory Diseases (KATRD). The questionnaire consisted of 6 domains and 27 items. Responses were analyzed using agreement rates, interquartile ranges, and content validity ratios to determine consensus levels.

Results: Consensus was reached on defining clinical remission as a composite of no exacerbations, no systemic corticosteroid use, sustained symptom control (ACT ≥20 on at least three occasions over 12 months), and stabilization and optimization of pulmonary function while on maintenance treatment. Experts agreed that pulmonary function should be assessed based on clinical judgment rather than absolute thresholds. Complete remission was additionally defined as fulfilling all clinical remission criteria with normalization of type 2 inflammation (blood eosinophils <300/μL and FeNO <25 ppb).

Conclusion: This Delphi consensus provides a regionally relevant and pragmatic framework for defining remission in severe asthma. These statements may help guide clinical practice, inform guideline development, and support future research on remission as a treatment goal.

Keywords: Delphi survey; clinical remission; severe asthma.

21

Review

Expert Rev Respir Med

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. 2025 Dec 9:1-12.

doi: 10.1080/17476348.2025.2600698. Online ahead of print.

What is the role of the IgE-mediated allergy in severe asthma?

Daniela Muti [1], Plamena Novakova [2], Silviya Novakova [3], Denislava Nedeva [4], Herberto Chong Neto [5], Angelica Tiotiu [6 7]

Affiliations Expand

- PMID: 41342580

- DOI: 10.1080/17476348.2025.2600698

Abstract

Introduction: Severe asthma (SA) is a heterogenous disease with multiple clinical phenotypes. 'Early atopic asthma' is the predominant phenotype in children with SA. This phenotype is also identified in adults with SA. However, the role of immunoglobulin E (IgE)-mediated allergy in SA is still under debate.

Areas covered: This review summarizes current evidence linking IgE-mediated sensitization to SA. Electronic search was realized in Medline and PubMed databases by using the following terms: 'severe asthma,' 'IgE-mediated' associated with 'environmental allergens,' 'aeroallergens,' 'house dust mites,' 'pollens,' 'pets,' 'moulds,' 'cockroach,' 'food allergy,' 'drug allergy,' 'venom allergy,' 'atopic dermatitis,' 'eczema,' 'anaphylaxis.' Exposure to most aeroallergens of SA patients with atopy is associated with an increased risk of severe exacerbations. Children with food allergy have more severe asthma, poor symptoms control, and a high hospitalization rate. More limited evidence exists for the other IgE-mediated conditions and SA.

Expert opinion: IgE-mediated pathways play central role in the pathogenesis of various allergic diseases, including asthma. However, the allergic burden seems to be more important in children with SA than in adults. Future research may provide a better understanding of the role of IgE-mediated allergy in SA and coexisting allergic diseases with improvement in their clinical outcomes.

Keywords: Aeroallergens; anaphylaxis; drugs-allergies; food-allergies; severe asthma; venoms-allergies.

. 2025 Dec 13:thorax-2025-223457.

doi: 10.1136/thorax-2025-223457. Online ahead of print.

Multidisciplinary, non-pharmacological breathlessness intervention service for patients with moderately severe to severe COPD: a randomised controlled trial

Tracy A Smith [1 2], Mary M Roberts [3 2 4 5], Tim Luckett [5], Jin-Gun Cho [3 2 4], Ester Klimkeit [3], Heather Stephenson [3], Nicola McCaffrey [6], Adrienne Kirby [7], John R Wheatley [3 2 4]

Affiliations Expand

- PMID: 41309286

- DOI: 10.1136/thorax-2025-223457

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is an often-progressive respiratory disease associated with disabling breathlessness. Breathlessness intervention services (BIS), which coach patients to self-manage breathlessness using non-pharmacological strategies, are effective in a variety of populations, including those with cancer and serious respiratory disease. This study aimed to compare the impact of the Westmead Breathlessness Service in people with moderate to severe COPD.

Methods: We analysed 113 participants randomised (1:1) with moderate/severe COPD (forced expiratory volume in 1 s (FEV_1)/forced vital capacity <0.70 and FEV_1 ≤60% predicted) and disabling breathlessness (modified Medical Research Council (mMRC) Breathlessness Score ≥2) to either an 8-week intervention involving breathing techniques, handheld fan use, exercise, energy conservation, dietetic advice (n=54) or 8-week wait-list control group (n=59). The primary outcome was change in Chronic Respiratory Questionnaire (CRQ) Mastery of breathlessness subscale. Secondary outcomes included change in other CRQ subscales (Fatigue, Emotion and Dyspnoea), exertional breathlessness intensity/unpleasantness (0-10 Numerical Rating Scale Score), anxiety and depression. Difference in change over 8 weeks between groups was compared using ANCOVA; p<0.05 statistically significant.

Findings: Participants were aged 70.9 (±8.5) years, 50% female, mean FEV_1 =0.8 L (±0.3 L; 34% predicted), mMRC Breathlessness Score 3 (IQR 3-4). CRQ-Mastery improved following intervention compared with control (between-group difference 0.5 units; 95% CI 0.2 to 0.8; p=0.0262) using modified intention-to-treat analysis. Better CRQ-Dyspnoea and CRQ-Fatigue were seen in the intervention group (between-group difference-CRQ-Dyspnoea 0.4 units; CI 0.1 to 0.7; p=0.005, and CRQ-Fatigue 0.4 units; CI 0.1 to 0.7; p=0.014). Exertional breathlessness intensity

(difference -0.8 units; CI -1.4 to -0.2; p=0.013) and breathlessness unpleasantness (difference -1.2 units; CI -1.7 to -0.6; p=0.001) also improved.

Interpretation: An 8-week BIS improved CRQ-Mastery, Dyspnoea and Fatigue, exertional breathlessness intensity and unpleasantness in people with severe COPD.

Keywords: COPD Exacerbations; Palliative Care; Perception of Asthma/Breathlessness.

Conflict of interest statement

Competing interests: None declared.

Full text links

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Cite

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Thorax

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. 2025 Dec 15;81(1):61-70.

doi: 10.1136/thorax-2024-222795.

Time to diagnosis and long-term outcomes for adults presenting with breathlessness

Urvee Karsanji [1], Claire A Lawson [2], Emily Petherick [3], Kamlesh Khunti [4], Gillian Doe [1], Jennifer K Quint [5], Alex Bottle [5], Michael C Steiner [1], Rachael A Evans [6]

Affiliations Expand

- PMID: 41285477

- DOI: 10.1136/thorax-2024-222795

Abstract

Background: The impact of delays to diagnosis for individuals presenting with chronic breathlessness is unknown. We investigated the time to diagnosis after

presenting with chronic breathlessness and associations with future unplanned hospitalisation and mortality.

Methods: A retrospective cohort study using the UK Clinical Practice Research Datalink involving adults with a first recorded code for breathlessness and no pre-existing cardiorespiratory disease. Adjusted Cox regression was used to investigate the associations with unplanned hospitalisation and mortality during all follow-up and within 2 years after the first code of breathlessness between those with and without a diagnosis, and using landmark analysis for time to diagnosis.

Results: 66 909/101 369 (66%) of adults with a first recorded code for breathlessness received an explanatory diagnosis during a median 5 years of follow-up. 43 394 (43%) of adults received an explanatory diagnosis within 2 years and had a higher risk (HR (95% CI)) of unplanned hospitalisation (1.25, 1.19 to 1.31) and mortality (1.84, 1.42 to 2.38) in the subsequent 2 years compared with adults without a diagnosis. In those with a recorded diagnosis, waiting ≥6 months was associated with increased mortality (6-24 months: 3.33 (2.13 to 5.20); ≥24 months: 13.30 (8.98 to 19.80)).

Conclusion: We describe better outcomes in adults coded for breathlessness without subsequent explanatory diagnoses. In adults with an explanatory diagnosis, waiting ≥6 months for a diagnosis was associated with reduced survival. Diagnostic pathways for chronic breathlessness need to differentiate between these two groups and achieve earlier diagnosis in those at higher risk.

Keywords: Asthma; Bronchiectasis; COPD epidemiology; Clinical Epidemiology; Interstitial Fibrosis; Symptom Assessment.

Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure. KK is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC).

- Cited by 1 article

Supplementary info

MeSH termsExpand

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Cite

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Editorial

Thorax

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. 2025 Dec 15;81(1):7.

doi: 10.1136/thorax-2025-224038.

Why asthma progresses to COPD: environmental and genetic drivers

Yankai Xia [1 2]

Affiliations Expand

- PMID: 41125389

- DOI: 10.1136/thorax-2025-224038

No abstract available

Keywords: Asthma; COPD epidemiology.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication typesExpand

Full text links

Proceed to details

Cite

25

Editorial

Thorax

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. 2025 Dec 15;81(1):1-2.

doi: 10.1136/thorax-2025-223499.

Occupational asthma: still an underestimated burden?

Filippo Liviero [1]

Affiliations Expand

- PMID: 41047245

- DOI: 10.1136/thorax-2025-223499

No abstract available

Keywords: Asthma Epidemiology; Occupational Lung Disease.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication typesExpand

Full text links

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26

Editorial

Thorax

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. 2025 Dec 15;81(1):5-6.

doi: 10.1136/thorax-2025-223595.

Home monitoring of asthma using oscillometry: seeking the signal in the noise

David A Kaminsky [1]

Affiliations Expand

- PMID: 41047239

- DOI: 10.1136/thorax-2025-223595

No abstract available

Keywords: Lung Physiology; Paediatric asthma.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication typesExpand

Full text links

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27

Observational Study

Thorax

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. 2025 Dec 15;81(1):42-50.

doi: 10.1136/thorax-2024-222744.

Day-to-day variability indices improve utility of oscillometry in paediatric asthma

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Affiliations Expand

- PMID: 40555499

- DOI: 10.1136/thorax-2024-222744

Abstract

Background: Oscillometry may provide the feasible and sensitive tool for objective remote monitoring of paediatric asthma.

Methods: Observational study of school-aged healthy, well-controlled and poorly-controlled asthma performing daily home-based oscillometry for 3-4 months, alongside objective measures of asthma control (Asthma Control Questionnaire weekly and Asthma Control Test monthly), medication use and exacerbations. Day-to-day variability calculated as coefficient of variation (CV) for resistance at 5 Hz (R5), reactance at 5 Hz (X5) and area under reactance curve (AX). Our objective was to examine feasibility, whether day-to-day variability was increased in asthma and correlations with asthma control and exacerbation burden. Clinical exacerbation patterns were examined using principal component analysis and k-means clustering of oscillometry, symptoms, breathing parameters and adherence.

Results: Feasibility was 74.9±16.0% in health (n=13, 93.7±16.2 days) and 80.6±12.9% in asthma (n=42, 101.6±24.9 days; 17 well-controlled and 27 poorly-controlled asthma). Increased day-to-day variability in all oscillometry indices occurred in asthma versus health (all p≤0.002), with CV R5 the best discriminator (area under receiver operating characteristics curve 0.88, p<0.001). CV R5 increased during exacerbation and correlated with all asthma control measures and exacerbation burden. Correlations remained when examining non-exacerbation oscillometry data. Two exacerbation patterns were found based on oscillometry data in the pre-exacerbation period, characterised by severity of impairment of R5, X5, AX and CV R5 (n=12, more severe). Findings were similar using post-exacerbation period oscillometry data (n=8, more severe). Symptoms did not differ across exacerbation patterns.

Conclusions: Home-based oscillometry monitoring was highly feasible over extended periods in school-aged asthmatics. Day-to-day oscillometry variability was increased in asthma compared with health, reflected asthma control and exacerbation burden and identified differing exacerbation patterns.

Keywords: Asthma; Paediatric Lung Disaese; Paediatric asthma; Respiratory Measurement.

Conflict of interest statement

Competing interests: None declared.

- **Cited by 1 article**

Supplementary info

Publication types, MeSH termsExpand

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Cite

28

Multicenter Study

Thorax

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. 2025 Dec 15;81(1):22-32.

doi: 10.1136/thorax-2024-222307.

Occupational exposures and incidence of asthma over two decades in the European Community Respiratory Health Survey

Sheikh M Alif [1 2 3], Geza Benke [3], Hans Kromhout [4], Michael J Abramson [3], Manolis Kogevinas [5], Debbie Jarvis [6], Nicole Le Moual [7], Shyamali Dharmage [8], Vivi Schlünssen [9], Kjell Torén [10], Dan Norback [11], Theodore Lytras [12], Anne-Elie Carsin [5 13], Cecilie Svanes [14], Mario Olivieri [15], Sandra Dorado-Arenas [16], Isabel Urrutia [16], Silvia Pascual Erquicia [16], Sofie Acke [17], Hayat Bentouhami [17], Gunilla Wieslander [11], Nicola Murgia [18], Jesús Martínez-Moratalla [19], Bénédicte Leynaert [7], Katja Radon [20], Jessica Gerlich [20], Dennis Nowak [20], Simona Villani [21], Mathias Holm [10], Giuseppe Verlato [22], Angelo D'Errico [23], Per Bakke [24], Trude Duelien Skorge [24], Torgeir Storaas [25], Anna Dahlman-Höglund [26], Johan Hellgren [26], David Miedinger [27], Torben Sigsgaard [9], Paul D Blanc [28], Jan-Paul Zock [29]

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- PMID: 40306950

- DOI: 10.1136/thorax-2024-222307

Abstract

Background: While short-term occupational exposures to many agents are associated with increased risk of asthma, the long-term consequences of exposure have not been well understood. We investigated the effects of occupational exposures over two decades on the incidence of asthma.

Methods: This population-based, multicentre cohort was assessed at baseline (European Community Respiratory Health Survey (ECRHS)1) and followed up twice over 20 years (ECRHS2 and ECRHS3). This analysis included data for 5591 participants with complete work histories and free of asthma at baseline. Incident

adult-onset asthma was defined as either an asthma attack, woken by an attack of shortness of breath and/or current asthma medication in the last 12 months before each timepoint, without asthma at a previous survey. An updated asthma-specific job exposure matrix was used to estimate exposures to asthmagens. Adjusted Poisson models were fitted with generalised estimating equations to estimate asthma incidence.

Results: Ever high exposure to high molecular weight *sensitisers* (rate ratio (RR)=1.31; 95% CI 1.15 to 1.63), *irritants* (RR=1.29; 1.09-1.54), biocides (RR=1.42; 1.12-1.79), only low exposure to low molecular weight *sensitisers* (RR=1.26; 1.08-1.47), mites (RR=1.48; 1.12-1.94) and reactive chemicals (RR=1.24; 1.06-1.45) were associated with increased incidence of asthma. Asthma incidence also increased with ever high or cumulative exposure to these exposures and for specific exposure to wood dust, cleaning agents and bleach. The population-attributable fraction for adult-onset asthma due to occupational exposures was 18% (16.9-19.4%).

Conclusion: This strengthens the evidence that occupational exposures to sensitisers and chemical irritants contribute substantial risk and a substantive attributable fraction of adult-onset asthma. Control of implicated hazardous exposures and periodic screening of exposed workers should be considered.

Keywords: Asthma; Clinical Epidemiology; Occupational Lung Disease.

Conflict of interest statement

Competing interests: MJA reports investigator-initiated grants from Pfizer, Boehringer-Ingelheim, Sanofi and GSK for unrelated research. He has conducted an unrelated consultancy for Sanofi. He has also received a speaker's fee from GSK. DJ reports grants from the European Commission, during the conduct of the study. VS reports grants from The Wood Dust Foundation (Project No. 444508795), during the conduct of the study. The remaining authors have nothing to disclose.

Supplementary info

Publication types, MeSH terms

"rhinitis"[MeSH Terms] OR rhinitis[Text Word]

1

Sci Rep

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. 2025 Dec 16.

doi: 10.1038/s41598-025-31902-5. Online ahead of print.

A retrospective cohort study on the association between allergic rhinitis, sublingual immunotherapy, and COVID-19 symptomatology

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Affiliations Expand

- PMID: 41402361

- DOI: 10.1038/s41598-025-31902-5

No abstract available

Keywords: Allergic rhinitis; COVID-19; Olfaction disorders; Respiratory symptoms; SARS-CoV-2; Sublingual immunotherapy.

Conflict of interest statement

Declarations. Competing interests: The authors declare no competing interests. Ethical approval: Ethical approval for this study was granted by the Ethics Committee of the First Affiliated Hospital with Nanjing Medical University (2023-SR-446) in accordance with the ethical standard of the Declaration of Helsinki. All participants gave informed consent prior to the survey.

- 54 references

Supplementary info

Grants and fundingExpand

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2

Review

Eur J Med Res

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. 2025 Dec 13.

doi: 10.1186/s40001-025-03685-y. Online ahead of print.

Association between early-life antibiotic exposure and gut microbiome alterations linked to allergic diseases in children: a systematic review

F N U Sameeha [1], Seerat Riaz [1], Muhammad Nouman Aslam [1], Abida Perveen [2]

Affiliations Expand

- PMID: 41390460

- DOI: 10.1186/s40001-025-03685-y

Free article

Abstract

Background: Early-life exposure to antibiotics has been implicated in the disruption of gut microbiota development, potentially contributing to the onset of allergic diseases in childhood. This systematic review aimed to evaluate the association between early antibiotic exposure, gut microbiome alterations, and the risk of developing allergic conditions such as asthma, atopic dermatitis, and allergic rhinitis.

Methods: This review followed PRISMA 2020 guidelines. A comprehensive search of PubMed, Embase, Web of Science, and the Cochrane Library was conducted up to [insert date]. Eligible studies included observational and interventional designs involving participants from the prenatal stage to 10 years of age. Data were extracted on antibiotic type, exposure timing, microbiome changes, and allergic outcomes. Study quality was assessed using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias tool for randomized trials.

Results: Fifteen studies involving over 1.5 million children met the inclusion criteria. The majority reported that antibiotic exposure during the prenatal period or the first two years of life was significantly associated with an increased risk of allergic diseases, particularly asthma and atopic dermatitis. Several studies also documented alterations in gut microbiota composition, including reduced Bifidobacterium and increased Clostridium and Klebsiella spps. Antibiotic type, duration, and timing of exposure were key factors influencing microbiota disruption and allergy development.

Conclusion: There is growing evidence that early-life antibiotic exposure may predispose children to allergic diseases through gut microbiota disturbances. These findings support the cautious use of antibiotics during pregnancy and early childhood and underscore the need for further research into microbiota-preserving interventions and long-term outcomes.

Keywords: Allergic diseases; Antibiotics; Asthma; Atopic dermatitis; Children; Early-life exposure; Gut microbiome.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: Not applicable. Competing interests: The authors declare no competing interests.

- **37 references**

Supplementary info

Publication typesExpand

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Cite

3

Allergy

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. 2025 Dec 13.

doi: 10.1111/all.70182. Online ahead of print.

EAACI Guidelines on the Importance of Green Space in Urban Environments for Allergy and Asthma Prevention

Tari Haahtela [1], Liam O'Mahony [2], Claudia Traidl-Hoffmann [3], Mubeccel Akdis [4], Ozlem Ceylan [5], Panagiotis Chaslaridis [6], Athanasios Damialis [7], Stefano Del Giacco [8], Antti Lauerma [1], Kari C Nadeau [9], Inês Paciência [10], Isabella Pali-Schöll [11 12], Oscar Palomares [13], Harald Renz [14 15 16], Jurgen Schwarze [17], Marilyn Urrutia-Pereira [18 19], Carina Venter [20], Donata Vercelli [21 22 23 24], Tonya Winders [25], Cezmi A Akdis [4], Marek Jutel [26 27], Ioana Agache [28]

Affiliations Expand

- **PMID: 41388798**

- **DOI: 10.1111/all.70182**

Abstract

The allergy and asthma epidemic in urban societies following World War II is mostly caused by changes in the environment, diet and lifestyle. Disconnection of urban populations from the wider environment has reduced the protective factors building up immunological resilience. The European Academy of Allergy and Clinical Immunology (EAACI) guidelines on greenness impact on allergy and asthma follow the Grading of Recommendations, Assessment, Development and Evaluation

(GRADE) approach and provide eight recommendations encouraging greenness exposure to support immune health. Controlled follow-up studies are still scarce, and the strength of evidence is generally low or moderate at best. For primary prevention of allergy and asthma, most of the evidence indicates beneficial effects. Exposure is also useful for secondary prevention. Asthma patients may feel better and need less medication by combining green space exposure with physical activity. During the high-pollen season, effective seasonal medication is necessary for patients with pollen allergy. In urban planning, implementing appropriate green infrastructure and easy access to green space promotes immune health and reduces risks of air pollution and heatwaves. These EAACI guidelines are the first recommendations highlighting the importance of urban green spaces on immune health and call for prioritising innovative research in this field.

Keywords: allergic rhinitis; asthma; atopic dermatitis; biodiversity; climate change; green space; greenness; guidelines; nature loss; nature-based solutions.

- 125 references

Supplementary info

Grants and fundingExpand

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4

Review

Int Forum Allergy Rhinol

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. 2025 Dec 11.

doi: 10.1002/alr.70078. Online ahead of print.

The Role of Artificial Intelligence in Chronic Rhinosinusitis: A Scoping Review

Nicola M Pereira [1], Sarah J Wie [1], Karena Zhao [1], Michelle Demetres [2], Ashutosh Kacker [1]

Affiliations Expand

- **PMID: 41376460**

- **DOI: 10.1002/alr.70078**

Abstract

Background: In the modern medical landscape, artificial intelligence (AI) is becoming an increasingly common tool for the diagnosis and management of chronic pathologies. Chronic rhinosinusitis (CRS) comprises a significant part of the practice of otolaryngology and thus provides ample opportunity for AI optimization of diagnosis and management.

Objective: With increasing interest in AI, this scoping review aims to map the current landscape of AI applications in CRS, identifying trends, gaps, and future opportunities.

Methods: A comprehensive literature search was performed in the following databases from inception-April 2024: Ovid MEDLINE, Ovid EMBASE, Web of Science, and The Cochrane Library. Studies retrieved were then screened for eligibility. The inclusion criteria included studies whose methods included the use of any form of AI for the diagnosis or management of chronic rhinosinusitis. Any studies that were non-English language publications, publications older than 2003, studies analyzing acute rhinosinusitis, and studies involving pediatric populations were excluded. Discrepancies were resolved by consensus.

Results: 573 records were screened, with 49 studies included in the final review. The studies were qualitatively analyzed according to the type of AI used, study objectives, application of AI, training variables for AI in CRS, and AI accuracy reporting. Commonly used forms of AI included deep learning (36.7%), neural networks (24.5%), convolutional neural networks (10.2%), and random forest models (6.1%). The majority (55%) of studies were focused on applying AI to the diagnosis of CRS. The remaining studies used AI to predict prognostic outcomes in CRS (29%) and to assess patient response to treatment or inform patient treatment plans (12%). Some studies aimed to identify biomarkers or clinical variables for the diagnosis or prognosis of CRS (37%), while others used AI to subtype CRS (33%) or assess radiologic characteristics using AI (20%). CT imaging, tissue or blood eosinophil counts, clinical or demographic patient characteristics, histopathology characteristics, blood and tissue cytokines, and nasal endoscopy findings were all variables used to train the AI models. Classification metrics and regression metrics were used to assess AI model performance.

Conclusions: AI is a promising tool in the management of CRS, though it remains in its early stages. Current applications show significant progress in diagnosis, subtyping, and prognosticating in CRS, but there are few studies that analyze the utility of AI for surgical planning, economic evaluation, or interactive clinical tools. This review underscores the potential of AI for transforming an otolaryngologist's approach to CRS.

Keywords: asthma; chronic rhinosinusitis; rhinitis; rhinosinusitis; sinusitis.

- 55 references

Supplementary info

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Cite

5

J Occup Health

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. 2025 Dec 10:uiaf071.

doi: 10.1093/joccuh/uiaf071. Online ahead of print.

Association between allergic rhinitis and work productivity in a non-clinical setting: a cross-sectional study

Yasuhiro Sekine [1], Kazuhiro Watanabe [1 2], Hyogo Horiguchi [3], Go Muto [3], Eriko Miyajima [4], Naoki Kikuchi [1], Akizumi Tsutsumi [1]

Affiliations Expand

- PMID: 41368811

- DOI: 10.1093/joccuh/uiaf071

Free article

Abstract

Objective: Allergic rhinitis (AR) is a prevalent condition in Japan that negatively affects workers by reducing their productivity. However, previous studies primarily focused on patients with severe AR symptoms. This exploratory study aimed to examine the association between AR, including mild cases, and reduced work productivity in the general working population.

Methods: A questionnaire survey was conducted between March and April 2024, recruiting adult workers living in the Kanto region through a healthcare center and affiliated companies. Absenteeism, presenteeism, and weekly economic costs were

compared between individuals with and without AR. Multiple regression analysis was performed to examine the association between AR severity and productivity. A causal mediation analysis was also conducted to explore the indirect effects of depressive symptoms, positive and negative affect, and sleep quality on the association between AR and presenteeism.

Results: Of the 555 participants, 347 (62.5%) reported having AR, while 208 (37.5%) reported not having AR or were unsure. No significant differences were observed in absenteeism or presenteeism between the AR and non-AR/unknown groups. In the AR group, AR severity was significantly associated with increased presenteeism (unstandardized partial regression coefficient B=4.19 [95% confidence interval (CI): 3.48-4.90], p<0.001). Causal mediation analysis revealed a significant total natural indirect effect (TNIE) only for depressive symptoms (TNIE=5.246 [95% CI: 0.059-10.432], p=0.047).

Conclusions: In the non-clinical setting, the overall impact of AR on work productivity may be limited among Japanese workforces.

Keywords: absenteeism; depressive symptoms; economic cost; mediation analysis; pollen allergy; presenteeism.

chronic cough

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Respir Investig

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. 2025 Dec 12;64(1):101353.

doi: 10.1016/j.resinv.2025.101353. Online ahead of print.

Identification of individuals with COPD using biometric voice and cough sound features

Yasushi Obase [1], Susumu Fukahori [2], Jun Iriki [3], Takahiro Takazono [4], Yusei Tsukamoto [3], Shinnosuke Takemoto [2], Noriho Sakamoto [5], Yusuke Hamanaka [6], Hideaki Watanabe [6], Kazumi Hirano [6], Chizu Fukushima [7], Tomoya Nishino [8], Hiroshi Mukae [5]

Affiliations Expand

- PMID: 41389529

- DOI: 10.1016/j.resinv.2025.101353

Abstract

Background: Chronic obstructive pulmonary disease (COPD), a major global health burden linked to smoking, is frequently underdiagnosed due to low awareness and delayed symptom recognition. This study explored the feasibility of non-invasive voice and cough sound analysis for COPD identification.

Methods: In this prospective study, 55 participants (26 with COPD, 29 without) underwent pulmonary function testing and provided sociodemographic and clinical data. Speech and cough sounds were recorded three times per participant and processed using acoustic feature extraction, feature selection via the minimum redundancy maximum relevance algorithm, and logistic regression classification. Model performance was evaluated using four-fold cross-validation. Statistical analysis was conducted with JMP software ($p < 0.05$).

Results: The vowel sound/u/showed statistically significant discriminatory ability in the mixed-gender cohort, but sensitivity and specificity were both below 80 %, indicating limited diagnostic performance. When restricted to male participants, both metrics exceeded 80 %, suggesting higher discriminatory power. Smartphone recordings yielded comparable accuracy to integrated circuit recorders. Adding COPD assessment test scores and smoking history did not improve classification.

Conclusions: Voice analysis may offer a non-invasive screening approach for COPD. However, this study was limited to male participants and a single disease target, restricting generalizability. Future research will expand to include related respiratory conditions such as bronchiectasis and assess performance across sexes and disease types.

Keywords: COPD screening; Machine learning; Non-invasive biomarker; Voice sound analysis.

Conflict of interest statement

Declaration of competing interest Takahiro Takazono received honoraria for lecture fee from Insmed, Asahikasei, Shionogi, Pfizer, and MSD, and research grants from

GSK, Asahikasei, and Shionogi; Hiroshi Mukae received honoraria for lecture fee from Asahi Kasei Pharma Corporation, AstraZeneca K.K., Chugai Pharmaceutical Co., Ltd., Gilead Sciences Inc., GlaxoSmithKline K.K, Insmed Incorporated, Kyorin Pharmaceutical Co., Ltd., MSD Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Novartis Pharma K.K, Pfizer Inc., SHIONOGI Co., Ltd., and Taisho Pharma Co., Ltd., and research grants from FUJIFILM Toyama Chemical Co., Ltd, Kyorin Pharmaceutical Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Otsuka Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd., Taisho Pharma Co., Ltd., and SHIONOGI Co., Ltd. and Donations from Taiho Pharmaceutical Co., Ltd., and Taisho Pharma Co., Ltd.; the other authors have no conflict of interest.

Cite

2

Practice Guideline

Respiration

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. 2025 Dec 12:1-59.

doi: 10.1159/000549999. Online ahead of print.

Diagnosis and treatment of adult patients with cough

Peter Kardos, Sven Becker, Kai-Roland Heidenreich, Ludger Klimek, Thomas Köhnlein, Joachim Labenz, Norbert Mülleneisen, Dorothea Pfeiffer-Kascha, Isabell Pink, Helmut Sitter, Frederik Trinkmann, Heinrich Worth, Cordula Winterholler

- PMID: 41385480

- DOI: 10.1159/000549999

Free article

Abstract

This is the 4th edition of the S2k cough Guideline (based on a structured consensus among a representative committee) of the German Respiratory Society (DGP) for specialists, written by respiratory, internal medicine, allergy, ear-nose-throat,

gastroenterology specialists, speech therapists and physiotherapists - accredited by their respective scientific societies. Importantly, a patient representative was also involved. The Guideline was coordinated under the guidance of a representative from AWMF (Association of the Scientific Medical Societies in Germany). With regard to specific questions, we intend to supplement the cough guideline of the German Society of General and Family Medicine (DEGAM). Compared to the earlier versions 1-3 of the DGP cough guideline, which had the character of a monograph, the concept of this guidelines is completely new. In a modified Delphi process, the authors developed 12 key questions; they were answered in the guideline conference and the recommendations were graded strong), weak or insufficient on the basis of the available evidence. A brief scientific background to the respective questions was then compiled by expert groups of authors. In some cases, new diagnostic algorithms were created for acute, subacute and chronic cough. The significantly reduced scope and improved overview make the guideline easier to use in daily practice. It has also been incorporated into the Leila Pro smartphone Application and can be accessed using its convenient functions (see https://www.leila.de/de/).

Supplementary info

Publication typesExpand

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Cite

3

Eur Respir J

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. 2025 Dec 11:2501435.

doi: 10.1183/13993003.01435-2025. Online ahead of print.

A multi-country cohort study evaluating the prevalence, risk factors, lung function and clinical outcomes of chronic bronchitis in low- and middle-income countries

Nicole M Robertson [1 2 3], Arun K Sharma [4 3], Mingling Yang [1 2], Santa K Das [5], Trishul Siddharthan [2 6], Suzanne L Pollard [1], Natalie A Rykiel [1 2], Patricia Alupo [7], Oscar Flores-Flores [2 8], Bruce Kirenga [7], Ram K Chandyo [9], Shumonta A Quaderi [10], Laxman Shrestha [4], Robert A Wise [1], John R Hurst [10], William Checkley [11 2]; Global Excellence in COPD outcomes (GECo) Study Investigators

Affiliations Expand

- **PMID: 41381225**

- **DOI: 10.1183/13993003.01435-2025**

Abstract

Background: Chronic bronchitis affects up to 40% of individuals with COPD and may serve as an early predictor of the disease and development of COPD. We investigated the prevalence, risk factors, and clinical outcomes associated with chronic bronchitis in three low- and middle-income countries (LMICs).

Methods: We conducted a population-based study of adults aged ≥40 years in Bhaktapur (Nepal), Lima (Peru), and Nakaseke (Uganda). Chronic bronchitis was defined as a productive cough several days per week for over four weeks. Multivariable log-binomial regression identified risk factors and outcomes associated with chronic bronchitis.

Results: Among 9664 participants (mean age 56.2 years, 51.0% male, 66.9% ever smokers), chronic bronchitis prevalence was 9.7%, with 31.5% of those also having COPD. Significant risk factors included older age (adjusted RR=1.54 per 19.8 years, 95% CI 1.4-1.7), male sex (1.18, 1.05-1.34), prior tuberculosis (1.45, 1.14-1.83), prior asthma diagnosis (2.11, 1.84-2.42), pack-years of tobacco use (1.16 per 10 pack-years, 1.14-1.18), family history of chronic respiratory diseases (1.69, 1.50-1.91), second-hand smoke exposure (1.45, 1.28-1.64), lower socioeconomic status quartile (1.22,1.07-1.39), and indoor biomass exposure (1.45, 1.13-1.64). Participants with chronic bronchitis experienced more breathlessness, worse respiratory health (higher St. George's Respiratory Questionnaire scores), and higher hospitalization rates (all p<0.001).

Conclusions: Chronic bronchitis is common in LMIC settings and is associated with multiple modifiable risk factors, including second-hand smoke, biomass exposure, and prior respiratory disease. Addressing these factors may reduce disease burden and improve quality of life.

4

Tuberc Respir Dis (Seoul)

. 2025 Dec 9.

doi: 10.4046/trd.2025.0104. Online ahead of print.

Cough Assessment in Chronic Respiratory Diseases (COASESS): Findings from A Prospective Multicenter Cross-Sectional Study

Tai Joon An [1], Hyeon-Kyoung Koo [2], Chin Kook Rhee [3], Yee Hyung Kim [4], Sung-Kyoung Kim [5], Kyung Hoon Min [6], Deog Kyeom Kim [7], Jong-Wook Shin [8], Hyoung Kyu Yoon [1], Woo-Jung Song [9], Jin Woo Kim [10], Ji-Yong Moon [11]

Affiliations Expand

- PMID: 41365251

- DOI: 10.4046/trd.2025.0104

Free article

Abstract

Background: Cough is a key symptom of chronic respiratory diseases such as asthma, idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disease (COPD), and bronchiectasis (BE). Some patients develop chronic cough (CC), defined as lasting over eight weeks, yet its characteristics remain unclear. This study aimed to characterize CC across different chronic respiratory diseases using validated cough assessment tools.

Methods: This multicenter, prospective cross-sectional study (the COASESS study) was conducted at 10 university hospitals. CC was assessed for intensity (numeric rating scale, NRS), frequency (cough symptom score, CSS), and quality of life (cough assessment tool [COAT], Leicester Cough Questionnaire [LCQ]). Cough hypersensitivity was evaluated using the Cough Hypersensitivity Questionnaire (CHQ). Age, sex, and smoking status were also recorded.

Results: Of 303 enrolled patients, 266 with chronic respiratory diseases were analyzed. Asthma patients were younger, more often female, and never-smokers, while COPD and IPF patients were older male ever-smokers ($P < 0.001$). COAT, LCQ, NRS, and CSS scores differed significantly across diseases, with asthma and IPF showing greater symptom burden and poorer quality of life than COPD or BE ($P < 0.001$). CHQ total scores were similar across groups, but asthma patients more often reported triggers like talking and post-nasal drip.

Conclusions: This study identified distinct CC characteristics across chronic respiratory diseases. Asthma and IPF were associated with greater symptom burden, and cough hypersensitivity varied by underlying condition. These findings support the need for disease-specific CC assessment and management.

Keywords: Asthma; Bronchiectasis; Chronic Obstructive Pulmonary Disease; Chronic cough; Cough Hypersensitivity; Idiopathic pulmonary fibrosis; Structural lung diseases.

Full text links

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Cite

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Tuberc Respir Dis (Seoul)

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. 2025 Dec 9.

doi: 10.4046/trd.2025.0164. Online ahead of print.

Objective Assessment of Cough: Listening to the Patient's Voice: A Narrative Review

Tai Joon An [1]

Affiliations Expand

- **PMID: 41362086**

- **DOI: 10.4046/trd.2025.0164**

Free article

Abstract

Cough is one of the most common yet least quantifiable respiratory symptoms. Despite its prevalence-affecting up to 10% of adults worldwide-objective measurement remains challenging. Conventional descriptors such as "frequent" or "severe" are inherently subjective and poorly reproducible, limiting clinical interpretation and standardization. Over the past five decades, technological advances have transformed cough assessment from manual counting and provocation testing to automated acoustic monitoring and neurophysiologic imaging. Modern validated systems such as the Leicester Cough Monitor and VitaloJAK™ provide reproducible measures of cough frequency, now accepted as regulatory trial endpoints. In contrast, cough intensity remains difficult to capture objectively. Physiologic tools including peak cough flow, esophageal manometry, and electromyography provide mechanistic insights but are invasive and impractical for real-world use. Acoustic amplitude serves as a promising

noninvasive surrogate, yet suffers from ambient noise interference and lack of cross-device calibration. Functional MRI and experimental brain PET have further revealed cortical and subcortical dysregulation underlying cough hypersensitivity, reframing chronic cough as a disorder of aberrant sensory processing. However, these approaches remain research tools, constrained by cost, accessibility, and limited validation. The future of cough assessment lies in integrated, multimodal systems that combine physiologic, acoustic, and neuroimaging signals through AI-based analytics. Such approaches could transform cough into a measurable digital biomarker-an objective "fifth vital sign." Realizing this vision will require collaborative efforts among clinicians, engineers, and policymakers to ensure validation, standardization, and clinical applicability.

Keywords: Biomarkers; Chronic Cough; Cough; Cough Hypersensitivity Syndrome; Monitoring, Physiologic.

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Eur J Med Chem

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. 2025 Dec 15:300:118116.

doi: 10.1016/j.ejmech.2025.118116. Epub 2025 Sep 7.

Development of a P2X3 receptor antagonist derived from eliapixant with improved properties for the treatment of chronic cough

Yang Zang [1], Qun Li [1], Yang Li [1], Xiaohua Ding [1], Ruibin Liu [1], Lifei Liu [1], Hongna Sun [1], Lihan Qu [1], Xuejun Zhang [2]

Affiliations Expand

- PMID: 40946532

- DOI: 10.1016/j.ejmech.2025.118116

Abstract

The P2X3 receptor is an ATP-activated ion channel primarily expressed on peripheral sensory neurons. Its activation triggers cough reflex pathways, making it an attractive target for treating chronic cough and the discovery of P2X3 receptor

antagonist has been a long-term pursuit by academia and pharmaceutical companies. However, preliminary antagonists have been hampered by taste disturbances or drug-induced liver injury. Our strategy described herein are maintaining a moderate selectivity between P2X3 and P2X2/3 receptors and replacing the metabolically labile motif with 3-methylbutan-2-ol. These discovery efforts lead to the identification of HW091077, a P2X3 receptor antagonist with an optimal balance of potency, selectivity, PK and metabolic properties that has advanced into clinical trials for the treatment of chronic cough.

Keywords: ATP-Gated ion channel receptor; Antagonist; Chronic cough; P2X3.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary info

MeSH terms, SubstancesExpand

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Cite

"bronchiectasis"[MeSH Terms] OR bronchiectasis[Text Word]

1

Sarcoidosis Vasc Diffuse Lung Dis

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. 2025 Dec 15;42(4):17112.

doi: 10.36141/svdld.v42i4.17112.

The prevalence of interstitial lung disease and bronchiectasis in rheumatoid arthritis: A systematic review and meta-analysis

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Affiliations Expand

- PMID: 41396107

- DOI: 10.36141/svdld.v42i4.17112

Abstract

Background and aim: Rheumatoid arthritis (RA) is associated with an increased risk of interstitial lung disease (ILD) and bronchiectasis. Understanding the prevalence of these diseases is essential for timely diagnosis and management. Our aim was to estimate the prevalence of ILD and bronchiectasis in RA patients.

Study design and methods: A systematic literature search was performed on PubMed, Embase, and Google Scholar to identify all studies performing HRCT in consecutive RA patients. Articles were screened by three independent authors in accordance with PRISMA guidelines. Random-effects meta-regression was performed to estimate the prevalence according to RA duration and C-reactive protein.

Results: Twenty-four studies comprising 2,532 RA patients were included. The estimated prevalence of ILD at the time of RA diagnosis was 8.5% (95% CI: 4.4-12.5%), increasing by 3.0 percentage points (95% CI: 2.1-3.9%) per year after RA diagnosis (P<0.0001, R^2=95%). The estimated prevalence of bronchiectasis at RA diagnosis was 8.2% (95% CI: 1.6-14.7%), increasing 1.1 percentage points (95% CI: 0.3-1.9) per year after RA diagnosis (P<0.01, R^2=34%). Bronchiectasis prevalence was strongly associated with C-reactive protein and increased by 3.1 percentage points (95% CI: 0.9-5.4) per unit increase in CRP (mg/dL) (p<0.01, R2=77%) Conclusion: Bronchiectasis and ILD are common pulmonary manifestations of RA, particularly in patients with long-term disease. Possibly due to the cumulative effect of chronic inflammation. Therefore, we suggest HRCT for all patients with respiratory symptoms or RA duration exceeding 5 years. This approach may facilitate earlier detection of preclinical ILD and timely intervention.

2

Respir Investig

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. 2025 Dec 12;64(1):101353.

doi: 10.1016/j.resinv.2025.101353. Online ahead of print.

Identification of individuals with COPD using biometric voice and cough sound features

Yasushi Obase [1], Susumu Fukahori [2], Jun Iriki [3], Takahiro Takazono [4], Yusei Tsukamoto [3], Shinnosuke Takemoto [2], Noriho Sakamoto [5], Yusuke Hamanaka [6], Hideaki Watanabe [6], Kazumi Hirano [6], Chizu Fukushima [7], Tomoya Nishino [8], Hiroshi Mukae [5]

Affiliations Expand

- PMID: 41389529

- DOI: 10.1016/j.resinv.2025.101353

Abstract

Background: Chronic obstructive pulmonary disease (COPD), a major global health burden linked to smoking, is frequently underdiagnosed due to low awareness and delayed symptom recognition. This study explored the feasibility of non-invasive voice and cough sound analysis for COPD identification.

Methods: In this prospective study, 55 participants (26 with COPD, 29 without) underwent pulmonary function testing and provided sociodemographic and clinical data. Speech and cough sounds were recorded three times per participant and processed using acoustic feature extraction, feature selection via the minimum redundancy maximum relevance algorithm, and logistic regression classification. Model performance was evaluated using four-fold cross-validation. Statistical analysis was conducted with JMP software ($p < 0.05$).

Results: The vowel sound/u/showed statistically significant discriminatory ability in the mixed-gender cohort, but sensitivity and specificity were both below 80 %, indicating limited diagnostic performance. When restricted to male participants, both metrics exceeded 80 %, suggesting higher discriminatory power. Smartphone recordings yielded comparable accuracy to integrated circuit recorders. Adding COPD assessment test scores and smoking history did not improve classification.

Conclusions: Voice analysis may offer a non-invasive screening approach for COPD. However, this study was limited to male participants and a single disease target, restricting generalizability. Future research will expand to include related respiratory conditions such as bronchiectasis and assess performance across sexes and disease types.

Keywords: COPD screening; Machine learning; Non-invasive biomarker; Voice sound analysis.

Conflict of interest statement

Declaration of competing interest Takahiro Takazono received honoraria for lecture fee from Insmed, Asahikasei, Shionogi, Pfizer, and MSD, and research grants from GSK, Asahikasei, and Shionogi; Hiroshi Mukae received honoraria for lecture fee from Asahi Kasei Pharma Corporation, AstraZeneca K.K., Chugai Pharmaceutical Co., Ltd., Gilead Sciences Inc., GlaxoSmithKline K.K, Insmed Incorporated, Kyorin Pharmaceutical Co., Ltd., MSD Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Novartis Pharma K.K, Pfizer Inc., SHIONOGI Co., Ltd., and Taisho Pharma Co., Ltd., and research grants from FUJIFILM Toyama Chemical Co., Ltd, Kyorin Pharmaceutical Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Otsuka Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd., Taisho Pharma Co., Ltd., and SHIONOGI Co., Ltd. and Donations from Taiho Pharmaceutical Co., Ltd., and Taisho Pharma Co., Ltd.; the other authors have no conflict of interest.

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Chest

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. 2025 Dec 10:S0012-3692(25)05826-X.

doi: 10.1016/j.chest.2025.12.001. Online ahead of print.

Aspergillus fumigatus sensitization is associated with high-risk bronchiectasis

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Affiliations Expand

- **PMID: 41386457**

- **DOI: 10.1016/j.chest.2025.12.001**

Free article

Abstract

Background: Fungal sensitization is an increasingly recognized endophenotype in chronic respiratory disease, however, its role in bronchiectasis remains poorly

defined. This study aims to provide the most comprehensive evaluation to date of fungal sensitization and its clinical relevance in bronchiectasis using an expanded panel of crude and recombinant fungal allergens.

Research question: What is the prevalence and clinical implications of fungal sensitization in bronchiectasis?

Study design and methods: We conducted an international, multi-centre evaluation of fungal sensitization across six tertiary centres in four countries (Singapore, Malaysia, United Kingdom and Italy) prospectively recruiting N=277 individuals with bronchiectasis. Using a comprehensive, expanded allergen panel including 11 crude and 24 recombinant fungal allergens (total: 35 allergens and 9,695 individual assays), we assessed sensitization responses in relation to clinical characteristics, exacerbation frequency and geographic origin. Low baseline exacerbations is defined as < 3, and high as ≥ 3 in the preceding 12 months of study recruitment.

Results: Sensitization to recombinant Aspergillus fumigatus (rAsp f) links to bronchiectasis severity. Measurable responses to rAsp f allergens 12, 15, and 17 associates with severe (hospitalized) exacerbations. particularly in those with low baseline exacerbations (low-risk) . 'Sensitized' low-risk individuals demonstrate significantly greater disease severity and higher occurrence of bronchiectasis-COPD overlap (BCO) compared to non-sensitized, low-risk individuals , a relationship absent in those with high baseline exacerbations . Polysensitization to the same allergens confers further additional risks of severe (hospitalized) exacerbations. Notably, sensitized Asians to rAsp f allergens 12, 15, and 17 demonstrate poorest clinical outcomes with increased symptoms, poorer lung function, and severe disease.

Interpretation: Aspergillus fumigatus sensitization, particularly to rAsp f allergens 12, 15, and 17 is a clinically significant and potentially treatable trait in bronchiectasis. This is of highest relevance in individuals with lower baseline exacerbation frequency and Asian descent.

Keywords: Asian; Aspergillus sensitization; bronchiectasis; exacerbations; fungi.

. 2025 Dec 11;30(1):1231.

doi: 10.1186/s40001-025-03604-1.

The cellular triangle in bronchiectasis: the interplay network and regulatory mechanisms of neutrophils, macrophages, and epithelial cells

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- PMID: 41373005
- PMCID: PMC12696920
- DOI: 10.1186/s40001-025-03604-1

Abstract

Bronchiectasis is a chronic airway disorder characterized by persistent inflammation and structural damage, driven by dynamic interactions among neutrophils, macrophages, and epithelial cells. While current therapies-such as airway clearance techniques, inhaled antibiotics, and macrolides-provide symptomatic and antimicrobial benefits, they remain largely reactive and fail to address the underlying inflammatory networks that sustain disease progression. This review focuses on the central role of the neutrophil-macrophage-epithelial cellular triad in bronchiectasis pathogenesis. We synthesize evidence detailing how these cells communicate via cytokines, proteases, and extracellular traps to perpetuate a self-amplifying cycle of infection, inflammation, and tissue remodeling. By moving beyond a pathogen-centric perspective, this review aims to establish a coherent framework for understanding immune-epithelial crosstalk as a driver of disease heterogeneity and treatment resistance. Ultimately, we highlight how decoding these cellular circuits may reveal novel therapeutic targets capable of disrupting disease chronicity and advancing precision management in bronchiectasis.

Keywords: Bronchiectasis; Epithelial cells; Interplay network; Macrophages; Neutrophils.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: Not applicable. Consent for publication: Not applicable. Competing interest: The authors declare that they have no competing interests.

- 72 references

- 1 figure

Supplementary info

Publication types, MeSH terms, Grants and fundingExpand

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Jpn J Radiol

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. 2025 Dec 11.

doi: 10.1007/s11604-025-01917-z. Online ahead of print.

Automated interstitial lung abnormalities detection at CT: external validation and potential recognition of traction bronchiectasis/bronchiolectasis

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- PMID: 41372552

- DOI: 10.1007/s11604-025-01917-z

Abstract

Purpose: An artificial intelligence (AI) system for detecting interstitial lung abnormalities (ILA) was previously developed but requires external validation. This study aimed to examine the robustness across different populations and investigate associations between the system outputs and traction bronchiectasis/bronchiolectasis severity patterns.

Materials and methods: CT scans from population-based samples of the Rotterdam Study (2018-2019) and the Age Gene/Environment Susceptibility Reykjavik (AGES-Reykjavik) Study (baseline CT: 2002-2006, follow-up CT: 2007-2011) were used in

this secondary analysis of the two cohorts. The AI system calculated ILA probability score (AI score) in the range from 0 to 1. Three experienced readers evaluated independently all CT scans for ILA, and two chest radiologists assessed traction bronchiectasis/bronchiolectasis using the 4-scale traction bronchiectasis/bronchiolectasis index (TBI) for severity by consensus. Receiver operating characteristic (ROC) analysis and Kruskal-Wallis test were used for statistical analysis.

Results: The system analyzed 932 CT scans of the Rotterdam Study (mean participant age, 79.6 years ± 4.3 (SD), 482 women) and 5242 CT scans of the AGES-Reykjavik Study (mean participant age, 76.4 years ± 5.6, 3032 women), and achieved area under the ROC curve of 0.841 (95% CI 0.804, 0.879) and 0.823 (95% CI 0.798, 0.847), respectively. AI scores correlated with readers' certainty, decreasing from unanimous ILA cases to No-ILA cases. Higher baseline AI scores correlated with greater severity of traction bronchiectasis/bronchiolectasis (TBI-3: 0.931 [IQR, 0.911-0.932], TBI-2: 0.738 [IQR, 0.406-0.880], TBI-1: 0.537 [IQR, 0.317-0.761], TBI-0: 0.250 [IQR, 0.136-0.455]).

Conclusion: The system demonstrated robust ILA detection performance across different populations, with AI scores showing associations with traction bronchiectasis/bronchiolectasis severity.

Keywords: Artificial intelligence; CT; External validation; Interstitial lung abnormalities; Machine learning; Traction bronchiectasis/bronchiolectasis.

Conflict of interest statement

Declarations. Conflict of interest: A.K., K.A., and M.O. are employees of Canon Medical Systems Corporation, Tochigi, Japan. M.K. is an employee of Canon Inc., Tokyo, Japan. D.W.L. received payment to institution for organization of a regional pulmonary hypertension course sponsored by Ferrer, MSD, and Johnson & Johnson, and received travel support for a perceptorship course at Aarhus University Hospital. He serves as a board member of the ILD section of the Dutch Association of pulmonary physicians (NVALT). M.W.V. receives funding from ZonMw Memorabel grant (No. 733050817), TAP-dementia ZonMw funded project (#10510032120003), Medical Delta research grant, and ABOARD public–private partnership (ZonMW #73305095007, Health ~ Holland #LSHM20106). She received honorarium paid to institution for an educational lecture to EISAI company (topic unrelated to the present manuscript). V.G. received grant payments from NIA grants N01-AG-12100 and HHSN271201200022C. D.C.C receives research grant from NIH. G.M.H. receives funding from NIH NHLBI grants R01 HL111024, R01 HL130974, and R01 HL135142, and received consulting fees from Gerson Lehrman Group and Boehringer Ingelheim, and lecture honoraria from Boehringer Ingelheim, and travel support for meetings from Boehringer Ingelheim. M.N. and H.H. received research grants to institution from Canon Medical Systems and Konica Minolta. H. H. also received consulting fees from Canon Medical Systems Inc. and Boehringer Ingelheim Inc. (less than $5,000 USD per year each). G.G. received grant payments from Landspitali Scientific Fund, University of Iceland Research Fund, and Icelandic Research Fund. K.A., M.O., M.K., and H.H. are co-inventors on US patent application number 63/610,842. M.O. holds stock options in Institute for Advanced Diagnosis for Rare Diseases & Conditions K.K. Ethical approval: This study was a secondary

analysis of de-identified imaging data from two previously approved cohort studies. The Rotterdam Study was approved by the Medical Ethics Committee (MEC 02.1015), and the AGES-Reykjavik Study was approved by the Institutional Review Board (VSN 00–063). As this study involved only retrospective analysis of existing anonymized imaging data, additional ethical approval was not required. Informed consent: Written informed consent was obtained from all participants in the original cohort studies. As this study used only de-identified data, additional informed consent was not required.

- 32 references

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Tuberc Respir Dis (Seoul)

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. 2025 Dec 9.

doi: 10.4046/trd.2025.0104. Online ahead of print.

Cough Assessment in Chronic Respiratory Diseases (COASESS): Findings from A Prospective Multicenter Cross-Sectional Study

Tai Joon An [1], Hyeon-Kyoung Koo [2], Chin Kook Rhee [3], Yee Hyung Kim [4], Sung-Kyoung Kim [5], Kyung Hoon Min [6], Deog Kyeom Kim [7], Jong-Wook Shin [8], Hyoung Kyu Yoon [1], Woo-Jung Song [9], Jin Woo Kim [10], Ji-Yong Moon [11]

Affiliations Expand

- PMID: 41365251

- DOI: 10.4046/trd.2025.0104

Free article

Abstract

Background: Cough is a key symptom of chronic respiratory diseases such as asthma, idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disease (COPD), and bronchiectasis (BE). Some patients develop chronic cough (CC), defined as lasting over eight weeks, yet its characteristics remain unclear. This

study aimed to characterize CC across different chronic respiratory diseases using validated cough assessment tools.

Methods: This multicenter, prospective cross-sectional study (the COASESS study) was conducted at 10 university hospitals. CC was assessed for intensity (numeric rating scale, NRS), frequency (cough symptom score, CSS), and quality of life (cough assessment tool [COAT], Leicester Cough Questionnaire [LCQ]). Cough hypersensitivity was evaluated using the Cough Hypersensitivity Questionnaire (CHQ). Age, sex, and smoking status were also recorded.

Results: Of 303 enrolled patients, 266 with chronic respiratory diseases were analyzed. Asthma patients were younger, more often female, and never-smokers, while COPD and IPF patients were older male ever-smokers (P < 0.001). COAT, LCQ, NRS, and CSS scores differed significantly across diseases, with asthma and IPF showing greater symptom burden and poorer quality of life than COPD or BE (P < 0.001). CHQ total scores were similar across groups, but asthma patients more often reported triggers like talking and post-nasal drip.

Conclusions: This study identified distinct CC characteristics across chronic respiratory diseases. Asthma and IPF were associated with greater symptom burden, and cough hypersensitivity varied by underlying condition. These findings support the need for disease-specific CC assessment and management.

Keywords: Asthma; Bronchiectasis; Chronic Obstructive Pulmonary Disease; Chronic cough; Cough Hypersensitivity; Idiopathic pulmonary fibrosis; Structural lung diseases.

doi: 10.1007/s00330-025-12188-7. Online ahead of print.

Quantitative CT of emphysema, wall thickness and mucus plugs in alpha-1-antitrypsin deficiency: relationship to clinical outcomes

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Affiliations Expand

- **PMID: 41364209**

- **DOI: 10.1007/s00330-025-12188-7**

Abstract

Objectives: Alpha-1-antitrypsin deficiency (AATD) is a rare genetic disorder leading to chronic obstructive pulmonary disease (COPD). Emphysema is the major structural damage visible on CT scans. However, there is little knowledge on the association between other structural abnormalities, such as bronchiectasis (BE), airway wall thickening (WT) or mucus plugs (MP), and clinical features.

Materials and methods: Retrospective study between 2008 and 2022 at one University Hospital of Bordeaux on all consecutive AATD patients. Bronchial and parenchymal alterations were evaluated with an (artificial intelligence) AI-driven Normalized Volume of Airway Abnormalities (NOVAA-CT) scoring system, including BE, WT, MP and emphysema quantifications. We evaluated correlations between forced expiratory volume in 1-s (FEV1%), dyspnea severity through the mMRC scale and the occurrence of at least one exacerbation in the year following CT scan.

Results: Fifty-two AATD patients were included (median FEV1: 47% (40-65)). CT features of BE, WT and MP were present in 100%, 94.2% and 59% of the study population, respectively, with a lower versus upper lung predominance ($p < 0.05$). WT ($p < 0.001$) and BE ($p = 0.04$) correlated with FEV1% but not mMRC ($p \geq 0.09$). Conversely, MP did not correlate with FEV1% ($p = 0.08$) but with mMRC ($p = 0.01$). Emphysema strongly correlated with both FEV1% and mMRC ($p < 0.001$). In multivariate analysis, after adjustment for age, genotype and tobacco consumption, the best predictor of exacerbation was WT (OR = 1.12 [1.02-1.22]; $p = 0.01$).

Conclusion: This study demonstrates that AI-assisted identification of structural airway abnormalities is frequent in AATD patients and carries distinct clinical significance. Among them, WT was the most robust predictor of exacerbations.

Key points: Question Emphysema is the major structural damage in alpha-1-antitrypsin deficiency (AATD). Clinical associations of bronchial abnormalities such as bronchiectasis (BE), mucus plugs (MP) and wall thickness (WT) are lacking. Findings Quantitative CT of BE and WT correlated with PFT ($p \leq 0.05$), while MP correlated with dyspnea scale ($p = 0.01$). The best predictor of exacerbation was WT (OR = 1.12 [1.02-1.24]). Clinical relevance AI-assisted identification of bronchial abnormalities is frequent in AATD patients in addition to emphysema alone and carries distinct clinical significance. These findings highlight the importance of comprehensive CT-based evaluations to better characterize disease phenotype and guide clinical management in AATD.

Keywords: Alpha-1-antitrypsin deficiency; Artificial intelligence; CT scan; Chronic obstructive pulmonary disease; Exacerbation.

Conflict of interest statement

Compliance with ethical standards. Guarantor: The scientific guarantor of this publication is Gael Dournes. Conflict of interest: The authors of this manuscript declare relationships with the following companies: Patrick Berger: GSK, AstraZeneca, Sanofi, Chiesi. Maeva Zysman: GSK, AstraZeneca, Menarini, Novartis, CSL Behring, Chiesi, Pfizer. Gael Dournes: Sanofi, AstraZeneca, Vertex Pharmaceuticals. The other authors do not have relationship of interest with the manuscript content. Statistics and biometry: One of the authors (Patrick Berger) has significant statistical expertise. No complex statistical methods were necessary for this paper. Informed consent: Written informed consent was waived by the Institutional Review Board. Ethical approval: Institutional Review Board approval was obtained. Study subjects or cohorts overlap: None. Methodology: Retrospective Observational Performed at one institution

- **37 references**

Full text links

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Tuberc Respir Dis (Seoul)

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. 2025 Dec 9.

doi: 10.4046/trd.2025.0067. Online ahead of print.

Clinical outcome prediction by high-resolution computed tomography and echocardiography assessment of pulmonary hypertension in patients with bronchiectasis

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Affiliations Expand

- **PMID: 41362089**

- **DOI: 10.4046/trd.2025.0067**

Free article

Abstract

Background: To evaluate the association between pulmonary hypertension and hospital admission rates in patients with bronchiectasis.

Methods: We retrospectively analyzed data from 130 bronchiectasis patients at the National Medical Center, Korea (November 2012 to October 2022). Pulmonary hypertension was evaluated using high-resolution computed tomography (CT) and echocardiography. Patients were categorized into two groups based on the diameter of the main pulmonary artery (mPA). Logistic regression analysis was performed to identify risk factors associated with hospitalization.

Results: 40 patients had suspected pulmonary hypertension on echocardiography. A higher percentage of patients with an mPA diameter > 29 mm (N=61) had a history of previous exacerbations, elevated echocardiographic parameters related to pulmonary hypertension, and reduced lung function compared to those with an mPA diameter ≤ 29 mm (N=69). In univariate analysis, the hospitalization group showed an increased main pulmonary artery (mPA) diameter; PA (mPA to aorta) ratio; involvement of lung lobes, cavities, and nodules; and increased systolic pulmonary artery pressure and peak tricuspid regurgitation velocity. In multivariate analysis, mPA diameter >29 mm (adjusted odds ratio [OR], 2.47; 95% confidence interval [CI], 1.14-5.32) and the involvement of more than two lobes (adjusted OR, 2.57; 95% CI, 1.14-5.77) were significant risk factors for hospitalization.

Conclusion: CT parameters demonstrated comparable accuracy to models incorporating echocardiographic data for predicting hospitalization in bronchiectasis patients.

Keywords: Bronchiectasis; Hospitalization; Main pulmonary artery diameter; Pulmonary hypertension.

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J Med Chem

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. 2025 Dec 11;68(23):24869-24889.

doi: 10.1021/acs.jmedchem.5c02638. Epub 2025 Nov 27.

Design, Synthesis, and Biological Evaluation of the Novel Neutrophil Elastase Inhibitor CHF-6333 for the Inhaled Treatment of Bronchiectasis

Elisabetta Armani [1], Andrea Rizzi [1], Daniela Miglietta [1], Irene Bassanetti [1], Francesco Amadei [1], Giandomenico Brogin [1], Carmelida Capaldi [1], Fabio Rancati [1], Chiara Carnini [1], Sergio Xanxo Fernandez [1], Maurizio Civelli [1], Paola Puccini [1], Marta Bellini [1], Andrew Jennings [2], Robert A Heald [2], Lilian Alcaraz [2], Jonathan M Sutton [2], Harry Finch [3], Mary Fitzgerald [3], Craig Fox [3], Gino Villetti [1]

Affiliations Expand

- PMID: 41307403

- DOI: 10.1021/acs.jmedchem.5c02638

Abstract

The inhibitors of neutrophil elastase (NE) have long attracted interest for the treatment of respiratory diseases. We report the breakthrough of a new potent, selective NE inhibitor with a 24 h duration of action: CHF-6333, is currently undergoing clinical studies for the inhaled treatment of bronchiectasis (BE). The story of the discovery project to identify novel small molecules that inhibit extracellular elastase in the lung with prolonged activity is described. Medicinal chemistry investigation, supported by docking studies, led to N-quaternary compounds with an *in vitro* profile suitable for inhalatory administration. Compound 15 emerged from *in vivo* pharmacokinetic and pharmacodynamic studies, also showing safety and no off-target effects *in vitro*. Salt screening of different counterions, in conjunction with *in vivo* local irritancy testing, aided in the selection of compound 15-xinafoate (CHF-6333). Efficacy in a lung injury model and no findings in non-GLP toxicity studies promoted CHF-6333 as a clinical candidate.

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Thorax

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. 2025 Dec 15;81(1):61-70.

doi: 10.1136/thorax-2024-222795.

Time to diagnosis and long-term outcomes for adults presenting with breathlessness

Urvee Karsanji [1], Claire A Lawson [2], Emily Petherick [3], Kamlesh Khunti [4], Gillian Doe [1], Jennifer K Quint [5], Alex Bottle [5], Michael C Steiner [1], Rachael A Evans [6]

Affiliations Expand

- PMID: 41285477

- DOI: 10.1136/thorax-2024-222795

Abstract

Background: The impact of delays to diagnosis for individuals presenting with chronic breathlessness is unknown. We investigated the time to diagnosis after presenting with chronic breathlessness and associations with future unplanned hospitalisation and mortality.

Methods: A retrospective cohort study using the UK Clinical Practice Research Datalink involving adults with a first recorded code for breathlessness and no pre-existing cardiorespiratory disease. Adjusted Cox regression was used to investigate the associations with unplanned hospitalisation and mortality during all follow-up and within 2 years after the first code of breathlessness between those with and without a diagnosis, and using landmark analysis for time to diagnosis.

Results: 66 909/101 369 (66%) of adults with a first recorded code for breathlessness received an explanatory diagnosis during a median 5 years of follow-up. 43 394 (43%) of adults received an explanatory diagnosis within 2 years and had a higher risk (HR (95% CI)) of unplanned hospitalisation (1.25, 1.19 to 1.31) and mortality (1.84, 1.42 to 2.38) in the subsequent 2 years compared with adults without a diagnosis. In those with a recorded diagnosis, waiting ≥6 months was associated with increased mortality (6-24 months: 3.33 (2.13 to 5.20); ≥24 months: 13.30 (8.98 to 19.80)).

Conclusion: We describe better outcomes in adults coded for breathlessness without subsequent explanatory diagnoses. In adults with an explanatory diagnosis, waiting ≥6 months for a diagnosis was associated with reduced survival. Diagnostic pathways for chronic breathlessness need to differentiate between these two groups and achieve earlier diagnosis in those at higher risk.

Keywords: Asthma; Bronchiectasis; COPD epidemiology; Clinical Epidemiology; Interstitial Fibrosis; Symptom Assessment.

Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure. KK is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC).

- Cited by 1 article

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11

Thorax

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. 2025 Dec 15;81(1):71-77.

doi: 10.1136/thorax-2024-222570.

Nocturnal gastro-oesophageal reflux and pulmonary abnormalities on chest CT in a general population: the Swedish CArdioPulmonary BioImage Study

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Affiliations Expand

- **PMID: 40784748**

- **DOI: 10.1136/thorax-2024-222570**

Free article

Abstract

Background: Nocturnal gastro-oesophageal reflux (nGER) is common in people with respiratory diseases, but its association with pulmonary abnormalities is not known.

Aim: Investigate the association between nGER and pulmonary abnormalities on chest CT in an adult general population.

Methods: In total, 28 846 individuals from the general population aged 50-64 years completed questionnaires and underwent chest CT, in the Swedish CArdioPulmonary BioImage Study (www.scapis.org). Participants with nGER

symptoms on ≥1 night per week were defined as having nGER. Chest CT was evaluated for bronchial wall thickening, bronchiectasis, reticular abnormalities, honeycombing, cysts and ground glass opacities. Ever-smoking, current asthma, inflammatory bowel disease and autoimmune disease were defined as risk factors for pulmonary abnormalities. Analyses were adjusted for sex, age, body mass index, education level and study centre.

Results: The prevalence of nGER was 9.4%. Among participants with risk factors for pulmonary abnormalities (n=4004), having nGER was positively associated with bronchial wall thickening (adjusted OR (aOR) (95% CI): 1.25 (1.07 to 1.48)) and reticular abnormalities (aOR (95% CI): 1.51 (1.04 to 2.17)), but negatively associated with cysts (aOR (95% CI): 0.68 (0.48 to 0.97)). Among participants without risk factors for CT abnormalities (n=2555), nGER did not relate with pulmonary abnormalities.

Conclusions: In a middle-aged general population, nGER was not associated with pulmonary abnormalities on chest CT. However, in the presence of other risk factors for pulmonary abnormalities, nGER was associated with bronchial wall thickening and reticular abnormalities. Persons with nGER and risk factors for pulmonary abnormalities should, therefore, be evaluated for respiratory disease and treated appropriately.

Keywords: Bronchiectasis; Imaging/CT MRI etc; Interstitial Fibrosis.

Conflict of interest statement

Competing interests: ÖIE reports fees from Boehringer Ingelheim, MSD and AstraZeneca for advisory boards and lectures, unrelated to this publication. IP reports fees from Boehringer Ingelheim for lectures and participation on advisory boards. MS reports research grants from Boehringer Ingelheim for pulmonary fibrosis research, payments for lectures and educational activities related to pulmonary fibrosis, and participation on advisory boards related to pulmonary fibrosis. Other authors have no conflicts of interest related to this work.

Supplementary info

MeSH terms