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

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Nat Commun

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The effect of type 2 diabetes genetic predisposition on non-cardiovascular comorbidities

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Affiliations Expand

- **PMID: 41073432**
- **PMCID: PMC12514310**
- **DOI: 10.1038/s41467-025-64927-5**

Abstract

Type 2 diabetes is associated with a range of non-cardiovascular non-oncologic comorbidities. To move beyond associations and evaluate causal effects between type 2 diabetes genetic predisposition and 21 comorbidities, we apply Mendelian randomization analysis using genome-wide association studies across multiple genetic ancestries. Additionally, leveraging eight mechanistic clusters of type 2 diabetes genetic profiles, each representing distinct biological pathways, we investigate causal links between cluster-stratified type 2 diabetes genetic predisposition and comorbidity risk. We identify causal effects of type 2 diabetes genetic predisposition driven by distinct genetic clusters. For example, the risk-increasing effects of type 2 diabetes genetic predisposition on cataracts and erectile dysfunction are primarily attributed to adiposity and glucose regulation mechanisms, respectively. We observe opposing effect directions across different genetic ancestries for depression, asthma and chronic obstructive pulmonary disease. Our findings leverage the heterogeneity underpinning type 2 diabetes genetic predisposition to prioritize biological mechanisms underlying causal relationships with comorbidities.

Conflict of interest statement

Competing interests: The authors have no competing interests.

- **101 references**
- **4 figures**

Supplementary info

MeSH termsExpand

Full text links

Cite

2

Randomized Controlled Trial

BMJ Open Respir Res

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. 2025 Oct 10;12(1):e003615.

doi: 10.1136/bmjresp-2025-003615.

Sputum colour charts to guide antibiotic self-treatment of acute exacerbation of chronic obstructive pulmonary disease: the Colour-COPD RCT

Eleni Gkini [1], Joshua De Soyza [2], Daniella A Spittle [3], Paul Robert Ellis [4], Sarah Tearne [1], Peymane Adab [4], Rachel Jordan [4], Nawar Diar Bakerly [5 6], Alice Margaret Turner [7]

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- PMID: 41073133

- DOI: 10.1136/bmjresp-2025-003615

Abstract

Background: Chronic obstructive pulmonary disease (COPD) patients are encouraged to manage exacerbations (acute exacerbation of COPD (AECOPD)) through self-management (SM) plans. Since only around half of AECOPD are bacterial, and sputum colour correlates with bacterial load, it may help guide antibiotic use. This pragmatic randomised controlled trial (RCT) assessed the safety and effectiveness of using a sputum colour chart in UK primary care.

Methods: The multicentre RCT, Colour COPD randomised COPD adults who had ≥2 AECOPD or ≥1 AECOPD hospital admission in the preceding year. The primary objective was to assess the non-inferiority of the Bronkotest sputum colour chart compared with usual care, with hospital admission for AECOPD at 12 months as the primary outcome. Secondary outcomes included second courses of treatment requirement and quality of life (CAT score). Nested substudies examined daily symptoms via e-diaries and sputum culture.

Results: 115 severe COPD patients (global obstructive lung disease(GOLD) D, 54% Medical Research Council (MRC) 4 or 5, CAT score 24) were randomised. A trend towards more hospital admissions (32% vs 16%, relative risk (RR) 1.95 (0.92-4.18)) and increased antibiotic use within 14 days (34% vs 18%, adjusted relative risk (aRR) 1.80 (0.85-3.79)) was seen in the colour chart group. From 38 sputum substudy patients, 57 samples were received (42 stable, 15 during AECOPD), with 30% containing potentially pathogenic bacterium (PPB). Purulent sputum was more frequent in bronchiectasis, independent of disease state (stable vs exacerbation) or PPB presence, suggesting sputum colour alone does not reliably guide antibiotic use.

Conclusion: Under-recruitment precluded definitive conclusions. However, sputum colour is unlikely to be a useful addition to COPD SM in primary care.

Trial registration number: The UK's Clinical Study Registry: ISRCTN14955629 (https://doi.org/10.1186/ISRCTN14955629; registration date: 11 Number 2020).

Keywords: COPD Exacerbations; Pulmonary Disease, Chronic Obstructive.

Conflict of interest statement

Competing interests: AMT was funded via her institution from the NIHR HTA for the studies described in this report. She has also received funding to attend conferences from Boehringer Ingelheim and AstraZeneca, honoraria for talks or advisory boards about COPD from AstraZeneca and GlaxoSmithKline and via her Institution has received grants for work in COPD from AstraZeneca, Chiesi and GlaxoSmithKline. She was on the NIHR HTA prioritisation committee B 01/03/2020-31/03/2024. EG was funded via her institution from the NIHR HTA for work described in this report. ST was funded via her institution from the NIHR HTA for work described in this report. PA was funded via her institution from the NIHR HTA for work described in this report. RJ was funded via his institution from the NIHR HTA for work described in this report. DAS was funded via her institution from the NIHR HTA for work described in this report. PRE was funded by the University of Birmingham and University Hospitals Birmingham, for his role as an academic clinical lecturer, during which he conducted work described in this report. All other authors have no competing interest to declare.

Supplementary info

Publication types, MeSH terms, SubstancesExpand

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Cite

3

Review

Respir Med

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. 2025 Oct 8:248:108409.

doi: 10.1016/j.rmed.2025.108409. Online ahead of print.

Non-pharmacological interventions for fatigue in patients with chronic obstructive pulmonary disease: a systematic review and network meta-analysis

Xiaona Zhang [1], Jiali Xue [2], Yan Chang [3], Rui Zhang [3], Jie Zhao [3], Xindan Li [3], Hongyan Lu [4], Xirui Jiang [5], Fang Yu [3], Pengfei Yang [6]

Affiliations Expand

- PMID: 41072774

- DOI: 10.1016/j.rmed.2025.108409

Abstract

Background: Fatigue is a common and debilitating symptom in patients with chronic obstructive pulmonary disease (COPD). It limits daily activities, lowers perceived health, and diminishes the overall quality of life. Although several interventions have been demonstrated to alleviate fatigue, the relative effectiveness of these interventions remains unclear.

Objective: To assess and compare the efficacy of various non-pharmacological interventions for managing fatigue in patients with COPD, and to provide evidence-based recommendations for the design of intervention programs.

Methods: A comprehensive literature search was conducted across MEDLINE, Cochrane Library, Web of Science, Embase, CINAHL, CNKI, Wanfang Database, CBM, and the VIP Chinese journal full-text database to identify randomized controlled trials and quasi-experimental studies evaluating non-pharmacological interventions for COPD-related fatigue. The search covered all records from the inception of each database up to August, 2025. The network meta-analysis was conducted using Stata 16.0 and Addis 1.16.8 software.

Results: The analysis included 35 studies involving 2565 patients with COPD and examined 12 distinct non-pharmacological interventions. Results from the network meta-analysis demonstrated that acupressure [standardized mean difference (SMD) = -20.58, 95 %CI (-36.35, -5.19), P < 0.05], aerobic exercise [SMD = -12.80, 95 %CI (-22.96, -2.57), P < 0.05], pulmonary rehabilitation [SMD = -20.07, 95 %CI (-32.61, -6.98), P < 0.05], and progressive muscle relaxation [SMD = -16.99, 95 %CI (-28.83, -5.57), P < 0.05] were significantly effective in alleviating COPD-related fatigue. Ranking probability analysis further suggested that acupressure (0.25) was the most effective intervention, followed by pulmonary rehabilitation (0.19) and progressive muscle relaxation (0.15). The sensitivity analysis indicated that the ranking probability of acupressure was influenced by the quasi-experimental studies.

Conclusion: Pulmonary rehabilitation and progressive muscle relaxation therapy provide significant therapeutic advantages and should be prioritized as key non-pharmacological strategies for managing fatigue in patients with COPD.

Trial registration: INPLASY registration number: 202290072.

Keywords: Advanced care planning; Chronic obstructive pulmonary disease; Fatigue; Network meta-analysis; Non-pharmacological intervention; Palliative care.

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

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Am J Respir Crit Care Med

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. 2025 Oct 10.

doi: 10.1164/rccm.202501-0262OC. Online ahead of print.

Mucus Plugs-associated Gene Expression Identifies Pathophysiology Shared with Chronic Bronchitis

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Affiliations Expand

- PMID: 41072469

- DOI: 10.1164/rccm.202501-0262OC

Abstract

Rationale: Mucus plug formation and chronic bronchitis are manifestations of mucus pathology in chronic obstructive pulmonary disease. Identifying gene expression changes related to mucus pathology could provide insight into its pathogenesis.

Objectives: To investigate gene expression changes in individuals with mucus plugs, identify related biological pathways, and assess whether mucus plug-related gene expression associates with clinical features of other mucus pathologies.

Methods: We studied 290 participants from the Detection of Early Lung Cancer Among Military Personnel 2 study with mainstem bronchial brush bulk RNA-sequencing data (n = 204 discovery, n = 86 validation). We scored mucus plugging based on the number of lung segments with mucus plugs identified on chest computed tomography scans and used correlative analysis to identify differentially expressed genes and examine their association with chronic bronchitis symptoms.

Results: 76 participants (37%) in the discovery set had mucus plugs. Differentially expressed genes were broadly epithelial- or immune-related. Epithelial-related genes show decreased expression of genes involved in cilia maintenance and microtubule function and increased expression of genes related to epithelial maintenance and protection. Expression patterns of epithelial-related genes are associated with chronic bronchitis symptoms. Immune-related genes are enriched for innate and adaptive pathways. Expression of immune genes varies by lung function and was more weakly associated with mucus plugs than that of epithelial-related genes. Findings were replicated in an independent validation set.

Conclusion: Several distinct gene expression patterns are linked to the presence of mucus plugs, highlighting biological pathways involved in mucus pathophysiology. Variability in gene expression suggests a spectrum of mucus pathophysiology contributes to mucus plugs and chronic bronchitis symptoms.

Keywords: COPD; mucus dysfunction; transcriptomics.

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Curr Opin Pulm Med

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. 2025 Oct 9.

doi: 10.1097/MCP.0000000000001226. Online ahead of print.

Lung transplantation for chronic obstructive pulmonary disease patients: an overview

Talli Ida Naamani [1], Veronique Verplancke, Geert M Verleden

Affiliations Expand

- **PMID: 41065562**
- **DOI: 10.1097/MCP.0000000000001226**

Abstract

Purpose of review: To provide an overview of current indications for lung transplantation (LTx) in COPD patients, to describe the different transplantation

options, to compare the outcome of COPD and alpha1-antitrypsin deficiency (AATD) patients versus non-AATD COPD patients and to discuss the possible complications, also specifically related to COPD, AATD patients and the transplantation procedure.

Recent findings: Some 30-50% of all lung LTx worldwide are performed in COPD patients, with the majority being operated via double lung transplantation (DLTx). Unilateral lung transplantation (SLTx) remains an option, depending on the donor availability and the center's experience. The mean survival after LTx for COPD remains somewhat lower compared to other underlying diseases, especially after SLTx, which may lead to specific complications such as native lung hyperinflation and development of a native lung cancer.

Summary: LTx for end-stage COPD remains an accepted treatment modality in selected patients, which increases the QOL and the survival. The global 5-year survival is around 60%; somewhat better for AATD, compared to non-AATD COPD and after DLTx compared to SLTx. The best procedure of choice remains a matter for further discussion, although most centers prefer to perform DLTx, certainly in patients with underlying AATD.

Keywords: alpha1 antitrypsin deficiency; chronic obstructive pulmonary disease; double lung; lung transplantation; single lung.

- 39 references

Full text links

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Cite

6

BMC Pulm Med

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. 2025 Oct 8;25(1):458.

doi: 10.1186/s12890-025-03941-1.

Impulse oscillometry for the detection of small airway dysfunction in patients with chronic respiratory symptoms, preserved ratio impaired spirometry and COPD

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Affiliations Expand

- PMID: 41063069
- PMCID: PMC12505595
- DOI: 10.1186/s12890-025-03941-1

Abstract

Background: Persistent chronic airway inflammation and progressive airflow limitation are typical features of chronic obstructive pulmonary disease (COPD). Emerging evidence indicates that small airway dysfunction (SAD) plays a critical role in driving the sustained pathological progression of COPD. Preserved ratio impaired spirometry (PRISm) represents a spirometric pattern characterized by a reduced forced expiratory volume in 1 second (FEV_1) despite a preserved ratio. Current evidence inadequately elucidates the pathophysiological role of SAD and its intricate interplay with PRISm and COPD progression. On the other hand, impulse oscillometry (IOS) can be used as a complementary tool to spirometry to detect SAD. Detection of SAD in patients with chronic respiratory symptoms could help in the diagnosis of PRISm and COPD when spirometry is not achievable.

Objective: To investigate the diagnostic value of IOS for identifying SAD in patients with chronic respiratory symptoms, PRISm and COPD.

Methods: Between September 2021 and July 2023, 552 symptomatic patients without known structural lung disease who underwent both spirometry and IOS on the same day in the outpatient clinic were evaluated. The correlations between spirometry and the IOS parameters, and the ROC curves of the IOS parameters for SAD patients and COPD patients were analyzed.

Results: Among the 552 patients included in the study, 96 patients had COPD, 39 patients had PRISm, and 417 patients had chronic cough. Among 456 chronic cough patients with preserved ratio spirometry, the incidence of PRISm was 8.55%. Based on spirometry-defined SAD, the incidence of SAD in the PRISm population was 71.8%, which was significantly higher than the 9.35% of the non-PRISm population. With increasing COPD GOLD stage, the IOS parameters R5-R20, R5, Fres, and Ax increased, whereas the traditional lung function parameters and X5 decreased. R5-R20, X5, Fres, and AX of COPD GOLD stage 1 patients were not substantially different from those of PRISm patients. In PRISm patients, R5-R20, R5 and Fres were strongly correlated with $FEF_{25\%-75\%}$. R5-R20, R5, X5, Fres and AX were significantly associated with FEV_1, FEV_1/FVC, FEV_1% predicted, $FEF_{50\%}$, $FEF_{75\%}$ and $FEF_{25\%-75\%}$ in COPD patients. Through ROC curve analysis, the cutoffs for identifying SAD in patients with chronic respiratory symptoms and PRISm patients were obtained, with R5-R20 values of 0.075 and 0.105 kPa/L/s, respectively. The values of R5 were 0.365 and 0.375 kPa/L/s, respectively. The Fres values are 16.31 Hz and 17.11 Hz, respectively. The cutoff for detecting COPD in all patients was 0.485 kPa/L/s for R5, 0.125 kPa/L/s for R5-R20, -0.155 kPa/L/s for X5, and 17.98 Hz for Fres. Fres had the highest AUC value for both SAD and COPD detection, and it detected COPD the most in all patients, with a prevalence of 24.1%. R5 detected SAD the most in patients with chronic respiratory symptoms, with a prevalence of 47.5%.

With a prevalence of 71.8%, spirometry identified SAD in patients with PRISm the most frequently.

Conclusion: Almost all IOS parameters Linked to the small airways were significantly different in the PRISm population compared with patients with chronic respiratory symptoms. SAD severity in PRISm patients is similar to that in GOLD stage 2 COPD patients. The IOS can assess the disease severity of COPD.

Keywords: COPD; Impulse oscillometry; Preserved ratio impaired spirometry (PRISm); Small airway dysfunction (SAD); Spirometry.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: The study involving human participants was approved by the Ethics Committee of Shaoxing People's Hospital in accordance with the Declaration of Helsinki. All patients signed informed consent to participate in this study, and all personal information was de-identified before further analyses. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests. Clinical trial number: Not applicable.

- 28 references
- 5 figures

Supplementary info

MeSH termsExpand

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NPJ Digit Med

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. 2025 Oct 8;8(1):602.

doi: 10.1038/s41746-025-01939-x.

Systematic review: digital biomarkers of fatigue in chronic diseases

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Affiliations Expand

- PMID: 41062803

- PMCID: PMC12508163

- DOI: 10.1038/s41746-025-01939-x

Abstract

This systematic review explores the relationship between digital biomarkers, measured using wearable devices, and fatigue in patients with chronic diseases. Studies included in this review focused on individuals with diseases or conditions in 13 broad categories: multiple sclerosis (MS); rheumatoid arthritis (RA); chronic obstructive pulmonary disease (COPD); long COVID; cancer; chronic fatigue syndrome (CFS); pulmonary sarcoidosis; Parkinson's disease; chronic stroke; chronic inflammatory rheumatic disease (CIRD); Inflammatory Bowel Diseases (IBD), Primary Sjogren's Syndrome (PSS), and Systemic Lupus Erythematosus (SLE). The review synthesizes findings on the correlation between objective digital biomarkers and self-reported fatigue, highlighting the potential for disease-specific digital biomarkers to inform personalized fatigue management. The results suggest that reduced physical activity, increased sedentary behavior and autonomic dysfunction are associated with fatigue levels across multiple disease conditions included in this review, though the strength of this association and the specific biomarkers involved vary across diseases.

Conflict of interest statement

Competing interests: SDD reports consultancy activity with Hoffmann-La Roche Ltd. outside of this study. Other authors declare no conflict of interest.

- 75 references
- 2 figures

Supplementary info

Grants and fundingExpand

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Review

Eur Respir Rev

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. 2025 Oct 8;34(178):250089.

doi: 10.1183/16000617.0089-2025. Print 2025 Oct.

Ultrasound innovations in diaphragm assessment: an integrative review of expanding clinical applications

Ivo Neto Silva [1 2 3 4], **Claire Bennett** [5], **José Alberto Duarte** [4 6], **Karim Bendjelid** [7 2]

Affiliations Expand

- **PMID: 41062171**
- **PMCID: PMC12505151**
- **DOI: 10.1183/16000617.0089-2025**

Abstract

Introduction: Diaphragm dysfunction is prevalent across various patient populations, requiring precise structural and functional assessment. Ultrasound, being bedside-accessible and radiation-free, has gained relevance for evaluating the diaphragm and other respiratory muscle. Recent advancements have introduced novel techniques that have expanding its assessment scope. This review aims to identify emerging ultrasound methods for quantitative diaphragm assessment in adults, emphasising reliability and clinical relevance.

Methods: A systematic literature search was conducted using keywords related to the diaphragm, ultrasound techniques and innovation. We included original studies on adult participants using innovative ultrasound methods extending beyond conventional assessments. Studies lacking original data, case reports, animal studies and studies on automated analysis techniques were excluded. Screening and data extraction followed a structured process, with one researcher extracting data and a second verifying accuracy. Results were categorised by reliability and by physiological and clinical outcomes.

Results: Of 1411 records screened, 288 full-text articles were reviewed, and 36 studies met inclusion criteria, with four additional studies identified *via* reference analysis. These studies, published between 2013 and 2024, explored seven innovative techniques: the area method, contrast-enhanced ultrasound, echogenicity/echodensity, excursion of the zone of apposition, shear wave/strain

elastography, speckle tracking and pulsed-wave tissue Doppler imaging. Studies focused on both healthy subjects and critically ill, surgical and COPD patients.

Conclusions: Recent ultrasound advancements enhance diaphragm assessment by evaluating muscle quality, functional mechanical properties and blood flow. These innovative methods also provide alternatives when conventional approaches are limited. Further research is essential to refine protocols, validate clinical applications and standardise assessments for broader implementation.

Conflict of interest statement

Conflict of interest: I. Neto Silva reports grants from the Private Foundation of the Geneva University Hospitals. C. Bennett, J.A. Duarte and K. Bendjelid report no disclosures.

- 112 references
- 2 figures

Supplementary info

Publication types, MeSH termsExpand

Full text links

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Comment

Eur Respir J

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. 2025 Oct 7;66(4):2501584.

doi: 10.1183/13993003.01584-2025. Print 2025 Oct.

Reply to: Decoding the eosinophil connection: implications for precision treatment of emphysematous in COPD

Clarus Leung [1 2], Janice M Leung [1 2], Don D Sin [3 2]

Affiliations Expand

- PMID: 41057217

- DOI: 10.1183/13993003.01584-2025

No abstract available

Conflict of interest statement

Conflict of interest: C. Leung has no potential conflicts of interest to disclose. J.M. Leung reports grants from Canadian Institutes of Health Research, Canadian Cancer Society, Heart and Stroke Foundation of Canada, BC Lung Foundation, Canada Research Chairs Program and GlaxoSmithKline Chair in COPD, payment or honoraria for lectures, presentations, manuscript writing or educational events from University of British Columbia, support for attending meetings from GlaxoSmithKline, and participation on a data safety monitoring board or advisory board for the Veterans Affairs EQuiP Study. D.D. Sin reports payment or honoraria for lectures, presentations, manuscript writing or educational events from GlaxoSmithKline, Boehringer Ingelheim and AstraZeneca, participation on a data safety monitoring board or advisory board with NHLBI, and is the Deputy Chief Editor of the European Respiratory Journal.

Comment on

- **Transcriptomic profiling of the airway epithelium in COPD links airway eosinophilia to type 2 inflammation and corticosteroid response.**

Leung C, Park HY, Li X, Koelwyn GJ, Tuong J, Vahedi SM, Leitao Filho FS, Yang JS, Eddy RL, Milne S, Ryu MH, Takiguchi H, Akata K, Ra SW, Moon JY, Kim HK, Cho Y, Yamasaki K, van Eeden SF, Shaipanich T, Lam S, Leung JM, Sin DD.Eur Respir J. 2025 May 6;65(5):2401875. doi: 10.1183/13993003.01875-2024. Print 2025 May.PMID: 39978857 Clinical Trial.

Supplementary info

Publication typesExpand

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Editorial

Eur Respir J

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. 2025 Oct 7;66(4):2501605.

doi: 10.1183/13993003.01605-2025. Print 2025 Oct.

The MUSIC trial: harmonising our understanding of inhaled corticosteroids and the COPD airway microbiome

Fernando Sergio Leitao Filho [1], Stephen Milne [2 3 4]

Affiliations Expand

- PMID: 41057215

- DOI: 10.1183/13993003.01605-2025

No abstract available

Conflict of interest statement

Conflict of interest: F.S. Leitao Filho and S. Milne were investigators on the DISARM trial discussed in this editorial, which was sponsored by AstraZeneca. S. Milne also reports payment or honoraria for lectures, presentations, manuscript writing or educational events from Chiesi Australia, support for attending meetings from GlaxoSmithKline and Sanofi Australia, participation on a data safety monitoring board or advisory board with GlaxoSmithKline, and is a member of the Executive of the Thoracic Society of Australia and New Zealand.

Comment on

- The effect of different inhaled corticosteroid and long-acting bronchodilator combinations on the airway microbiome in patients with severe COPD: a randomised trial (MUSIC).

Richardson H, Alferes De Lima Headley D, Clarke C, Veluchamy A, Rauchhaus P, Pollock J, Pembridge T, Cassidy D, Keir HR, Finch S, Hussain F, Band M, Smith A, Patel M, Paracha M, Choudhury G, Dhasmana D, Chaudhuri R, Short PM, Chalmers JD.Eur Respir J. 2025 Oct 7;66(4):2500287. doi: 10.1183/13993003.00287-2025. Print 2025 Oct.PMID: 40841147 Clinical Trial.

Supplementary info

Publication typesExpand

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Review

Respir Med

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. 2025 Oct 5:248:108401.

doi: 10.1016/j.rmed.2025.108401. Online ahead of print.

Sarcopenia as a treatable trait in COPD: From mechanisms to management

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Affiliations Expand

- PMID: 41057104

- DOI: 10.1016/j.rmed.2025.108401

Abstract

Sarcopenia is common in COPD, with prevalence ranging from 14 % to 67 % depending on setting, age, disease severity, and nutritional status, highlighting its clinical relevance and the need for standardized diagnostic criteria and routine screening, especially in older or more severe cases. It results from a complex interplay of systemic inflammation, oxidative stress, mitochondrial dysfunction, physical inactivity, hypoxia, malnutrition, hormonal imbalances, and structural muscle remodeling, all contributing to muscle catabolism and impaired regeneration. These factors form a vicious cycle that worsens functional decline, highlighting the need for multifaceted, integrated therapeutic approaches. Sarcopenia in COPD is a measurable, modifiable, and treatable trait linked to worse lung function, physical performance, and outcomes. Early detection using the EWGSOP2 algorithm, starting with SARC-F screening, muscle strength testing, and confirmation via imaging and targeted interventions, can enable timely, effective interventions to improve outcomes. Targeted sarcopenia treatment in COPD includes pulmonary rehabilitation, nutritional support, and behavioral strategies. Exercise and high-protein, vitamin D-rich diets improve muscle strength and function. Pharmacological options remain experimental. Multidisciplinary care involving pulmonologists, physiotherapists, dietitians, and primary care providers ensures early detection, individualized treatment, and better outcomes through integrated interventions that address both respiratory impairment and muscle loss. Despite promising advances, key research gaps remain in sarcopenia as a treatable trait in COPD, including the need for standardized diagnostic criteria, longitudinal studies, optimal intervention strategies, and integration of functional outcomes.

Future research should prioritize equity, mechanistic insights, and implementation science to refine personalized care and improve clinical outcomes in COPD.

Keywords: Chronic obstructive pulmonary disease; Sarcopenia; Treatable traits.

Conflict of interest statement

Declaration of competing interest We have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. Furthermore, we declare that this manuscript was not funded/sponsored, and no writing assistance was utilized in its production. Given their role as Deputy Editor (MC) and Editorial Board Member (CP), Mario Cazzola and Clive Page are not involved in the peer-review of this article and have no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to another journal editor.

Supplementary info

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Am J Respir Crit Care Med

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. 2025 Oct 7.

doi: 10.1164/rccm.202504-0854OC. Online ahead of print.

Maternal Smoking and CC-16: Implications for Lung Development and COPD Across the Lifespan

Joselyn Rojas-Quintero [1], Rosa Faner [2], Chia-Ying Chiu [3], Jeff T Kue [1], Yun Zhang [4 5], David Sanz Rubio [6 7], Adrianne S Colborg [8], Constanze A Jakwerth [9 10], Carsten B Schmidt-Weber [11], Anke-Hilse Maitland-van der Zee [12 13], Mahmoud I Abdel-Aziz [14], Aprile L Pilon [15], Caroline A Owen [16 17], Erin J Plosa [18], Gregory L Kinney [19], Sharon Mc-Grath Morrow [20 21], Mariacarolina G Gazzaneo [8], Nahir Cortes Santiago [22 23], Krithika Lingappan [24], Julie Ledford [25], Jason

Spence [26], Jennifer M Sucre [27], Maor Sauler [28], Tianshi David Wu [29], Alvar Agusti [30], Asa Wheelock [31 32], Sabina Illi [33], Erika von Mutius [34 35], Russell P Bowler [36], Bartolome Celli [37 38], Steven H Abman [39], J Michael Wells [3], Francesca Polverino [40 41]; ALLIANCE study group, ECLIPSE and COPDGene investigators

Affiliations Expand

- PMID: 41056135

- DOI: 10.1164/rccm.202504-0854OC

Abstract

Rationale: Early-life lung function trajectories predict long-term respiratory health, including COPD risk. Club Cell protein 16 (CC16) is a key determinant of lung health, with low levels associated with impaired lung development, reduced lung function, and COPD. Cigarette smoking lowers CC16, but it is unknown whether maternal smoking leads to persistent CC16 deficiency from early life, thereby disrupting lung development and predisposing to COPD risk and progression Methods: CC16 expression was analyzed across 4 human cohorts, in plasma samples (COPDGene [n=1,062] and ECLIPSE [n=2,164]), nasal brushings (ALLIANCE [n=63]), and peripheral lung sections (LTRC [n=44]) from participants with and without a history of maternal smoking exposure. Lung histology and respiratory mechanics were assessed in WT and *Cc16*$^{-/-}$ mice with and without maternal smoking exposure. Recombinant human (rh)CC16 effects on lung maturation were assessed in embryonic murine lung explants.

Results: Maternal smoking was linked to reduced circulating and airway CC16 in COPD patients, controls, and a preclinical murine COPD model. In human adults, lower CC16 correlated with accelerated lung function decline and emphysema progression, while in children it was associated with obstructive physiology and early small airway impairment. In both mice and humans, maternal smoking-induced CC16 reduction was accompanied by greater epithelial injury (fibrosis, inflammation, apoptosis, oxidative stress). In murine explants, smoking impaired lung branching, whereas rhCC16 restored branching via α2-integrin binding Conclusions: Maternal smoking reduces CC16 levels, disrupting lung development in ways that predispose to lifelong impairment of lung function and worse COPD outcomes. Defining the mechanisms by which CC16 regulates lung maturation is essential for establishing reliable outcome measures and designing trials aimed at preventing early COPD.

Keywords: CC16; COPD; Lung morphogenesis; Maternal smoke; lung function.

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Am J Respir Crit Care Med

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. 2025 Oct 7.

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Patient Factors and Clinical Efficacy of Early Identification and Treatment of COPD and Asthma

Arianne Tardif [1], G A Whitmore [2], Katherine L Vandemheen [3], Celine Bergeron [4 5], Louis-Philippe Boulet [6], Andréanne Côté [7], R Andrew McIvor [8], Erika Penz [9], Stephen K Field [10], Catherine Lemière [11], Irvin Mayers [12], Mohit Bhutani [13], Tanweer Azher [14], M Diane Lougheed [15], Samir Gupta [16], Nicole Ezer [17 18], Christopher J Licskai [19], Paul Hernandez [20], Martha Ainslie [21], Gonzalo G Alvarez [3], Sunita Mulpuru [22 23], Shawn D Aaron [24 25]

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- PMID: 41056133

- DOI: 10.1164/rccm.202505-1260OC

Abstract

Rationale: The Undiagnosed COPD and Asthma Population trial showed that early diagnosis and treatment of asthma and COPD by pulmonologists improved healthcare utilization, respiratory symptoms, and quality of life.

Objectives: To determine if the benefits of early diagnosis and treatment were greater in individuals with more advanced disease, or in individuals with asthma as opposed to COPD. We also assessed whether pulmonologist-directed care benefited asthma and COPD subgroups equally.

Methods: Case finding was used to identify undiagnosed adults with chronic respiratory symptoms in the community. Five hundred and eight newly diagnosed participants with COPD or asthma were randomized to a pulmonologist-care intervention or usual care. Low and high disease-burden categories for St. Georges Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT) were defined using a median-split of baseline scores, and MCID thresholds were used to define significant responses. Benefits of pulmonologist care were assessed by evaluating treatment effects within subgroups and by assessing treatment-by-subgroup interactions.

Measurements and main results: Patients with higher disease burden at diagnosis were more likely to benefit from early diagnosis and treatment compared to those with lower disease-burden. 71% of those with high disease-burden improved their

CAT by ≥ 2 points over 12 months compared to 47% with low disease burden; OR 2.78, 95% CI: 1.90 to 4.07, p<0.001. Similar results were seen for SGRQ and FEV1 improvements. In contrast, responses to early diagnosis and treatment were similar for those with asthma vs COPD. Individuals with asthma randomized to pulmonologist-directed care showed greater one-year improvements in CAT, SGRQ, SF36 and FEV1 compared to individuals randomized to primary care. However, individuals with COPD experienced similar improvements regardless of whether their treatment was managed by a pulmonologist or primary care provider. Treatment-by-disease interaction terms were not statistically significant.

Conclusions: Patients with greater disease burden who exhibited more advanced and symptomatic asthma and COPD at the time of diagnosis, benefited more from earlier diagnosis and treatment. Patients with asthma tended to derive greater benefit from pulmonologist-directed care than patients with COPD.

Keywords: Asthma; COPD; Case-finding; Disease burden; Early diagnosis.

Cite

14

Review

Expert Rev Respir Med

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. 2025 Oct 7:1-16.

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COPD and the burden of multimorbidity: navigating the complexity

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- PMID: 41054835

- DOI: 10.1080/17476348.2025.2569126

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a chronic condition that affects millions of people worldwide. The majority of patients with COPD have multiple coexisting chronic diseases, such as cardiovascular diseases, osteoporosis, lung cancer, and metabolic syndrome, a phenomenon that is known as multimorbidity. The coexistence of these diseases with COPD complicates diagnosis, treatment, and prognosis.

Areas covered: This review explores the underlining mechanisms that connect COPD and multimorbidity, such as shared risk factors and pathophysiological pathways. It also highlights the challenges in managing multimorbid patients and emphasizes the fact that the complexity of comorbidities may require a multidisciplinary approach in COPD management.

Expert opinion: Managing COPD in the context of multimorbidity requires a multidisciplinary approach. This approach should combine pharmacological and non-pharmacological treatments for COPD, adhere to evidence-based guidelines for managing comorbidities, and target modifiable shared risk factors to improve overall patient outcomes.

Keywords: Cardiovascular disease; chronic obstructive pulmonary disease; comorbidities; depression; lung cancer; metabolic syndrome; multimorbidity; obstructive sleep apnea.

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BMC Pulm Med

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Risk factors and outcomes of ventilator-associated pneumonia: an updated systematic review and meta-analysis

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- **PMID: 41053703**

- **PMCID: PMC12502355**

- **DOI: 10.1186/s12890-025-03932-2**

Abstract

Background: Ventilator-associated pneumonia (VAP) is a common complication in intensive care unit (ICU) patients, which increases morbidity rates and adversely affects outcomes. The associated risk factors and outcomes remain controversial. The aim of the present study is to explore the risk factors and clinical outcomes of patients with VAP.

Methods: Two investigators conducted independent systematic Literature searches of Pubmed, Cochrane Database, Scopus, Medline, Science Direct and Epistemonikos databases published from inception to November 2024. The Newcastle-Ottawa Scale (NOS) was used to assess study quality. A meta-analysis was performed using the random-effects Model. The systematic review protocol was registered in the CRDdatabase 42024538138 of the Prospective International Registry of Systematic Reviews (PROSPERO). A subgroup analysis, bivariate meta-regression, and sensitivity analysis were performed. Publication bias was assessed using a funnel plot and Egger's test. Certainty of evidence was assessed using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology.

Results: Twenty-two studies were included in the meta-analysis, with a total of 16,731 patients. Male gender odds ratio (OR) 1.30 (95% Confidence interval (CI) 1.18-1.44) p<0.05; the use of H2 blockers OR 2.24 (95% CI 1.50-3.37) p<0.05; tracheostomy OR 3.44 (95% CI 2.0-5.92) p<0.05; prior antibiotic treatment OR 1.52 (95% CI 1.08-2.15) p<0.05; reintubation OR 5.11 (95% CI 2.29-11.42) p<0.05; enteral feeding OR 4.73 (95% CI 2.54-8.78) p<0.05; Chronic Obstructive Pulmonary Disease (COPD) OR 1.52 (95% CI 1.10-2.09) p<0.05; impaired consciousness at hospital admission OR 3.14 (95% CI 1.28-7.69) p<0.05; nasogastric tube OR 2.94 (95% CI 1.56-5.53) p<0.05; use of neuromuscular blockers OR 1.30 (95% CI 1.13-1.49) p<0.05; trauma OR 1.47 (95% CI 1.12-1.93) p<0.05, and days of intubation prior to VAP OR 6.2 (95% CI 1.09-11.3). A p<0.05 significantly increased the risk of VAP. In patients with VAP, the average ICU stay was 12.7 days longer (95% CI: 9.6-15.8) p<0.05; the duration of mechanical ventilation was 12.3 days longer (95% CI: 9.27-15.34) p <0.05; the hospital stay was 16.1 days longer (95% CI: 10.8-21.5) p <0.05. The certainty of the evidence was low for most outcomes.

Conclusions: Male gender, use of H2 blockers, tracheostomy, prior antibiotic treatment, reintubation, enteral feeding, COPD, impaired consciousness at hospital admission, nasogastric tube, use of neuromuscular blockers, trauma and days of intubation prior to VAP significantly increased the risk of VAP. In patients with VAP, ICU stay, duration of mechanical ventilation, and hospital stay presented significant increases.

Supplementary Information: The online version contains supplementary material available at 10.1186/s12890-025-03932-2.

Keywords: Intensive care units; Mortality; Patient outcome assessment; Pneumonia ventilator associated; Risk factors.

Conflict of interest statement

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

- **68 references**
- **3 figures**

Supplementary info

Publication typesExpand

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16

Review

Heart Fail Rev

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doi: 10.1007/s10741-025-10566-3. Online ahead of print.

Heart failure and chronic obstructive pulmonary disease. A combination not to be underestimated

Damiano Magrì [1], Emiliano Fiori [2], Piergiuseppe Agostoni [3 4], Michele Correale [5], Massimo Piepoli [6], Savina Nodari [7], Matteo Beltrami [8], Stefania Paolillo [9], Pasquale Perrone Filardi [9], Alberto Palazzuoli [10]; Working Group on Heart Failure of the Italian Society of Cardiology

Affiliations Expand

- **PMID: 41053405**

- DOI: 10.1007/s10741-025-10566-3

Abstract

Chronic obstructive pulmonary disease (COPD) and heart failure (HF) frequently coexist and interact through complex and bidirectional hemodynamic mechanisms that amplify symptoms' burden and complicate clinical management. The present review explores the impact of COPD across the HF spectrum, particularly in HF with preserved ejection fraction (HFpEF), where comorbidities, such as COPD, exert a dominant role in disease expression. COPD-induced hyperinflation reduces cardiac preload and increases right ventricular afterload, while HF-related congestion impairs pulmonary function and gas exchange, illustrating a tight cardiorespiratory coupling. Diagnostic challenges stem from overlapping symptoms and the limited specificity of biomarkers, such as natriuretic peptides, especially in HFpEF. Cardiopulmonary exercise testing (CPET) emerges as a valuable tool for distinguishing between cardiac and pulmonary limitations and guiding individualized treatment strategies. From a therapeutic standpoint, β1-selective blockers are not only safe in COPD patients but are pivotal in those with HF with reduced ejection fraction (HFrEF), where they have been demonstrated to improve survival and reduce both HF and COPD exacerbations. Concerns regarding bronchodilator safety in HF remain largely theoretical, with current evidence supporting their continued use when clinically indicated. Ultimately, optimal care for patients with coexisting COPD and HF requires a phenotype-specific approach, incorporating insights from pathophysiology, diagnostic innovation, and evidence-based pharmacotherapy to improve outcomes in this challenging patient population.

Keywords: Cardiopulmonary exercise test; Cardiopulmonary interaction; Heart failure; Lung disease.

Conflict of interest statement

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

- 105 references

Supplementary info

Publication typesExpand

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Editorial

Thorax

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. 2025 Oct 6:thorax-2025-223930.

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Nocturnal reflux: an untapped target in lung disease?

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Affiliations Expand

- PMID: 41052929

- DOI: 10.1136/thorax-2025-223930

No abstract available

Keywords: Asthma Mechanisms; COPD exacerbations mechanisms; Clinical Epidemiology; Imaging/CT MRI etc; Interstitial Fibrosis.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication typesExpand

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doi: 10.1164/rccm.202507-1793ED. Online ahead of print.

Targeted Lung Denervation in COPD: Threading the Needle of Safe Interventions to Help the Sickest

Yukiko Kunitomo [1], Nirupama Putcha [2]

Affiliations Expand

- PMID: 41052462

- DOI: 10.1164/rccm.202507-1793ED

No abstract available

Keywords: COPD; Targeted Lung Denervation.

19

J Behav Med

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doi: 10.1007/s10865-025-00609-3. Online ahead of print.

The effectiveness of cognitive behavioral therapy for smoking cessation: A systematic review and meta-analysis

Jinyoung Chang [# 1], Jimin Kim [# 1], Eon Sook Lee [2], Yu Jin Paek [3], Hyeon-Jeong Lee [1], Miyoung Choi [1], Jin-Kyoung Oh [4], Eun-Jung Bae [5], Sang Hwa Shin [6], Yun Hee Kim [7], Kyung-Hyun Suh [8]

Affiliations Expand

- PMID: 41047437

- DOI: 10.1007/s10865-025-00609-3

Abstract

Cognitive Behavioral Therapy (CBT) is a commonly used intervention for smoking cessation. This PROSPERO-registered systematic review and meta-analysis (CRD42024581823) evaluated the long-term effectiveness of CBT in achieving abstinence for six months or longer. Sixteen randomized controlled trials (RCTs) involving 2,531 adults were included. Studies comparing CBT to minimal care and published in English or Korean were selected; those focusing on Acceptance and Commitment Therapy (ACT) or mindfulness were excluded. Results indicate that CBT significantly improves long-term cessation rates. Subgroup analyses showed that both CBT alone and CBT with pharmacotherapy were effective compared with minimal care. In particular, CBT demonstrated greater effectiveness among patients with smoking-related conditions such as COPD and cardiovascular disease. Risk of bias was generally rated as "some concerns," and the certainty of evidence was moderate. These findings support CBT's clinical utility, especially when integrated with pharmacological treatments or tailored to high-risk populations.

Keywords: Cognitive behavioral therapy; Meta-analysis; Smoking cessation; Systematic review.

Conflict of interest statement

Declarations. Conflict of interest: The authors declare no potential conflicts of interest concerning the research, authorship and/or publication of this article.

- 51 references

Supplementary info

Grants and fundingExpand

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Thorax

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. 2025 Oct 8:thorax-2024-222823.

doi: 10.1136/thorax-2024-222823. Online ahead of print.

Mobile health pulmonary rehabilitation (m-PR): a randomised controlled equivalence trial

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Affiliations Expand

- PMID: 40992935

- DOI: 10.1136/thorax-2024-222823

Abstract

Background: Mobile health (mHealth) is a novel model of care that may overcome barriers to pulmonary rehabilitation (PR) access. This study determined if mHealth PR was equivalent to centre-based PR (CB-PR) in improving exercise capacity and health status in people with chronic obstructive pulmonary disease (COPD).

Method: Single-blinded, multicentre, randomised controlled equivalence trial using an intention-to-treat analysis. Participants completed 8 weeks of either mHealth PR, using the mobile PR (m-PR) application and supported by telephone calls, or CB-PR. Co-primary outcomes, measured at baseline and end-intervention, were change in 6 minute walk distance (6MWD) and COPD assessment test (CAT) score, with an equivalence margin of 30 m and 2 points, respectively.

Results: 90 participants were randomised (mean (SD), m-PR n = 44: age 75 (7) years; forced expiratory volume in one second (FEV_1) 58 (15) % predicted; CB-PR n = 46: age 75 (6) years; FEV_1 55 (14) % predicted) with 38 m-PR participants and 42 CB-PR participants completing at least one primary outcome. At end-intervention, there was no between-group difference in 6MWD (mean difference (MD) 13 m, 95% CI -6 to 31), indicating equivalence of m-PR to CB-PR. There was a significant between-group difference in CAT score (MD -4.9 points, 95% CI -7.2 to -2.6), with both limits of the CI exceeding the equivalence margin, indicating superiority of m-PR.

Conclusion: An mHealth PR programme resulted in equivalent improvements in exercise capacity and superior improvements in health status when compared with CB-PR in people with COPD. mHealth PR could be effective as a management option for people with COPD with adequate digital literacy.

Trial registration number: ACTRN12619001253190.

Keywords: COPD Exacerbations; Emphysema; Exercise; Pulmonary Rehabilitation.

Conflict of interest statement

Competing interests: ZJM is the managing director of the Better Breathing Foundation, which has contributed PhD scholarship funding to SEB. All other authors declare that they have no competing interests.

Full text links

21

J Am Heart Assoc

. 2025 Oct 7;14(19):e039231.

doi: 10.1161/JAHA.124.039231. Epub 2025 Sep 19.

Dynamic Increase of the C_2HEST Score in Relation to the Development of Incident Atrial Fibrillation: A Longitudinal Cohort Study

Yan-Guang Li [1], Yi-Jie Liu [1], Li-Li Wang [1], Qiao-Yuan Li [1], Tao Zhang [1], Xu Liu [1], Qin-Chao Wu [1], Yan Yin [1], Shao-Min Chen [2], Jin Bai [2], Daniele Pastori [3 4], Gregory Y H Lip [4 5], Yun-Long Wang [1]

Affiliations Expand

- PMID: 40970537

- DOI: 10.1161/JAHA.124.039231

Free article

Abstract

Background: The risk of incident atrial fibrillation (AF) increases with accumulating risk factors. Baseline-only risk assessment may not reflect the real risk of incident AF. We aimed to evaluate the performance of the dynamic change of the C_2HEST score (C2: coronary artery disease/chronic obstructive pulmonary disease (1 point each); H: hypertension (1 point); E: elderly (age ≥75 years, 2 points); S: systolic/diastolic heart failure (2 points); and T: thyroid disease (hyperthyroidism, 1 point) C_2HEST) score to assess the risk of incident AF during follow-up.

Methods: The present study data were retrieved from the Information Management and Big Data Center of Peking University Hospital Group. Patients without AF at baseline were enrolled. New-onset comorbidities were recorded during follow-up. The change in the C_2HEST score was analyzed. The baseline and the change in C_2HEST scores were compared for the prediction of incident AF.

Results: A total of 120 133 patients were included in the final analysis. During 346 400 patient-years of follow-up, 2304 developed incident AF (0.67 per 100 patient-years). The mean C_2HEST score increased significantly from 1.62 to 2.96 (P<0.05). A

significant proportion of patients had newly diagnosed comorbidities (61.9% with ΔC2HEST ≥1 in AF and 14.6% with C2HEST ≥1 in non-AF). The change in C2HEST scores showed better performance compared with the baseline score, as assessed by area under curve analyses (ΔC2HEST 0.821 [0.811-0.830], baseline 0.758 [0.747-0.769]), decision curve analysis, and positive net reclassification index.

Conclusions: The risk for incident AF is not static and increases with the accumulation of new comorbidities. The change in C2HEST score had better prediction in assessing individual risk of incident AF compared with the baseline score.

Keywords: C2HEST; atrial fibrillation; real world; risk factors.

Supplementary info

MeSH termsExpand

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Randomized Controlled Trial

Eur Respir J

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. 2025 Oct 7;66(4):2500287.

doi: 10.1183/13993003.00287-2025. Print 2025 Oct.

The effect of different inhaled corticosteroid and long-acting bronchodilator combinations on the airway microbiome in patients with severe COPD: a randomised trial (MUSIC)

Hollian Richardson [1], Daniela Alferes De Lima Headley [1], Clare Clarke [1], Abirami Veluchamy [2], Petra Rauchhaus [3], Jennifer Pollock [1], Thomas Pembridge [1], Diane Cassidy [1], Holly R Keir [1], Simon Finch [1], Furrah Hussain [3], Margaret Band [3], Andrew Smith [4], Manish Patel [4], Mohammad Paracha [5], Gourab Choudhury [6], Devesh Dhasmana [7 8], Rekha Chaudhuri [9], Philip M Short [10], James D Chalmers [11]

Affiliations Expand

- PMID: 40841147

- DOI: 10.1183/13993003.00287-2025

Abstract

Background: The microbiome is associated with exacerbation risk, quality of life and mortality in COPD. Inhaled corticosteroid (ICS) treatment has been reported to alter the microbiome through modulating host defence. How ICS alters the microbiome and whether effects are equal between different ICS preparations is debated. The aim of the MUSIC trial was to investigate whether commonly used ICS therapies have different effects on the airway microbiome in COPD.

Methods: This was a multicentre randomised controlled trial. After a 4-week washout period during which they withdrew from ICS, patients with COPD (forced expiratory volume in 1 s <50% predicted at baseline and/or a history of two or more exacerbations per year) were randomised to one of four treatments (budesonide/formoterol 400/12 µg (BF400), fluticasone/salmeterol 500/50 µg (FS500), fluticasone/salmeterol 250/50 µg (FS250) or aclidinium/formoterol 340/12 µg, twice daily). Patients were followed-up for 3 months with monthly induced sputum, oropharyngeal and nasopharyngeal swabs for bacterial load and 16S rRNA sequencing to characterise the microbiome. Inflammatory markers were measured in sputum and blood. The primary outcome was bacterial load in oropharyngeal swabs comparing BF400 *versus* FS500, with sputum bacterial load the key secondary end-point.

Results: 122 participants started the washout period. ICS withdrawal was poorly tolerated; 61 participants withdrew before randomisation with 45 experiencing an exacerbation. 61 patients were randomised. No statistically significant differences were observed for the primary comparison of BF400 *versus* FS500 in oropharyngeal bacterial load. There was, however, a significant increase in sputum bacterial load with FS500 compared to BF400 by month 3. This difference was not seen with FS250. No significant differences in microbiome α-diversity were observed over time. Adverse events were similar between the groups.

Conclusion: FS500 increased sputum but not upper airway bacterial loads. ICS withdrawal was poorly tolerated in severe COPD.

Conflict of interest statement

Conflict of interest: H.R. Keir reports payment or honoraria for lectures, presentations, manuscript writing or educational events from Insmed Incorporated. A. Smith reports grants from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Oncimmune and Roche, and consultancy fees from AstraZeneca, GSK and Chiesi. M. Patel reports support for attending meetings from Chiesi. M. Paracha reports consultancy fees from AstraZeneca and GSK, and participation on a data safety monitoring board or advisory board with AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Oncimmune and Roche. G. Choudhury reports grants from AstraZeneca and GSK, payment or honoraria for lectures, presentations, manuscript writing or educational events from GSK, AstraZeneca and Chiesi, and participation on a data safety monitoring board or advisory board with AstraZeneca. R.

Chaudhuri reports grants from AstraZeneca, payment or honoraria for lectures, presentations, manuscript writing or educational events from GSK, AstraZeneca, Teva, Chiesi and Sanofi, participation on a data safety monitoring board or advisory board with GSK, AstraZeneca and Celltrion, and support for attending meetings from Sanofi and GSK. P.M. Short reports payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, and support for attending meetings from Chiesi. J.D. Chalmers is Chief Editor of the European Respiratory Journal, and reports grants from AstraZeneca, Genentech, Gilead Sciences, GSK, Insmed, Grifols, Novartis and Boehringer Ingelheim, and consultancy fees from AstraZeneca, Chiesi, GSK, Insmed, Grifols, Novartis, Boehringer Ingelheim, Pfizer, Janssen, Antabio and Zambon. The remaining authors have no potential conflicts of interest to disclose.

Comment in

- The MUSIC trial: harmonising our understanding of inhaled corticosteroids and the COPD airway microbiome.

Leitao Filho FS, Milne S.Eur Respir J. 2025 Oct 7;66(4):2501605. doi: 10.1183/13993003.01605-2025. Print 2025 Oct.PMID: 41057215 No abstract available.

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

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J Public Health (Oxf)

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. 2025 Oct 10:fdaf132.

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Workplace productivity losses due to multimorbidity: findings from an Australian longitudinal population survey, 2009-21

Mohammad Afshar Ali [1], Syed Afroz Keramat [2], Christine Y Lu [1 3]

Affiliations Expand

- PMID: 41071372

- DOI: 10.1093/pubmed/fdaf132

Abstract

Background: While productivity loss has been studied in various populations, the impact of multimorbidity on workplace productivity at a population level remains understudied. This study estimates the productivity losses attributable to multimorbidity.

Method: Using data from four waves of the Household, Income and Labour Dynamics in Australia (HILDA) survey, we investigated the relationship between multimorbidity and productivity loss. Negative binomial and logistic regression models were employed to analyze absenteeism, presenteeism, and working hour tension as measures of productivity loss.

Results: We found a significant association between multimorbidity and increased absenteeism, presenteeism and working hour tension. After controlling for socio-economic, demographic, health, and workplace-related factors, individuals with multimorbidity had a 1.07-fold higher rate of absenteeism (incidence rate ratios: 1.07; 95% CI: 1.02-1.13) compared to those without serious illness. Their odds of experiencing presenteeism were three times higher, and the incidence of working hour tension was 32% higher. On average, the annual cost of absenteeism was AU$265.20 higher for individuals with multimorbidity than for those without serious illness.

Conclusion: Our results underscore the need for evidence-based workplace policies to support the productivity and well-being of employees living with multimorbidity.

Keywords: health services; morbidity and mortality; public health.

Cite

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Geroscience

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. 2025 Oct 8.

doi: 10.1007/s11357-025-01927-9. Online ahead of print.

Psycho-socio-economic factors and cardiorenal multimorbidity in middle to older-aged adults: cross-sectional results from the Canadian Longitudinal Study on Aging

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Affiliations Expand

- **PMID: 41062867**

- **DOI: 10.1007/s11357-025-01927-9**

Abstract

Psycho-socio-economic factors (PSEFs) such as income, education, housing, and social support are known to influence health outcomes, yet their relationship with cardiorenal multimorbidity (CRM) remains poorly understood. This study aimed to estimate the prevalence of CRM and examine its associations with PSEFs in a large, nationally representative Canadian sample. We analyzed baseline data from 19,370 participants (mean age: 60 years; 49.8% men) in the Canadian Longitudinal Study on Aging, a prospective cohort of community-dwelling adults aged 45-85 years recruited between 2010 and 2015. CRM was defined as the co-existence of at least one cardiovascular disease and kidney disease. PSEFs assessed included household income, education, homeownership, marital status, employment status, and psychosocial variables. Survey-weighted multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for prevalent CRM. The overall prevalence of CRM was 0.83% (160 individuals), equivalent to 3.90 per 1000 individuals (95% CI 2.81-5.41). Prevalence increased with age and was higher among men than women (4.57 vs. 3.35 per 1000) and slightly higher in rural than urban areas (4.47 vs. 3.84 per 1000). Homeownership was associated with significantly lower odds of CRM (OR = 0.56; 95% CI 0.33-0.94). A household income of $50 K-99 K was associated with lower odds of CRM (OR = 0.63; 95% CI 0.39-1.00). No other PSEFs showed clear associations with prevalent CRM. CRM is relatively uncommon but shows variation by age, sex, and geography. Among the PSEFs assessed, homeownership and, to a lesser extent, moderate income were associated with reduced odds of prevalent CRM. These findings highlight the potential role of housing and economic stability in mitigating CRM risk. Longitudinal studies are needed to assess the impact of PSEFs on the development and progression of CRM over time.

Keywords: CLSA; Cardiorenal multimorbidity; Cross-sectional study; Psycho-socio-economic factor.

Conflict of interest statement

Declarations. Ethics approval: Ethics approval for CLSA data collection was granted by 13 research ethics boards across Canada. All participants provided informed consent. Ethics approval for this secondary analysis was obtained from the University of Manitoba Health Research Ethics Board (HS26767). Conflict of interest: The authors declare no competing interests.

- **34 references**

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Review

Ann Med

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. 2025 Dec;57(1):2569988.

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Multimorbidity quantification from the perspective of precision management: challenges and strategies

Xinyi Huang [1 2], Xiangyun Guo [3], Yiwen Gan [3], Aili Xu [1], Kai Sun [1], Hao Shen [4], Zitong Niu [3], Yafeng Zhang [5], Yang Guo [3], Yong Ma [3], Yili Zhang [3], Xu Wei [1]

Affiliations Expand

- PMID: 41062115

- PMCID: PMC12509298

- DOI: 10.1080/07853890.2025.2569988

Abstract

Background: Global healthcare systems face growing challenges from multimorbidity as populations age rapidly. However, progress in multimorbidity research is limited by the lack of consensus on its definition and measurement. This standardization is a critical prerequisite for identifying high-risk populations, refining interventions, and ensuring consistency in medical research, all of which are essential for precision management in healthcare.

Methods: This paper provides a comprehensive review of recent studies (2011-2024) on multimorbidity and comorbidity, retrieved from databases including Web of Science, PubMed, China National Knowledge Infrastructure (CNKI), and WanFang, using relevant keywords up to September 2024.

Conclusion: This paper reviews the definition of multimorbidity, with a particular emphasis on distinguishing it from frailty and disability. In addition, it offers an overview of widely used clinical multimorbidity assessment tools. This paper further

examines key challenges in quantifying multimorbidity, focusing on three critical aspects. First, it emphasizes the necessity of developing population-specific quantification models and integrating modifiable risk factors into multimorbidity frameworks, which are crucial for precision management by enabling early intervention and mitigating disease burden. Second, it highlights the analysis of disease interactions to clarify potential mechanisms of disease progression and their association with adverse outcomes. Finally, the seamless integration of multimorbidity quantification with healthcare information systems is essential to optimize personalized management and improve treatment outcomes.

Keywords: Multimorbidity; challenges; management; quantification.

Conflict of interest statement

Xinyi Huang, Xiangyun Guo, Yiwen Gan, Aili Xu, Kai Sun, Hao Shen, Zitong Niu, Yafeng Zhang, Yang Guo, Yong Ma, Yili Zhang and Xu Wei declare that they have no conflict of interest.

- 100 references
- 2 figures

Supplementary info

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4

Eur J Public Health

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. 2025 Oct 8:ckaf063.

doi: 10.1093/eurpub/ckaf063. Online ahead of print.

Multimorbidity and the indirect cost of productivity loss from health-related work absenteeism in Belgium

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Affiliations Expand

- PMID: 41060679

- DOI: 10.1093/eurpub/ckaf063

Abstract

This cross-sectional observational study aims to estimate the number of days absent from work due to health-related problems among employed individuals with multimorbidity and to quantify the lost productivity value from these absences. Data were obtained from the Belgian Health Interview Survey 2018, comprising employed individuals aged 15-64 (N = 4096). We examined 12 chronic conditions and 57 dyads. The Human Capital Approach was used by multiplying the reported number of days absent by the average wage per person per day, utilizing stratified gross wages from the Belgian Statistical Office. Approximately one-third of the study population reported multimorbidity. For individuals with zero to four+ chronic conditions, mean days of absence were 5.5 (95% CI: 2.3-8.8), 6.8 (95% CI: 2.9-10.7), 14.8 (95% CI: 10-19.6), 24 (95% CI: 17.8-30.2), and 36.2 (95% CI: 30.4-42), respectively. Depression (€3089; 95% CI: 2129-4049), diabetes (€2315; 95% CI: 962-3668), arthropathies (€1972; 95% CI: 1101-2844), and cancer (€1848; 95% CI: 598-3099), as standalone conditions, were associated with the greatest productivity losses. The effects were amplified up to seven times with the co-occurrence of multiple chronic conditions. We estimated 34.2 million days absent or €7.5 billion in lost productivity due to health-related work absenteeism among working-age employed individuals with multimorbidity in 2018. At the population level, the coexistence of two musculoskeletal disorders was linked to the highest aggregated productivity loss. At the individual level, the coexistence of a mental health condition and a somatic condition was associated with the highest average productivity loss per capita. The indirect cost due to health-related absence from work for individuals with multimorbidity in Belgium is high, and in many cases, exceeds the direct cost of treatment.

Supplementary info

Grants and fundingExpand

Full text links

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Cite

5

Aging Clin Exp Res

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. 2025 Oct 8;37(1):289.

doi: 10.1007/s40520-025-03133-1.

Burden of multimorbidity and verbal phonemic fluency in cognitively healthy and mildly impaired older adults: findings from a real-world study

Elisa Fabbri [1 2], Virginia Boccardi [3], Anna Giulia Guazzarini [3 4], Ilenia Murasecco [3], Francesco Melis [3], Patrizia Bastiani [3], Paolo Muratori [5 6], Carmelinda Ruggiero [3], Patrizia Mecocci [3 4]

Affiliations Expand

- PMID: 41060330

- PMCID: PMC12507945

- DOI: 10.1007/s40520-025-03133-1

Abstract

Objective: To examine the association between burden of multimorbidity and cognitive function in older adults with normal cognition or mild cognitive impairment (MCI).

Methods: Data from electronic health records of 898 individuals cognitively healthy or with MCI were included. Burden of multimorbidity was assessed using Cumulative Illness Rating Scale-Geriatrics (CIRS-G) total score, while cognitive function was evaluated using a comprehensive battery of neuropsychological tests. Age, sex, education, basic activities of daily living and instrumental activities of daily living scores, and total number of current medications were covariates. Spearmen's correlations and multivariate regression models investigated the cross-sectional association between burden of multimorbidity and cognitive function.

Results: At a first exploratory analysis, higher CIRS-G score was significantly and negatively correlated with Addenbrooke's Cognitive Examination Revised (ACE-R) total score, ACE-R Fluency Score, ACE-R Visual-spatial score, Digit Span Test Forward, Verbal Fluency Test, Visual Search Test and Coloured Progressive Matrices, while it was positively correlated with Trail Making Test A. Fitting fully-adjusted models and independent of all covariates, the inverse association between CIRS-G score and Verbal Fluency Test was confirmed (P <.001), while no significant association was found with other cognitive tests. Noteworthy, we excluded that specific disease categories could have driven the association.

Conclusions: The burden of multimorbidity is associated with impaired verbal phonemic fluency in individuals with normal cognition or MCI. Although further studies are required to confirm it, impaired verbal phonemic fluency may be an early sign of cognitive decline in older adults with multimorbidity, with potential implications for prevention strategies.

Keywords: Aging; Cognition; Multimorbidity; Verbal fluency.

Conflict of interest statement

Declarations. Competing interests: The authors declare no competing interests. Sponsor's role: None.

- 74 references
- 1 figure

Supplementary info

MeSH termsExpand

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Cite

6

Mayo Clin Proc

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. 2025 Oct 6:S0025-6196(25)00360-X.

doi: 10.1016/j.mayocp.2025.06.021. Online ahead of print.

Multimorbidity and the Risk of Sudden Cardiac Death: Findings From a Prospective Cohort Study

Jari A Laukkanen [1], Jussi Kauhanen [2], Sudhir Kurl [3], Carl J Lavie [4], Setor K Kunutsor [5]

Affiliations Expand

- PMID: 41055632

- DOI: 10.1016/j.mayocp.2025.06.021

Abstract

Objective: To assess the prospective associations of multimorbidity status and level with the risk of sudden cardiac death (SCD).

Methods: Multimorbidity was defined as the presence of at least two multiple long-term conditions (hypertension, cardiovascular disease, type 2 diabetes, chronic

kidney disease, chronic bronchitis, and other chronic lung conditions) among 2598 men 42 to 61 years of age who were recruited into the KIHD (Kuopio Ischemic Heart Disease) study from March 1, 1984, to December 31, 1989. Hazard ratios with 95% CIs were estimated.

Results: During a median follow-up of 27.8 years, 296 SCDs were recorded. In analysis adjusted for several established cardiovascular risk factors including socioeconomic and lifestyle characteristics, the HR (95% CI) for SCD comparing men with multimorbidity vs no multimorbidity was 1.97 (95% CI, 1.54 to 2.51). Compared with men with no multimorbidity, the corresponding adjusted HRs (95% CIs) for SCD were 1.93 (95% CI, 1.50 to 2.47) for men with two to three conditions and 2.66 (95% CI, 1.34 to 5.28) for men with four to five conditions.

Conclusion: In middle-aged and older men, multimorbidity is strongly linked to an increased risk of SCD, independent of known cardiovascular risk factors. Furthermore, the risk of SCD rises progressively with the number of coexisting health conditions.

Review

Expert Rev Respir Med

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. 2025 Oct 7:1-16.

doi: 10.1080/17476348.2025.2569126. Online ahead of print.

COPD and the burden of multimorbidity: navigating the complexity

Maria Kallieri [1], Georgios Hillas [1], Konstantinos Bartziokas [1], Stelios Loukides [1], Dimitrios Toumpanakis [2]

Affiliations Expand

- PMID: 41054835

- DOI: 10.1080/17476348.2025.2569126

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a chronic condition that affects millions of people worldwide. The majority of patients with COPD have multiple coexisting chronic diseases, such as cardiovascular diseases, osteoporosis, lung cancer, and metabolic syndrome, a phenomenon that is known as multimorbidity. The coexistence of these diseases with COPD complicates diagnosis, treatment, and prognosis.

Areas covered: This review explores the underlining mechanisms that connect COPD and multimorbidity, such as shared risk factors and pathophysiological pathways. It also highlights the challenges in managing multimorbid patients and emphasizes the fact that the complexity of comorbidities may require a multidisciplinary approach in COPD management.

Expert opinion: Managing COPD in the context of multimorbidity requires a multidisciplinary approach. This approach should combine pharmacological and non-pharmacological treatments for COPD, adhere to evidence-based guidelines for managing comorbidities, and target modifiable shared risk factors to improve overall patient outcomes.

Keywords: Cardiovascular disease; chronic obstructive pulmonary disease; comorbidities; depression; lung cancer; metabolic syndrome; multimorbidity; obstructive sleep apnea.

8

Sci Rep

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. 2025 Oct 5;15(1):34651.

doi: 10.1038/s41598-025-20134-2.

A body shape index modifies the association between air pollution and cardiometabolic multimorbidity

Zhao-Wei Wang [#1], Chengwu Hu [#1], Bo Zhou [2], Mei-Ping Wan [3]

Affiliations Expand

- PMID: 41047374
- PMCID: PMC12497869
- DOI: 10.1038/s41598-025-20134-2

Abstract

Long-term exposure to air pollution is associated with cardiometabolic diseases, but the modifying role of body shape distribution on cardiometabolic multimorbidity (CMM) remains unknown. This study investigated whether A Body Shape Index (ABSI), a measure of abdominal adiposity, modifies the relationship between air pollution and CMM in Chinese middle-aged and older adults. We included 11,838 participants aged ≥ 45 years from the China Health and Retirement Longitudinal Study (CHARLS) Wave 3 (2015). CMM was defined as the coexistence of ≥ 2 cardiometabolic diseases (diabetes, heart disease, and stroke). ABSI was calculated as waist circumference/(BMI^(2/3) × height^(1/2)). Individual exposure to air pollutants-including particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), ≤ 10 μm (PM_{10}), and ≤ 1 μm (PM_1); sulfur dioxide (SO_2); nitrogen dioxide (NO_2); and ozone (O_3)-was assessed using satellite-based spatiotemporal models. Generalized linear models examined associations between air pollution and CMM, with interaction terms to evaluate ABSI's modification effects. The final analysis included 10,487 participants, with 6,896 (65.8%) having cardiometabolic multimorbidity (CMM). All six air pollutants (PM2.5, PM10, SO2, NO2, O3, PM1) showed significant positive associations with CMM prevalence. In fully adjusted models, the odds ratios per interquartile range (IQR) increase ranged from 1.104 (95% CI 1.041-1.173) for O3 to 1.298 (95% CI 1.204-1.401) for PM1. ABSI was independently associated with increased CMM risk, with each IQR (0.005) increase associated with 14.2% higher odds (OR = 1.142, 95% CI 1.085-1.201). Significant interaction effects were observed between ABSI and all six examined air pollutants (P-interaction < 0.10). Stratified analyses revealed substantially stronger associations between air pollution and CMM among participants in the highest ABSI tertile compared to the lowest tertile. For example, PM1 showed an OR of 1.428 (95% CI 1.285-1.587) in the highest ABSI group versus weaker associations in lower ABSI groups. All sensitivity analyses confirmed the robustness of these findings. This study provides the first evidence that A Body Shape Index significantly modifies the association between long-term air pollution exposure and cardiometabolic multimorbidity in Chinese middle-aged and older adults. Individuals with higher ABSI values, indicating greater abdominal adiposity, experienced substantially stronger associations between air pollutant exposure and CMM risk. These findings suggest that central body fat distribution creates a metabolically vulnerable phenotype that amplifies environmental health risks. The results highlight the importance of considering body shape distribution when assessing air pollution health impacts and support targeted prevention strategies for high-risk individuals with central obesity in polluted environments. The demonstrated interaction

between environmental and metabolic factors underscores the need for integrated approaches to cardiometabolic disease prevention that address both air quality improvement and obesity management.

Keywords: ABSI; Air pollution; Cardiometabolic diseases; Cardiometabolic multimorbidity.

Conflict of interest statement

Declarations. Competing interests: The authors declare no competing interests. Ethical approval and consent to participate: Not explicitly stated in the manuscript, but as the study used data from the China Health and Retirement Longitudinal Study (CHARLS), ethical approval was likely obtained from the institutional review board of Peking University.

- 29 references

Supplementary info

MeSH terms, SubstancesExpand

Full text links

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J Am Heart Assoc

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. 2025 Oct 7;14(19):e041834.

doi: 10.1161/JAHA.125.041834. Epub 2025 Sep 19.

Population-Based Study on the Coexistence of Metabolic Dysfunction-Associated Steatotic Liver Disease and Chronic Kidney Disease

Rachel Sze Jen Goh [1], Jaycie Koh [2], Made Ayu Utami Intaran [3], Yiphan Chin [4], Gwyneth Kong [4], Bryan Chong [4], Jobelle Chia [3], Mark Y Chan [1 5], Anurag Mehta [6], Mark Muthiah [7 8], Muhammad Shahzeb Khan [9 10 11], Nicholas Ws Chew [1 5]

Affiliations Expand

- PMID: 40970538

- DOI: 10.1161/JAHA.125.041834

Free article

Abstract

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) and chronic kidney disease (CKD) are important cardiovascular risk factors. However, the prognostic impact of coexisting MASLD and CKD remains understudied.

Methods: This study cohort used the NHANES (National Health and Nutrition Examination Survey) 2007 to 2018 database, examining outcomes in adults with varying MASLD and CKD statuses. The primary outcome was all-cause mortality. Secondary outcomes included coronary heart disease, heart failure, stroke, and cancer. Cox regression model was constructed to investigate the relationship between MASLD/CKD and all-cause mortality, adjusted for age, prior coronary heart disease, body mass index, smoking, poverty-to-income ratio, lipid-lowering and glucose-lowering medications. Sensitivity analysis was performed with hepatic fibrosis and CKD.

Results: Among 14 818 participants (mean follow-up: 6.9 ± 3.4 years), a majority of participants had MASLD(-)/CKD(-) (50.8%), followed by MASLD(+)/CKD(-) (34.8%), MASLD(+)/CKD(+) (7.7%), and MASLD(-)/CKD(+) (6.7%). MASLD(+)/CKD(+) (n = 1142) had the highest rates of obesity (77.6%), hypertension (77.5%), dyslipidemia (67.0%), and diabetes (49.7%), with the highest risk of coronary heart disease (risk ratio [RR], 1.79 [95% CI, 1.13-2.82],*P* = 0.013) and heart failure (RR 2.33 [95% CI, 1.07-5.08], *P* = 0.033). Socioeconomic disparities were observed, with lower-income individuals predominantly in the group with MASLD(+)/CKD(+) (*P* < 0.001). MASLD(+)/CKD(+) (adjusted hazard ratio [aHR], 3.28 [95% CI, 1.89-5.70], *P* < 0.001) and MASLD(-)/CKD(+) (aHR, 2.18 [95% CI, 1.33-3.66], *P* = 0.002) phenotypes were independent mortality predictors. Although MASLD(-)/CKD(+) and MASLD(+)/CKD(+) had unfavorable 10-year prognoses, survival was worse in those with both hepatic fibrosis and CKD (*P* < 0.001).

Conclusions: MASLD(+)/CKD(+) phenotype increases the risk of cardiometabolic multimorbidity and independently predicts mortality. Mortality risk increased progressively in individuals with both advanced hepatic fibrosis and CKD.

Keywords: cardiovascular disease; chronic kidney disease; metabolic dysfunction-associated steatotic liver; mortality.

Supplementary info

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

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Allergy

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. 2025 Oct 13.

doi: 10.1111/all.70097. Online ahead of print.

Efficacy of Dupilumab in Asthma: Focus on Early, Progressive, and Long-Lasting Effects on Small Airways

Matteo Martini [1 2], Leonardo Antonicelli [3], Maria Stella Garritani [1], Maria Chiara Braschi [1], Angelica Di Vincenzo [1 2], Giada Torresi [1], Marco Gallifuoco [1], Ilaria Claudi [2], Maria Giovanna Danieli [2 4 5], Federico Mei [6 7], Gianluca Moroncini [2 8], Mario Andrea Piga [9], Maria Beatrice Bilò [1 2 5]

Affiliations Expand

- PMID: 41078173

- DOI: 10.1111/all.70097

No abstract available

Keywords: asthma; dupilumab; oscillometry; reactance; small airway dysfunction.

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Allergy

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. 2025 Oct 13.

doi: 10.1111/all.70091. Online ahead of print.

Antibiotics for Acute Wheezing and Asthma Exacerbations: An EAACI Position Paper and Systematic Review

Anne-Lotte Redel [1 2], Wojciech Feleszko [3], Marina Atanaskovic-Markovic [4], Alessandra Arcolaci [5], Avraham Beigelman [6], Cristina Boccabella [7], Matteo Bonini [8 9], Gert-Jan Braunstahl [1 2], Francesca Cefaloni [7], Aspasia Karavelia [10], Gerdien Tramper-Stranders [11 12]

Affiliations Expand

- PMID: 41078060

- DOI: 10.1111/all.70091

Abstract

Introduction: Antibiotics are frequently prescribed in preschool wheezing episodes and acute asthma exacerbations (AAEs), even though antibiotics are not recommended as standard AAE treatment.

Objective: To systematically present relevant literature about the clinical effects of antibiotics for AAE and conclude with recommendations.

Methods: Systematic search was conducted in Medline ALL, Embase, Web of Science Core Collection, and Cochrane Central Register of Controlled Trials. Primary outcomes included AAE duration and length of hospital stay, while secondary outcomes incorporated AAE severity, treatment failure, AAE recurrence risk, spirometry, health costs, and adverse events.

Selection criteria: Randomised controlled trials and cohort studies were included if they investigated the clinical effect of antibiotics in AAE compared to placebo/standard care.

Results: Fifteen studies were included. Evidence for clinical effects of antibiotics in AAE treatment is scarce. Macrolides seem to shorten AAE duration in children; for adults, there is a lack of data. Antibiotics were associated with a longer hospital admission in retrospective observational studies, without evidence in randomised trials. Procalcitonin-guided treatment led to a reduction of antibiotic prescriptions without adverse outcomes.

Conclusion: Limited evidence is available that macrolides shorten AAE duration in preschool wheezers. For other age groups, there is no clear evidence of beneficial effects of antibiotics.

Keywords: antibiotics; asthma; exacerbation; treatment.

- 44 references

Supplementary info

Grants and fundingExpand

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Cite

3

J Allergy Clin Immunol

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. 2025 Oct 10:S0091-6749(25)00977-7.

doi: 10.1016/j.jaci.2025.09.013. Online ahead of print.

Guideline adherence to aeroallergen-focused activities in adult asthma care: Insights from an online survey

Patrick K Gleeson [1], Knashawn H Morales [2], Hannah J Lee [3], Olajumoke O Fadugba [3], Priya J Patel [3], Audreesh Banerjee [4], Andrea J Apter [3], Jason D Christie [4], Meeta Prasad Kerlin [5]

Affiliations Expand

- PMID: 41074890

- DOI: 10.1016/j.jaci.2025.09.013

No abstract available

Keywords: Guideline adherence; health education; physicians' practice patterns; respiratory hypersensitivity; surveys and questionnaires.

Conflict of interest statement

Disclosure statement Supported by the National Institutes of Health National Heart, Lung, and Blood Institute (awards R01HL162354, R01HL141608, R01HL143364, and K24HL115354) and by the Patient-Centered Outcomes Research Institute (award AS-1307-05218). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the article. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or other funding agencies. Declaration of potential conflict of interest: K. H. Morales owns stock in Altria Group, British American Tobacco PLC, and Phillip Morris International. The rest of the authors declare that they have no relevant conflicts of interest.

Supplementary info

Publication typesExpand

Full text links

4

Review

Cell Biosci

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. 2025 Oct 10;15(1):137.

doi: 10.1186/s13578-025-01486-8.

Roles of glucagon-like peptide 1 receptor agonists in immune cell biology and autoimmune/autoinflammatory diseases

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Affiliations Expand

- PMID: 41074143
- PMCID: PMC12512578
- DOI: 10.1186/s13578-025-01486-8

Abstract

Glucagon-like peptide-1 (GLP-1) is a gut-derived hormone essential for maintaining glucose homeostasis through multiple physiological pathways: triggering insulin release, inhibiting glucagon secretion, delaying gastric emptying, enhancing feelings of fullness, and suppressing appetite. Since GLP-1 is prone to degradation by dipeptidyl peptidase 4, GLP-1 receptor agonists (GLP-1RAs) have been developed to surmount this degradation challenge. At present, GLP-1RAs have become highly effective treatments for managing type 2 diabetes mellitus and obesity. Beyond their well-established benefits for blood sugar regulation and weight control, GLP-1RAs also exhibit various biological activities associated with both insulinotropic effects and immunoregulation. These effects have been demonstrated through in vitro studies, preclinical models, and clinical observations. This review aims to explore the effects of GLP-1R signaling on various immune cells and evaluate the therapeutic potential of GLP-1RAs in autoimmune and autoinflammatory diseases, including psoriasis, inflammatory bowel diseases, rheumatoid arthritis, asthma, multiple sclerosis, Sjögren's syndrome, and systemic lupus erythematosus.

Keywords: Autoimmune diseases; Autoinflammatory diseases; GLP-1; GLP-1 receptor agonists; Immunoregulation.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: Not applicable. Consent for publication: Not applicable. Competing interests: The authors declare no conflicts of interest.

- 292 references
- 3 figures

Supplementary info

Publication types, Grants and fundingExpand

Full text links

Cite

5

Nat Commun

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. 2025 Oct 10;16(1):9042.

doi: 10.1038/s41467-025-64927-5.

The effect of type 2 diabetes genetic predisposition on non-cardiovascular comorbidities

Ana Luiza Arruda [#1,2], Ozvan Bocher [#3,4], Henry J Taylor [#5,6,7], Davis Cammann [#8], Satoshi Yoshiji [9,10,11], Xianyong Yin [12,13], Chi Zhao [14], Jingchun Chen [8], Alexis C Wood [15], Ken Suzuki [16], Josep M Mercader [9,17,18], Cassandra N Spracklen [14], James B Meigs [9,19,20], Marijana Vujkovic [21,22,23], George Davey Smith [24], Jerome I Rotter [25], Benjamin F Voight [21,22,26,27], Andrew P Morris [28,29], Eleftheria Zeggini [30,31]

Affiliations Expand

- **PMID: 41073432**
- **PMCID: PMC12514310**

- DOI: 10.1038/s41467-025-64927-5

Abstract

Type 2 diabetes is associated with a range of non-cardiovascular non-oncologic comorbidities. To move beyond associations and evaluate causal effects between type 2 diabetes genetic predisposition and 21 comorbidities, we apply Mendelian randomization analysis using genome-wide association studies across multiple genetic ancestries. Additionally, leveraging eight mechanistic clusters of type 2 diabetes genetic profiles, each representing distinct biological pathways, we investigate causal links between cluster-stratified type 2 diabetes genetic predisposition and comorbidity risk. We identify causal effects of type 2 diabetes genetic predisposition driven by distinct genetic clusters. For example, the risk-increasing effects of type 2 diabetes genetic predisposition on cataracts and erectile dysfunction are primarily attributed to adiposity and glucose regulation mechanisms, respectively. We observe opposing effect directions across different genetic ancestries for depression, asthma and chronic obstructive pulmonary disease. Our findings leverage the heterogeneity underpinning type 2 diabetes genetic predisposition to prioritize biological mechanisms underlying causal relationships with comorbidities.

Conflict of interest statement

Competing interests: The authors have no competing interests.

- 101 references
- 4 figures

Supplementary info

MeSH termsExpand

Full text links

Cite

6

Ann Allergy Asthma Immunol

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. 2025 Oct 8:S1081-1206(25)01201-3.

doi: 10.1016/j.anai.2025.09.015. Online ahead of print.

Effect of tezepelumab on asthma exacerbations co-occurring with infection-attributed acute respiratory illnesses

Wojciech Feleszko [1], Marco Caminati [2], James E Gern [3], Sebastian L Johnston [4], Claudio Marchese [5], Deborah Clarke [6], Christopher S Ambrose [7], Andrew W Lindsley [8]

Affiliations Expand

- PMID: 41072729

- DOI: 10.1016/j.anai.2025.09.015

Abstract

Background: Tezepelumab, a human monoclonal antibody, blocks the activity of thymic stromal lymphopoietin (TSLP). In the phase 2b PATHWAY (NCT02054130) and phase 3 NAVIGATOR (NCT03347279) studies, tezepelumab reduced exacerbations and improved lung function, asthma control, and health-related quality of life versus placebo in patients with severe, uncontrolled asthma.

Objective: This post hoc analysis of PATHWAY and NAVIGATOR evaluated the incidence of asthma exacerbations co-occurring with documented acute respiratory illnesses attributed to infections.

Methods: Patients were randomized 1:1 to receive tezepelumab 210 mg subcutaneously or placebo every 4 weeks for 52 weeks. The incidence of asthma exacerbations co-occurring with respiratory illness-related adverse events (AEs) was assessed. Co-occurrence was defined as at least 1 day of overlap between a respiratory illness-related AE and the asthma exacerbation period beginning 7 days before the start of the exacerbation until the end of the asthma exacerbation.

Results: Of the 1334 patients (tezepelumab, n = 665; placebo, n = 669) included, 312 experienced at least one asthma exacerbation co-occurring with a respiratory illness-related AE attributed to an infection. The incidence of asthma exacerbation co-occurring with a respiratory illness-related AE was lower in the tezepelumab group than the placebo group overall (18.2% vs 28.6%; exposure-adjusted incidence difference [EAID]: -11.1 [95% CI: -15.75, -6.41]) and among patients with perennial allergy (EAID, -11.6 [95% CI: -17.44, -5.69]) and without perennial allergy (EAID, -10.2 [95% CI: -18.16, -2.10]).

Conclusion: Tezepelumab reduced asthma exacerbations attributed to respiratory infections in patients with severe, uncontrolled asthma compared with placebo, irrespective of perennial allergy status.

Keywords: TSLP; acute respiratory illnesses; asthma; infections; tezepelumab.

Conflict of interest statement

Declaration of competing interest W. Feleszko has received speaker fees from AstraZeneca. M. Caminati has received fees from AstraZeneca for serving on

advisory boards and has received speaker fees from GSK and Sanofi. J. E. Gern has received consulting fees from AstraZeneca, Arrowhead Pharmaceuticals, and Meissa Vaccines; and owns stock options in Meissa Vaccines. S. L. Johnston has received fees from AstraZeneca and GSK for serving on advisory boards and has received grant income from GSK. C. Marchese, D. Clarke, and C. S. Ambrose are employees of AstraZeneca and may hold stock or stock options in AstraZeneca. A. W. Lindsley is an employee of Amgen and owns stock in Amgen.

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Am J Respir Cell Mol Biol

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. 2025 Oct 10.

doi: 10.1165/rcmb.2024-0580OC. Online ahead of print.

SERPINB10 Promotes Neutrophilic Airway Inflammation in Asthma

Weiqiang Kong [1], Chunli Huang [2], Lu Zhao [2], Gongqi Chen [3], Wei Gu [2], Huiru Jie [2], Zhen Wang [2], Tiantian Xiong [2], Lingling Yi [4], Yuchen Feng [2], Guohua Zhen [5]

Affiliations Expand

- PMID: 41072019

- DOI: 10.1165/rcmb.2024-0580OC

Abstract

A subset of severe asthma is characterized by neutrophilic airway inflammation in which epithelial activation of the NLRP3 inflammasome pathway is implicated. Recent reports link SERPINB10 to neutrophil activation in inflammatory disease. We hypothesized that SERPINB10 contributes to neutrophilic inflammation in asthma. Since viral infection triggers airway neutrophilia in asthma, we sensitized mice with house dust mite (HDM) and challenged them with HDM and poly(I:C), a viral double-stranded RNA analog. Compared to wild-type mice, *Serpinb10*$^{-/-}$ mice exhibited reduced neutrophil counts in bronchoalveolar lavage cells and alleviated inflammatory cell infiltration around airways. Expression of inflammatory cytokines such as Il-1β and Il-6 was also decreased in lung tissues from *Serpinb10*$^{-/-}$ mice. In cultured HBE cells, *SERPINB10* knockdown decreased IκBα phosphorylation and

suppressed poly(I:C)-induced expression of IL-1β and IL-6. Moreover, the expression of NLRP3 and pro-IL-1β in lung tissues of *Serpinb10*$^{-/-}$ mice was decreased. Conversely, *SERPINB10* overexpression enhanced IL-1β and IL-6 expression in HBE cells, which was blocked by either an IκBα phosphorylation inhibitor or an NLRP3 inhibitor. Of note, SERPINB10 expression in bronchial brushings from non-eosinophilic asthma patients was enhanced and significantly correlated with the severity of airflow limitation, and the expression of NLRP3, IL-1β, and IL-6. Altogether, SERPINB10 promotes IL-1β and IL-6 expression by upregulating NF-κB and NLRP3 signaling in airway epithelial cells, thereby driving neutrophilic airway inflammation in asthma. SERPINB10 is a potential therapeutic target for airway neutrophilia in asthma.

Keywords: SERPINB10; asthma; epithelial cells; neutrophilic airway inflammation.

Full text links

Cite

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Eur Ann Allergy Clin Immunol

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. 2025 Oct 10.

doi: 10.23822/EurAnnACI.1764-1489.417. Online ahead of print.

Analysis of trends in single inhaler triple therapy (SITT) use and clinical characteristics of patients with severe asthma: data from the IRSA registry

F Menzella [1], M Martini [2], M B Bilò [2 3], L Antonicelli [4], L Cecchi [5], F de Michele [6], A Vaghi [7], A Musarra [8], C Micheletto [9]

Affiliations Expand

- **PMID: 41070812**

- **DOI: 10.23822/EurAnnACI.1764-1489.417**

No abstract available

Keywords: Triple therapy; asthma; biomarkers; exacerbations; lung function.

Full text links

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Eur Ann Allergy Clin Immunol

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. 2025 Oct 10.

doi: 10.23822/EurAnnACI.1764-1489.416. Online ahead of print.

Real-life efficacy of Tezepelumab in patients with failure to other biologic drugs

J C Miralles-López [1], J J Cortés Collado [2], Y Petryk Petryk [3], F-J Bravo-Gutierrez [4], R Andújar-Espinosa [5], M Ramírez Hernández [6], M Castilla-Martínez [7], C Díaz-Chantar [8], I Ibarra-Calabuig [3], J Valverde-Molina [9] [10], V Pérez-Fernández [11], Re-Asgramur Group [12]

Affiliations Expand

- PMID: 41070810

- DOI: 10.23822/EurAnnACI.1764-1489.416

No abstract available

Keywords: Tezepelumab; failure previous drugs; real-life efficacy; severe asthma.

Supplementary info

Publication typesExpand

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Eur Respir J

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. 2025 Oct 9:2501229.

doi: 10.1183/13993003.01229-2025. Online ahead of print.

Exhaled nitric oxide (FeNO) and the response to prednisolone for asthma attacks in patients treated with anti-IL5/5Rα therapy: a prospective observational study

Imran Howell [1], Mahdi Mahdi [2], Hafiz R Mahmood [2], Laura Bermejo-Sanchez [2], Catherine Borg [2], Sanjay Ramakrishnan [3], James Melhorn [2], Gabriel Lavoie [4], Nayia Petousi [2], Timothy S C Hinks [2], Mona Bafadhel [5], Ian D Pavord [2]

Affiliations Expand

- PMID: 41067871

- DOI: 10.1183/13993003.01229-2025

No abstract available

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11

Respir Med

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. 2025 Oct 7:108402.

doi: 10.1016/j.rmed.2025.108402. Online ahead of print.

Comparison of oscillometry ratios between IOS and AOS in patients with asthma and COPD

Philipp Suter [1], Robert Greig [1], Chris RuiWen Kuo [1], Rory Chan [1], Brian Lipworth [2]

Affiliations Expand

- PMID: 41067289

- DOI: 10.1016/j.rmed.2025.108402

Abstract

The forced oscillation technique (FOT) enables effort-independent assessment of small airway dysfunction (SAD) in obstructive lung diseases. We compared resistance and reactance ratios between two FOT modalities-impulse oscillometry (IOS) and airwave oscillometry (AOS), in patients with asthma and COPD. We retrospectively analysed paired pre- and post-bronchodilator IOS and AOS measurements from 82 patients (58 asthma, 24 COPD). Resistance (R5-R20/R5 for IOS; R5-R19/R5 for AOS) and reactance (X5/AX) ratios were compared using correlation and Bland-Altman analyses. Resistance ratios showed significant agreement between devices, with minimal mean differences. Reactance ratios were also significantly correlated but were higher with IOS than AOS. This difference increased at higher X5/AX ratios, likely due to device specific signal characteristics and calibration differences. Post-bronchodilator improvements were observed with both devices, with a greater change in X5/AX using IOS ($p < 0.05$). In conclusion resistance ratios were comparable between IOS and AOS, supporting their clinical use across devices. In contrast, reactance ratios differed, highlighting the need for device-specific normative values and improved standardization. FOT-derived ratios may offer a practical alternative to absolute values for assessing SAD in asthma and COPD.

Keywords: AOS; IOS; obstructive pulmonary disease; oscillometry derived ratios; spirometry.

Conflict of interest statement

Declaration of Competing Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Philipp Suter reports a relationship with AstraZeneca UK Limited that includes: speaking and lecture fees. Philipp Suter reports a relationship with GSK that includes: speaking and lecture fees. Philipp Suter reports a relationship with Lung League Fribourg (Switzerland) that includes: funding grants without influence on work reported in this paper. Robert Greig reports a relationship with AstraZeneca UK Limited that includes: speaking and lecture fees. Chris Kuo reports personal fees from AstraZeneca. Chris Kuo reports personal fees from Chiesi. Chris Kuo reports non-financial support from GSK outside the submitted work. Rory Chan reports a relationship with AstraZeneca UK Limited that includes: speaking and lecture fees and travel reimbursement. Rory Chan reports a relationship with Vitalograph UK Ltd that includes: consulting or advisory. Rory Chan reports a relationship with Thorasys that includes: speaking and lecture fees. Brian J Lipworth reports a relationship with AstraZeneca UK Limited that includes: consulting or advisory, funding grants, speaking and lecture fees, and travel reimbursement. Brian J Lipworth reports a relationship with GSK that includes: non-financial support. Brian J Lipworth reports a relationship with Sanofi that includes: speaking and lecture fees. Brian J Lipworth reports a relationship with Circassia Pharmaceuticals Plc that includes: consulting or advisory and speaking and lecture fees. Brian J Lipworth reports a relationship with Teva UK Ltd that includes:

consulting or advisory, funding grants, speaking and lecture fees, and travel reimbursement. Brian J Lipworth reports a relationship with Chiesi Ltd that includes: consulting or advisory, funding grants, speaking and lecture fees, and travel reimbursement. Brian J Lipworth reports a relationship with Lupin Healthcare UK Ltd that includes: consulting or advisory. Brian J Lipworth reports a relationship with Glenmark Pharmaceuticals Limited that includes: consulting or advisory. Brian J Lipworth reports a relationship with Dr Reddy's Laboratories Ltd that includes: consulting or advisory. Brian J Lipworth reports a relationship with Sandoz UK Ltd that includes: consulting or advisory. Brian J Lipworth reports a relationship with Boehringer Ingelheim Ltd that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Brian J Lipworth reports a relationship with Mylan Pharmaceuticals Inc that includes: consulting or advisory and speaking and lecture fees. The son of Dr Brian Lipworth is presently an employee of AstraZeneca. 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.

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Pulmonology

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. 2025 Dec 31;31(1):2571016.

doi: 10.1080/25310429.2025.2571016. Epub 2025 Oct 9.

Severe acute asthma exacerbations under biological agents: A new therapeutic paradigm?

Diogo Antunes [1], Rita Oliveira [2], Marisa Paulino [1], Fernanda Paula Santos [2], Filipe Froes [2]

Affiliations Expand

- **PMID: 41063683**
- **DOI: 10.1080/25310429.2025.2571016**

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13

BMC Pulm Med

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. 2025 Oct 8;25(1):456.

doi: 10.1186/s12890-025-03919-z.

Determinants of adherence to inhaler use in patients with asthma: the role of knowledge, self-efficacy, and perceived barriers

Saeed Hosseininia [1], Sousan Mohammadikebar [1], Leila Motashakkeri [1], Aziz Kamran [2]

Affiliations Expand

- PMID: 41063043
- PMCID: PMC12505728
- DOI: 10.1186/s12890-025-03919-z

Abstract

Background: Adherence to inhaler therapy is a crucial determinant in the management and control of asthma. However, real-world evidence indicates that only 30-70% of patients adhere to prescribed treatments. This study aimed to identify the psychological and behavioral factors influencing inhaler adherence among patients with asthma.

Methods: This cross-sectional study was conducted on 300 patients with a confirmed diagnosis of asthma based on GINA criteria at Imam Khomeini Hospital, Ardabil, Iran, during the winter of 2021-2022. Participants were selected through a census sampling method. Data were collected using a researcher-developed questionnaire and analyzed statistically.

Results: Inhaler adherence was positively associated with patient knowledge, disease acceptance, treatment acceptance, self-efficacy, and perceived benefits of inhaler use. Conversely, fear of side effects and inhaler-related stigma were negatively associated with adherence ($P < 0.05$). Significant differences in

adherence-related variables (knowledge, disease and treatment acceptance, stigma, self-efficacy, and perceived benefits) were found across different educational levels and between urban and rural patients ($P < 0.05$).

Conclusions: Psychological and behavioral factors play a significant role in adherence to inhaler therapy in asthma patients. Regular assessment of patients' knowledge, beliefs, and behavioral patterns regarding inhaler use during clinical visits may enhance self-management and improve treatment outcomes.

Keywords: Asthma; Inhaler adherence; Self-efficacy; Stigma; Treatment acceptance.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human participants were approved by Biomedical Ethics Committee of Ardabil University of Medical Sciences (approval number IR.ARUMS.REC. 1399.056). Informed consent was obtained from all subjects and from the legal guardian(s) of the illiterate participants. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests. Clinical trial number: Not applicable.

- 36 references

Supplementary info

MeSH terms, SubstancesExpand

Full text links

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Sci Rep

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. 2025 Oct 8;15(1):35198.

doi: 10.1038/s41598-025-19056-w.

Machine learning reveals limited predictive value of clinical factors for asthma exacerbations

Erik Duijvelaar [1], Jack S Gisby [2], Hanneke Coumou [3], Jeroen Hoogland [4], Bart Hilvering [3], Anirban Sinha [5], Marijke Amelink [6], Els J M Weersink [3]

Affiliations Expand

- PMID: 41062600
- PMCID: PMC12508110
- DOI: 10.1038/s41598-025-19056-w

Abstract

While predictors of asthma exacerbation risk are generally well established, predictors of exacerbation severity remain largely undefined. Identifying robust clinical predictors of exacerbation severity is essential to support tailored management strategies and optimize resource allocation. This study leverages machine learning to evaluate the predictive value of clinical factors for exacerbation severity in a real-world emergency department setting. A retrospective cohort study was performed using medical records of 367 adults (644 exacerbations) who presented to the Amsterdam UMC emergency department between 2013 and 2020. Five severity outcomes were investigated: hospital admission, ICU admission, length of stay, oxygenation efficiency (SpO_2/FiO_2), and National Early Warning Score (NEWS). Associations were assessed using linear mixed models (LMM), and predictive modelling employed a machine learning approach combining LMMs with fivefold cross-validated least absolute shrinkage and selection operator (LASSO) regression. Exacerbation severity was most consistently associated with lung function, the presence of a radiographic chest infiltrate, C-reactive protein levels, blood neutrophil count and theophylline maintenance use. No significant associations were found for blood eosinophil count, age, comorbidities, symptom duration, triggers, allergic sensitization, ethnicity or exacerbation history within the preceding 12 months. Internally validated prediction models for hospital and intensive care admission achieved areas under the curve of 0.632 and 0.695, respectively. The strongest predictors explained 18.8% of variability in NEWS, 15.2% in oxygenation efficiency, and 9.0% in length of hospital stay. In these prediction models, a radiographic chest infiltrate, followed by theophylline maintenance use and blood neutrophil count, were most frequently associated across the five severity outcomes. To conclude, lung function and markers of acute respiratory infection were most frequently associated with asthma exacerbation severity. However, clinical and demographic variables have only modest predictive value, highlighting the need to identify additional robust predictors.

Keywords: Asthma; Exacerbations; Machine learning; Predictive modelling; Risk stratification; Treatable traits.

Conflict of interest statement

Declarations. Competing interests: The authors declare no competing interests. Ethics approval: Ethical approval for study conduction was obtained from the

ethical committee of the Amsterdam University Medical Centers (Amsterdam UMC), location Academic Medical Center (AMC). Written informed consent was waived by the ethical committee.

- 36 references
- 2 figures

Supplementary info

MeSH termsExpand

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Respir Med

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. 2025 Oct 6:108403.

doi: 10.1016/j.rmed.2025.108403. Online ahead of print.

Metformin use is associated with reduced systemic steroid courses among pediatric asthma patients with diabetes or elevated blood glucose levels

Erhan Ararat [1], Deepa Rastogi [2], Bradley C Martin [3]

Affiliations Expand

- PMID: 41061902

- DOI: 10.1016/j.rmed.2025.108403

Abstract

Background: Patients with asthma and abnormal glucose metabolism have increased asthma exacerbations, worse lung function, and higher health care utilization. Metformin, an insulin-sensitizing agent with anti-inflammatory properties, may modify these outcomes.

Objective: This study explored the association between metformin use and acute asthma exacerbations in children with asthma with elevated blood glucose or a type 2 diabetes diagnosis.

Methods: This observational study was conducted among children aged 10-17 years with asthma and evidence of type 2 diabetes, abnormal glucose, or serum glucose ≥200 mg/dL, using the Linked Network in TrinetX data. Two cohorts were constructed: a metformin treatment group and a comparison group without metformin. Groups were matched 1:1 using a propensity score algorithm on baseline characteristics. Negative binomial models were used to compare asthma-related healthcare utilizations and systemic steroid courses. Kaplan-Meier analysis using the log-rank test compared the time to-first asthma exacerbation.

Results: After propensity score matching, there were 536 children each in the metformin user and comparison groups. Metformin use was associated with a significantly lower rate of systemic corticosteroid courses, with a 42% reduction compared to the comparison group (IRR = 0.58; 95% CI: 0.40-0.85; p = 0.005). There was no difference in the median time to the first occurrence of asthma hospitalizations, ER visits, or systemic steroid courses between the metformin use and comparison group.

Conclusion: Metformin use was associated with a significantly lower rate of systemic corticosteroid courses, although no differences were observed in acute care utilization and in time to first asthma exacerbation.

Keywords: hospitalizations; insulin resistance; obesity; oral steroids; type 2 diabetes.

Conflict of interest statement

Declaration of Competing Interest ☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Erhan Ararat reports financial support was provided by University of Arkansas for Medical Sciences. 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.

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Ann Pharmacother

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. 2025 Oct 7:10600280251369941.

doi: 10.1177/10600280251369941. Online ahead of print.

Elevated Risk of Asthma Among Proton Pump Inhibitor Users: Evidence From Meta-Analysis

Sayed Aliul Hasan Abdi, Shabihul Fatma Sayed, Sumathi Nagarajan

- PMID: 41058147

- DOI: 10.1177/10600280251369941

No abstract available

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17

Case Reports

Acta Otorrinolaringol Esp (Engl Ed)

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. 2025 Oct 5:512291.

doi: 10.1016/j.otoeng.2025.512291. Online ahead of print.

Real-life outcomes of benralizumab treatment in chronic rhinosinusitis with nasal polyps: The BenREALizumab Study

Juan Maza-Solano [1], Vicente Merino-Bohórquez [2], Ana Gómez-Bastero [3], Julio Delgado-Romero [4], Serafín Sánchez-Gomez [5]

Affiliations Expand

- PMID: 41057094

- DOI: 10.1016/j.otoeng.2025.512291

Abstract

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a type 2 inflammatory disease with a significant impact on quality of life. Benralizumab has shown efficacy in severe eosinophilic asthma, but there is limited evidence for CRSwNP. A prospective observational study was conducted in a tertiary hospital with six adults with severe CRSwNP, according to EPOS2020 criteria, treated for 52 weeks. All had multiple surgeries (mean 3.3) and high cumulative exposure to systemic corticosteroids. Initially, they presented a high symptom and endoscopic burden (SNOT-22: 72; NPS: 5.2). After 16 and 52 weeks, significant improvements were observed in SNOT-22 (40.3 and 28.8), NPS (4.3 and 2.7), corticosteroid use, and complete eosinophil depletion. VAS scores improved, especially in smell, rhinorrhea, and general condition. No significant adverse events occurred. These preliminary results suggest that benralizumab may be effective in CRSwNP without associated asthma, although larger controlled studies are needed.

Keywords: Anticuerpos monoclonales; Benralizumab; Calidad de vida; Chronic rhinosinusitis with nasal polyps; Eosinophils; Eosinófilos; Evidencia real; Monoclonal antibodies; Quality of life; Real-world evidence; Rinosinusitis crónica con pólipos nasales.

Supplementary info

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Am J Respir Crit Care Med

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. 2025 Oct 7.

doi: 10.1164/rccm.202505-1260OC. Online ahead of print.

Patient Factors and Clinical Efficacy of Early Identification and Treatment of COPD and Asthma

Arianne Tardif [1], G A Whitmore [2], Katherine L Vandemheen [3], Celine Bergeron [4 5], Louis-Philippe Boulet [6], Andréanne Côté [7], R Andrew McIvor [8], Erika Penz [9], Stephen K Field [10], Catherine Lemière [11], Irvin Mayers [12], Mohit Bhutani [13], Tanweer Azher [14], M Diane Lougheed [15], Samir Gupta [16], Nicole

Ezer [17,18], Christopher J Licskai [19], Paul Hernandez [20], Martha Ainslie [21], Gonzalo G Alvarez [3], Sunita Mulpuru [22,23], Shawn D Aaron [24,25]

Affiliations Expand

- PMID: 41056133

- DOI: 10.1164/rccm.202505-1260OC

Abstract

Rationale: The Undiagnosed COPD and Asthma Population trial showed that early diagnosis and treatment of asthma and COPD by pulmonologists improved healthcare utilization, respiratory symptoms, and quality of life.

Objectives: To determine if the benefits of early diagnosis and treatment were greater in individuals with more advanced disease, or in individuals with asthma as opposed to COPD. We also assessed whether pulmonologist-directed care benefited asthma and COPD subgroups equally.

Methods: Case finding was used to identify undiagnosed adults with chronic respiratory symptoms in the community. Five hundred and eight newly diagnosed participants with COPD or asthma were randomized to a pulmonologist-care intervention or usual care. Low and high disease-burden categories for St. Georges Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT) were defined using a median-split of baseline scores, and MCID thresholds were used to define significant responses. Benefits of pulmonologist care were assessed by evaluating treatment effects within subgroups and by assessing treatment-by-subgroup interactions.

Measurements and main results: Patients with higher disease burden at diagnosis were more likely to benefit from early diagnosis and treatment compared to those with lower disease-burden. 71% of those with high disease-burden improved their CAT by ≥ 2 points over 12 months compared to 47% with low disease burden; OR 2.78, 95% CI: 1.90 to 4.07, p<0.001. Similar results were seen for SGRQ and FEV1 improvements. In contrast, responses to early diagnosis and treatment were similar for those with asthma vs COPD. Individuals with asthma randomized to pulmonologist-directed care showed greater one-year improvements in CAT, SGRQ, SF36 and FEV1 compared to individuals randomized to primary care. However, individuals with COPD experienced similar improvements regardless of whether their treatment was managed by a pulmonologist or primary care provider. Treatment-by-disease interaction terms were not statistically significant.

Conclusions: Patients with greater disease burden who exhibited more advanced and symptomatic asthma and COPD at the time of diagnosis, benefited more from earlier diagnosis and treatment. Patients with asthma tended to derive greater benefit from pulmonologist-directed care than patients with COPD.

Keywords: Asthma; COPD; Case-finding; Disease burden; Early diagnosis.

19

Editorial

Thorax

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. 2025 Oct 6:thorax-2025-223930.

doi: 10.1136/thorax-2025-223930. Online ahead of print.

Nocturnal reflux: an untapped target in lung disease?

Amanda T Goodwin [1 2 3]

Affiliations Expand

- PMID: 41052929

- DOI: 10.1136/thorax-2025-223930

No abstract available

Keywords: Asthma Mechanisms; COPD exacerbations mechanisms; Clinical Epidemiology; Imaging/CT MRI etc; Interstitial Fibrosis.

Conflict of interest statement

Competing interests: None declared.

Supplementary info

Publication typesExpand

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Curr Opin Pediatr

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. 2025 Oct 7.

doi: 10.1097/MOP.0000000000001514. Online ahead of print.

Early-life viral infections and asthma: new cells and ideas

Jie Lan [1], Alysia McCray [1], Emma Brown [1], Taylor Eddens [1 2]

Affiliations Expand

- PMID: 41051175

- DOI: 10.1097/MOP.0000000000001514

Abstract

Purpose of review: Asthma is among the most common conditions managed by pediatricians. This review summarizes recent advances in our immunologic understanding of asthma, focusing on cell types implicated in pathogenesis outside of the Th2 paradigm. Early-life respiratory viral infections are a key risk factor for the development of pediatric asthma. Literature detailing the epidemiologic and immunologic connection between early-life viral infections and asthma is also reviewed.

Recent findings: Asthma is an umbrella term used clinically, but the underlying immune mechanisms can be highly variable. These differing endotypes of asthma can be driven by distinct granulocyte, CD4 + T-cell, and innate-cell subsets, all with therapeutic implications. Early-life viral infection is a well described risk factor for asthma development. Understanding the differences in the immune system early in life, focused on the lung milieu, has shed light on the mechanisms connecting these two conditions.

Summary: Early-life respiratory viral infections and asthma have high prevalence in pediatrics, with the former raising the risk for the latter. Understanding the immunologic mechanisms is critical in understanding this connection. Further, our understanding of the drivers of asthma in pediatrics has expanded beyond the canonical pathways.

Keywords: asthma; early-life viral infection; lung immunology.

- 141 references

Full text links

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21

Review

Allergy

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. 2025 Oct 6.

doi: 10.1111/all.70087. Online ahead of print.

Asthma in Pregnancy

Eve Denton [1 2], Megan E Jensen [3], Bronwyn K Brew [3], Mark Hew [1 2], Vanessa E Murphy [3]

Affiliations Expand

- PMID: 41051000

- DOI: 10.1111/all.70087

Abstract

Asthma is one of the most common chronic diseases affecting pregnant women with variable prevalence around the world. Hormonally mediated and physical changes to the respiratory system occur during pregnancy and can impact asthma status unpredictably-some women improve, some worsen and some are stable. Increased maternal and foetal adverse outcomes are observed with uncontrolled asthma. Medication non-adherence increases in pregnancy, often because of concerns regarding the effect of medications on the developing foetus and is a major contributor to loss of asthma control. Certain comorbidities, particularly metabolic comorbidities, are more common in pregnant women with asthma and are increasingly understood to impact asthma and pregnancy outcomes. There is reassuring observational data to suggest the safety of omalizumab and dupilumab in pregnancy, but more studies are needed. This review highlights the current evidence regarding epidemiology, pregnancy-related respiratory changes, comorbidities and treatment of asthma in pregnancy.

Keywords: asthma; epidemiology; pregnancy; treatable traits; treatment.

- 206 references

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Editorial

Thorax

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. 2025 Oct 5:thorax-2025-223499.

doi: 10.1136/thorax-2025-223499. Online ahead of print.

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

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23

Editorial

Thorax

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. 2025 Oct 5:thorax-2025-223595.

doi: 10.1136/thorax-2025-223595. Online ahead of print.

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

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Review

Ear Nose Throat J

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. 2025 Oct 5:1455613251378726.

doi: 10.1177/01455613251378726. Online ahead of print.

Correlation Between Allergic Rhinitis, Asthma, and Laryngopharyngeal Reflux Disease: A Systematic Review

Baraa Ibrahim Awad [1], Laila Salah Aldokhail [2], Enar Mohammed Alotaibi [2], Hatem Mohammed Asiri [3], Yazeed Abdullah Asery [4], Nawaf Khalid Nahhas [4], Mohammed Halawani [4 5 6]

Affiliations Expand

- PMID: 41046361

- DOI: 10.1177/01455613251378726

Free article

Abstract

Background: Laryngopharyngeal reflux (LPR), allergic rhinitis (AR), and asthma are common airway disorders that often coexist, suggesting shared inflammatory mechanisms. LPR involves gastric reflux into the laryngopharynx, while AR and asthma are linked by the "united airway" hypothesis. Evidence indicates LPR may contribute to AR and asthma exacerbation, yet their interactions remain unclear. Understanding their interaction may enhance clinical outcomes.

Objective: This systematic review aimed to evaluate the associations between LPR, AR, and asthma by analyzing studies that examined these conditions in various patient populations.

Methodology: A comprehensive search of electronic databases, including PubMed, Scopus, and Google Scholar, was conducted for studies published up until 2024. Eligible studies were selected based on predefined inclusion criteria, and data on the prevalence, diagnostic methods, and associations between LPR, AR, and asthma were extracted. This systematic review was conducted and registered in PROSPERO (CRD42024588367). Statistical analysis was performed to determine the strength of the associations between these conditions.

Results: The review identified significant associations between LPR and both AR and asthma. Multiple studies confirmed a positive correlation between LPR and AR, with worse AR symptoms observed in patients with more severe LPR. Additionally, a strong association between LPR and asthma was observed, particularly in patients with poorly-controlled asthma. The analysis also revealed a robust relationship between AR and asthma, consistent with the "united airway" hypothesis, which posits that the upper and lower airways share common inflammatory pathways. These findings suggest that the coexistence of these conditions may exacerbate symptoms and complicate management.

Conclusion: This systematic review highlights the significant associations between LPR, AR, and asthma, emphasizing the importance of recognizing and addressing these comorbidities in clinical practice. The findings suggest that managing 1 condition may have a beneficial effect on the others, supporting a multidisciplinary approach to diagnosis and treatment.

Keywords: airway inflammation; allergic rhinitis; asthma; laryngopharyngeal reflux; systematic review.

Supplementary info

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Review

Expert Rev Respir Med

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. 2025 Oct 7:1-14.

doi: 10.1080/17476348.2025.2569844. Online ahead of print.

Advances in type 2-high asthma therapy: what remains missing?

Ahmad Z Al Meslamani [1], Anan S Jarab [2], Abdullah Elrefae [3]

Affiliations Expand

- **PMID: 41029975**

- DOI: 10.1080/17476348.2025.2569844

Abstract

Introduction: Type 2-high asthma (T2HA) accounts for most severe asthma morbidity and is driven by eosinophilic, IgE- and alarmin-mediated inflammation. Although five biologics are licensed, many patients remain symptomatic, corticosteroid-dependent or financially excluded.

Areas covered: PubMed, Embase, Web of Science, Scopus, Cochrane Library, EconLit, ClinicalTrials.gov and WHO-ICTRP were searched (1 January 2005 - 30 June 2025). Evidence from randomized trials, economic evaluations and translational studies on biologics, small-molecule drugs, cell-based and microbiome-directed interventions was synthesized across four domains: late-stage attrition, ultra-long-acting biologic limitations, slow small-molecule progress, and cost - access barriers. Durability, pediatric data and OCS-sparing potential were also examined.

Expert opinion: Phenotype-guided biologics have replaced corticosteroid escalation after two decades of research; nevertheless, plateaus in effectiveness, uncertain long-term safety profiles, and exorbitant costs persist. Future progress will depend on value-based pricing that facilitates global adoption, adaptive biomarker-anchored clinical trials, rational combination or bispecific therapeutics, and rigorous post-marketing surveillance of cell-based and microbiome-directed therapies. Delivering sustainable, equitable management of T2HA necessitates the coordination of scientific, regulatory, and economic mechanisms rather than focusing on increasingly narrow cytokine targets.

Keywords: Type 2-high asthma; biologic therapies; cost and accessibility; precision medicine; small-molecule drugs.

Supplementary info

Publication typesExpand

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

Int Forum Allergy Rhinol

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. 2025 Oct 11.

doi: 10.1002/alr.70047. Online ahead of print.

Budesonide Nasal Irrigation: An Effective Alternative Treatment for Allergic Rhinitis

Navarat Kasemsuk [1 2], Dichapong Kanjanawasee [2 3], Premyot Ngaotepprutaram [1 2], Triphoom Suwanwech [1 2], Torpong Thongngam [2 4], Mongkhon Sompornrattanaphan [2 4], Chamard Wongsa [2 4], Tharatham Phonmanee [1 2], Nicha Wiroonpanich [5], Sita Prakairungthong [5], Pattinee Juntrachu [5], Kawita Atipas [1 2], Pongsakorn Tantilipikorn [1 2]

Affiliations Expand

- PMID: 41075281

- DOI: 10.1002/alr.70047

No abstract available

Keywords: allergic rhinitis; budesonide nasal irrigation; intranasal corticosteroid; randomized-controlled trial.

- 5 references

Supplementary info

Grants and fundingExpand

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Ear Nose Throat J

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. 2025 Oct 9:1455613251382759.

doi: 10.1177/01455613251382759. Online ahead of print.

Two-Year Clinical Outcomes After Multipoint Impedance-Controlled Radiofrequency Ablation of the Posterior Nasal Nerve for Treatment of Chronic Rhinitis

David M Yen [1], Greg E Davis [2], Randall A Ow [3], Ellen M O'Malley [4], Anthony G Del Signore [5]

Affiliations Expand

- PMID: 41065547

- DOI: 10.1177/01455613251382759

Free article

Abstract

Objective: A person's quality of life can be deeply impacted by chronic rhinitis. We report 2-year outcomes in patients after treatment using a novel, multipoint, impedance-controlled, radiofrequency ablation device.

Methods: A prospective, multicenter, single-arm clinical study of posterior nasal nerve ablation in adults with chronic rhinitis. Efficacy assessments included the reflective total nasal symptom score (rTNSS), postnasal drip, cough, Eustachian Tube Dysfunction Questionnaire-7 (ETDQ-7), nasal obstruction symptom evaluation (NOSE), and mini-Rhinoconjunctivitis Quality of Life Questionnaire (mini-RQLQ).

Results: Seventy-five of 80 (94%) participants completed 2-year follow-up. Statistically significant improvements were observed in rhinitis symptoms, postnasal drip, cough, ear symptoms, and quality of life as evidenced by the mean change in rTNSS (-4.3), postnasal drip (-0.9), cough (-0.7), ETDQ-7 (-1.1), NOSE (-31.7), and mini-RQLQ (-1.7; $P < .0001$ for all). Allergic and nonallergic rhinitis subgroups demonstrated similar, significant improvement. No serious related adverse events were reported between the 9-month and 2-year follow-ups.

Conclusions: The data demonstrate consistent long-term efficacy and safety of a multipoint, impedance-controlled, radiofrequency ablation device for the treatment of chronic rhinitis. Significant improvements were observed in rhinitis symptoms, postnasal drip, cough, ear symptoms, and quality of life through 2-year follow-up.

Study registration: www.

Clinicaltrials: gov. Unique identifier NCT05591989.

Keywords: ETDQ-7; NOSE; allergic rhinitis; chronic rhinitis; impedance-controlled radiofrequency ablation; mini-RQLQ; nonallergic rhinitis; posterior nasal nerve ablation; quality of life; rTNSS.

Supplementary info

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Clin Otolaryngol

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. 2025 Oct 7.

doi: 10.1111/coa.70040. Online ahead of print.

The Role of Nasal Cytology in the Phenotyping and Monitoring of Chronic Rhinitis in Children

Damla Baysal Bakır [1], Özge Atay [1], Halime Yağmur [1], Gizem Kabadayı [1], Dilek Tezcan [1], Suna Asilsoy [1], Nevin Uzuner [1]

Affiliations Expand

- PMID: 41055895

- DOI: 10.1111/coa.70040

Abstract

Background: Local allergic rhinitis (LAR) is a rhinitis subtype characterised by an IgE-mediated response in the nasal mucosa. Although the nasal provocation test (NPT) is the diagnostic gold standard, it is impractical in many centres. Consequently, patients are often misclassified as having non-allergic rhinitis, delaying appropriate treatment. This study evaluated the role of nasal cytology in the classifying and monitoring paediatric allergic rhinitis (AR), distinguishing probable LAR (pLAR), and guiding treatment.

Methods: This retrospective study analysed data from 255 patients diagnosed with chronic rhinitis between March and June 2024. After applying exclusion criteria (recent allergy treatment, nasal deformities, incomplete records), 48 patients were included and grouped as pLAR (n = 11) or AR (n = 37). Nasal eosinophilia and atopy markers were assessed with clinical symptoms, before and after treatment.

Results: The mean age was 10.5 years (range: 3-17), with 64.6% male. AR was diagnosed in 77% and pLAR in 23%. Asthma was the most common comorbidity (37.5%). Persistent, moderate-severe symptoms were seen in 68.8%, with pollen sensitivity present in 76.3%. After treatment, both VAS scores and nasal eosinophil rates (NEOS%) significantly decreased in both groups ($p < 0.05$). NEOS% was higher in patients with atopic dermatitis and lower in those with adenoidal hypertrophy. AEC and NEOS% were positively correlated ($p < 0.001$), suggesting a link between systemic and local eosinophilia.

Conclusions: Patients with pLAR showed clinical and laboratory improvement similar to AR following treatment. Nasal cytology may be a useful diagnostic and monitoring tool in children with chronic rhinitis.

Keywords: allergic rhinitis; local allergic rhinitis; nasal cytology; paediatric chronic rhinitis.

- 21 references

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4

Review

Ear Nose Throat J

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. 2025 Oct 5:1455613251378726.

doi: 10.1177/01455613251378726. Online ahead of print.

Correlation Between Allergic Rhinitis, Asthma, and Laryngopharyngeal Reflux Disease: A Systematic Review

Baraa Ibrahim Awad [1], Laila Salah Aldokhail [2], Enar Mohammed Alotaibi [2], Hatem Mohammed Asiri [3], Yazeed Abdullah Asery [4], Nawaf Khalid Nahhas [4], Mohammed Halawani [4 5 6]

Affiliations Expand

- PMID: 41046361

- DOI: 10.1177/01455613251378726

Free article

Abstract

Background: Laryngopharyngeal reflux (LPR), allergic rhinitis (AR), and asthma are common airway disorders that often coexist, suggesting shared inflammatory mechanisms. LPR involves gastric reflux into the laryngopharynx, while AR and asthma are linked by the "united airway" hypothesis. Evidence indicates LPR may contribute to AR and asthma exacerbation, yet their interactions remain unclear. Understanding their interaction may enhance clinical outcomes.

Objective: This systematic review aimed to evaluate the associations between LPR, AR, and asthma by analyzing studies that examined these conditions in various patient populations.

Methodology: A comprehensive search of electronic databases, including PubMed, Scopus, and Google Scholar, was conducted for studies published up until 2024. Eligible studies were selected based on predefined inclusion criteria, and data on the prevalence, diagnostic methods, and associations between LPR, AR, and asthma were extracted. This systematic review was conducted and registered in PROSPERO (CRD42024588367). Statistical analysis was performed to determine the strength of the associations between these conditions.

Results: The review identified significant associations between LPR and both AR and asthma. Multiple studies confirmed a positive correlation between LPR and AR, with worse AR symptoms observed in patients with more severe LPR. Additionally, a strong association between LPR and asthma was observed, particularly in patients with poorly-controlled asthma. The analysis also revealed a robust relationship between AR and asthma, consistent with the "united airway" hypothesis, which posits that the upper and lower airways share common inflammatory pathways. These findings suggest that the coexistence of these conditions may exacerbate symptoms and complicate management.

Conclusion: This systematic review highlights the significant associations between LPR, AR, and asthma, emphasizing the importance of recognizing and addressing these comorbidities in clinical practice. The findings suggest that managing 1 condition may have a beneficial effect on the others, supporting a multidisciplinary approach to diagnosis and treatment.

Keywords: airway inflammation; allergic rhinitis; asthma; laryngopharyngeal reflux; systematic review.

chronic cough

Respir Investig

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. 2025 Oct 8;63(6):1246-1249.

doi: 10.1016/j.resinv.2025.08.009. Online ahead of print.

N-acetylcysteine inhalation improved sputum rheology in chronic productive cough: Clinical application in two cases

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Affiliations Expand

- **PMID: 41067161**

- DOI: 10.1016/j.resinv.2025.08.009

Abstract

This pilot study evaluated the effects of inhaled N-acetylcysteine (NAC) on sputum rheology in patients with chronic productive cough (CPC). Rheological measurements before and 30 min after inhalation were compared retrospectively in 16 outpatients receiving either NAC (n = 9) or bromhexine hydrochloride (BXH) (n = 7). NAC inhalation significantly reduced critical strain (γ_c), an indicator of sputum stringiness, from 2370 [1310-4390] % to 643 [389-700] % (median and interquartile range), with a significantly greater effect than BXH. This reduction was observed regardless of airway fungal colonization. In addition, two case reports, a 67-year-old man with bronchorrhea and a 79-year-old woman with refractory asthma, demonstrated improved quality-of-life scores evaluated with the Cough and Sputum Assessment Questionnaire (CASA-Q) and rheological improvement following 1-2 weeks of twice-daily NAC inhalation. These findings suggest that nebulized NAC may be a promising add-on therapy for refractory airway diseases characterized by high sputum stringiness (γ_c).

Keywords: Bromhexine hydrochloride; Chronic productive cough; Critical strain; N-acetylcysteine inhalation; Sputum rheology.

Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest.

Cite

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BMC Pulm Med

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. 2025 Oct 8;25(1):458.

doi: 10.1186/s12890-025-03941-1.

Impulse oscillometry for the detection of small airway dysfunction in patients with chronic respiratory symptoms, preserved ratio impaired spirometry and COPD

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Affiliations Expand

- **PMID: 41063069**

- **PMCID: PMC12505595**

- **DOI: 10.1186/s12890-025-03941-1**

Abstract

Background: Persistent chronic airway inflammation and progressive airflow limitation are typical features of chronic obstructive pulmonary disease (COPD). Emerging evidence indicates that small airway dysfunction (SAD) plays a critical role in driving the sustained pathological progression of COPD. Preserved ratio impaired spirometry (PRISm) represents a spirometric pattern characterized by a reduced forced expiratory volume in 1 second (FEV_1) despite a preserved ratio. Current evidence inadequately elucidates the pathophysiological role of SAD and its intricate interplay with PRISm and COPD progression. On the other hand, impulse oscillometry (IOS) can be used as a complementary tool to spirometry to detect SAD. Detection of SAD in patients with chronic respiratory symptoms could help in the diagnosis of PRISm and COPD when spirometry is not achievable.

Objective: To investigate the diagnostic value of IOS for identifying SAD in patients with chronic respiratory symptoms, PRISm and COPD.

Methods: Between September 2021 and July 2023, 552 symptomatic patients without known structural lung disease who underwent both spirometry and IOS on the same day in the outpatient clinic were evaluated. The correlations between spirometry and the IOS parameters, and the ROC curves of the IOS parameters for SAD patients and COPD patients were analyzed.

Results: Among the 552 patients included in the study, 96 patients had COPD, 39 patients had PRISm, and 417 patients had chronic cough. Among 456 chronic cough patients with preserved ratio spirometry, the incidence of PRISm was 8.55%. Based on spirometry-defined SAD, the incidence of SAD in the PRISm population was 71.8%, which was significantly higher than the 9.35% of the non-PRISm population. With increasing COPD GOLD stage, the IOS parameters R5-R20, R5, Fres, and Ax increased, whereas the traditional lung function parameters and X5 decreased. R5-R20, X5, Fres, and AX of COPD GOLD stage 1 patients were not substantially different from those of PRISm patients. In PRISm patients, R5-R20, R5 and Fres were strongly correlated with $FEF_{25\%-75\%}$. R5-R20, R5, X5, Fres and AX were significantly associated with FEV_1, FEV_1/FVC, FEV_1% predicted, $FEF_{50\%}$, $FEF_{75\%}$ and $FEF_{25\%-75\%}$ in COPD patients. Through ROC curve analysis, the cutoffs for identifying SAD in patients with chronic respiratory symptoms and PRISm patients were obtained, with R5-R20 values of 0.075 and 0.105 kPa/L/s, respectively. The values of R5 were 0.365 and 0.375 kPa/L/s, respectively. The Fres values are 16.31 Hz and 17.11 Hz, respectively. The cutoff for detecting COPD in all patients was 0.485 kPa/L/s for R5, 0.125 kPa/L/s for R5-R20, -0.155 kPa/L/s for X5, and 17.98 Hz for Fres. Fres had the highest AUC value for both SAD and COPD detection, and it detected COPD the most in all patients, with a prevalence of 24.1%. R5 detected SAD the

most in patients with chronic respiratory symptoms, with a prevalence of 47.5%. With a prevalence of 71.8%, spirometry identified SAD in patients with PRISm the most frequently.

Conclusion: Almost all IOS parameters Linked to the small airways were significantly different in the PRISm population compared with patients with chronic respiratory symptoms. SAD severity in PRISm patients is similar to that in GOLD stage 2 COPD patients. The IOS can assess the disease severity of COPD.

Keywords: COPD; Impulse oscillometry; Preserved ratio impaired spirometry (PRISm); Small airway dysfunction (SAD); Spirometry.

Conflict of interest statement

Declarations. Ethics approval and consent to participate: The study involving human participants was approved by the Ethics Committee of Shaoxing People's Hospital in accordance with the Declaration of Helsinki. All patients signed informed consent to participate in this study, and all personal information was de-identified before further analyses. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests. Clinical trial number: Not applicable.

- 28 references
- 5 figures

Supplementary info

MeSH termsExpand

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Minerva Med

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. 2025 Oct 7.

doi: 10.23736/S0026-4806.25.09808-8. Online ahead of print.

Amoxicillin/clavulanate as a cornerstone of antibiotic stewardship: integrating WHO AWaRe principles, Italian recommendations, and evidence-based practice

Roberto Mattina [1], Francesco Scaglione [2]

Affiliations Expand

- PMID: 41054784

- DOI: 10.23736/S0026-4806.25.09808-8

Abstract

Antimicrobial resistance (AMR) remains a critical global health concern, largely driven by inappropriate antibiotic use. To address this challenge, the World Health Organization (WHO) developed the AWaRe (Access, Watch, Reserve) classification, prioritizing the use of Access antibiotics - narrow-spectrum agents with proven efficacy and low resistance potential. Amoxicillin/clavulanate, included in the Access group, is widely endorsed in international and national guidelines, as a first-line option for common community-acquired infections. This Expert Opinion reviews the positioning of amoxicillin/clavulanate within stewardship frameworks, synthesizing its pharmacological characteristics, clinical evidence, and relevance in both Italian and global contexts. The combination of amoxicillin with the β-lactamase inhibitor clavulanic acid provides broad activity against key respiratory pathogens such as Haemophilus influenzae, and Moraxella catarrhalis, including β-lactamase-producing strains. Evidence from randomized controlled trials and meta-analyses demonstrates high bacteriological eradication and clinical cure rates across acute bacterial rhinosinusitis, otitis media, community-acquired pneumonia, and chronic bronchitis exacerbations. In pediatric populations, amoxicillin/clavulanate has shown significant efficacy in protracted bacterial bronchitis and chronic wet cough. Comparative data confirm its equivalence or superiority to macrolides and fluoroquinolones while maintaining a lower resistance selection potential and favorable tolerability. The integration of WHO AWaRe targets, Italian stewardship recommendations, and robust clinical evidence underscores the central role of amoxicillin/clavulanate in rational antibiotic prescribing. Its stewardship-aligned use - emphasizing short-course therapy, targeted prescribing, and avoidance in viral syndromes - represents a pragmatic and evidence-based strategy to optimize treatment outcomes while contributing to AMR mitigation in both national and global contexts.

. 2025 Oct 6.

doi: 10.1002/lary.70011. Online ahead of print.

Prospective Study of Long-Term Outcomes and the Patient Experience With Superior Laryngeal Nerve Block for Chronic Cough

Andrew T Peachman [1], Zachary T Root [2], Mohammad Bilal Alsavaf [2], Brandon Kim [3], Brad W deSilva [2], Laura Matrka [2]

Affiliations Expand

- PMID: 41053966

- DOI: 10.1002/lary.70011

Abstract

Objective: To characterize long-term response rates to the superior laryngeal nerve (SLN) block in a prospective fashion. Secondary objectives are to provide objective data to answer common pre-procedural questions and to identify factors that predict injection outcomes.

Methods: Prospective study from April 2021 to August 2024 of adult patients with refractory chronic cough undergoing SLN block. Response was measured via a yes/no question about improvement, cough severity index (CSI), and a 1-10 Likert scale grading cough impact on quality of life (QoL) taken at baseline, 2 weeks, and 6-9 months post-injection.

Results: One hundredtwenty-two patients were injected for cough, representing 249 injections. At 2 weeks after injection, 63.1% endorsed improvement on yes/no questioning ("initial improvers"), with significant improvement in both CSI and QoL scores ($p < 0.001$ for each). Of the initial improvers, 53.2% reported ongoing symptom improvement at long-term follow-up (6-9 months). Improvement occurred at an average of 4.3 days after injection and averaged 4.1 months in duration. 72.1% of improvers reported their degree of improvement as "a lot" or "completely." Side effects occurred in 44.2% of injections and were typically mild. No cough feature or clinical factor significantly predicted a positive response to the SLN block.

Conclusion: This prospective assessment indicates that nearly 2 in 3 refractory chronic cough patients respond positively to SLN block, with ~50% of these initial improvers endorsing ongoing improvement at long-term follow-up. Average duration of benefit is 4 months, and side effects are common. Predictive factors of a positive response to SLN block remain undefined.

Keywords: chronic cough; cranial neuropathy; intractable cough; irritable larynx syndrome; laryngeal hypersensitivity syndrome; laryngeal sensory neuropathy; neurogenic cough; neuropathic cough; refractory cough; superior laryngeal nerve block.

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

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Chest

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. 2025 Oct 9:S0012-3692(25)05493-5.

doi: 10.1016/j.chest.2025.09.122. Online ahead of print.

Research Letter: The Association Between Incident Nontuberculous Mycobacteria Isolation and Antibiotic Exposure in Patients with Bronchiectasis

Meghan Marmor [1], Amanda E Brunton [2], David Fraulino [3], Stephen J Ruoss [4], Emily Henkle [5], B Shoshana Zha [6], Mark Metersky [3], Kevin Winthrop [5]; Bronchiectasis and NTM Research Registry Investigators

Affiliations Expand

- PMID: 41076063

- DOI: 10.1016/j.chest.2025.09.122

No abstract available

Full text links

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Randomized Controlled Trial

BMJ Open Respir Res

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. 2025 Oct 10;12(1):e003615.

doi: 10.1136/bmjresp-2025-003615.

Sputum colour charts to guide antibiotic self-treatment of acute exacerbation of chronic obstructive pulmonary disease: the Colour-COPD RCT

Eleni Gkini [1], Joshua De Soyza [2], Daniella A Spittle [3], Paul Robert Ellis [4], Sarah Tearne [1], Peymane Adab [4], Rachel Jordan [4], Nawar Diar Bakerly [5 6], Alice Margaret Turner [7]

Affiliations Expand

- PMID: 41073133

- DOI: 10.1136/bmjresp-2025-003615

Abstract

Background: Chronic obstructive pulmonary disease (COPD) patients are encouraged to manage exacerbations (acute exacerbation of COPD (AECOPD)) through self-management (SM) plans. Since only around half of AECOPD are bacterial, and sputum colour correlates with bacterial load, it may help guide antibiotic use. This pragmatic randomised controlled trial (RCT) assessed the safety and effectiveness of using a sputum colour chart in UK primary care.

Methods: The multicentre RCT, Colour COPD randomised COPD adults who had ≥2 AECOPD or ≥1 AECOPD hospital admission in the preceding year. The primary objective was to assess the non-inferiority of the Bronkotest sputum colour chart compared with usual care, with hospital admission for AECOPD at 12 months as the primary outcome. Secondary outcomes included second courses of treatment requirement and quality of life (CAT score). Nested substudies examined daily symptoms via e-diaries and sputum culture.

Results: 115 severe COPD patients (global obstructive lung disease(GOLD) D, 54% Medical Research Council (MRC) 4 or 5, CAT score 24) were randomised. A trend towards more hospital admissions (32% vs 16%, relative risk (RR) 1.95 (0.92-4.18)) and increased antibiotic use within 14 days (34% vs 18%, adjusted relative risk (aRR) 1.80 (0.85-3.79)) was seen in the colour chart group. From 38 sputum substudy patients, 57 samples were received (42 stable, 15 during AECOPD), with 30% containing potentially pathogenic bacterium (PPB). Purulent sputum was more frequent in bronchiectasis, independent of disease state (stable vs exacerbation) or PPB presence, suggesting sputum colour alone does not reliably guide antibiotic use.

Conclusion: Under-recruitment precluded definitive conclusions. However, sputum colour is unlikely to be a useful addition to COPD SM in primary care.

Trial registration number: The UK's Clinical Study Registry: ISRCTN14955629 (https://doi.org/10.1186/ISRCTN14955629; registration date: 11 Number 2020).

Keywords: COPD Exacerbations; Pulmonary Disease, Chronic Obstructive.

Conflict of interest statement

Competing interests: AMT was funded via her institution from the NIHR HTA for the studies described in this report. She has also received funding to attend conferences from Boehringer Ingelheim and AstraZeneca, honoraria for talks or advisory boards about COPD from AstraZeneca and GlaxoSmithKline and via her Institution has received grants for work in COPD from AstraZeneca, Chiesi and GlaxoSmithKline. She was on the NIHR HTA prioritisation committee B 01/03/2020-31/03/2024. EG was funded via her institution from the NIHR HTA for work described in this report. ST was funded via her institution from the NIHR HTA for work described in this report. PA was funded via her institution from the NIHR HTA for work described in this report. RJ was funded via his institution from the NIHR HTA for work described in this report. DAS was funded via her institution from the NIHR HTA for work described in this report. PRE was funded by the University of Birmingham and University Hospitals Birmingham, for his role as an academic clinical lecturer, during which he conducted work described in this report. All other authors have no competing interest to declare.

Supplementary info

Publication types, MeSH terms, SubstancesExpand

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Am J Respir Crit Care Med

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. 2025 Oct 6.

doi: 10.1164/rccm.202508-2056VP. Online ahead of print.

Positioning Dipeptidyl Peptidase-1 Inhibitors in Bronchiectasis: No Drug Is an Island

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Affiliations Expand

- PMID: 41052432

- DOI: 10.1164/rccm.202508-2056VP

No abstract available

Keywords: DPP-1 inhibitors; brensocatib; bronchiectasis; neutrophilic inflammation; precision medicine.

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Clin Pharmacokinet

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. 2025 Oct 6.

doi: 10.1007/s40262-025-01575-4. Online ahead of print.

Spatial Pharmacokinetic and Pharmacodynamic Modeling in Airway Mucus

Yuchen Guo [1], Jinqiu Yin [1], Sirin Yonucu [1], Catherijne A J Knibbe [1 2], Tingjie Guo [1], J G Coen van Hasselt [3]

Affiliations Expand

- PMID: 41047457

- DOI: 10.1007/s40262-025-01575-4

Abstract

Background and objectives: Diseases such as cystic fibrosis (CF) and non-CF bronchiectasis can cause extensive mucus formation in the lung, which may affect drug distribution and effects. As such, quantitative understanding of drug distribution in mucus may guide treatment optimization. Here, we aimed to develop a modeling framework to evaluate spatial distribution of drugs in mucus with CF as a proof of concept. In a case study, we demonstrated how spatial PK models can be used to predict spatial antimicrobial pharmacodynamics (PD).

Methods: A spatial pharmacokinetic (PK) model in mucus was developed using discretized partial differential equations. Hypothetical drugs with realistic ranges for molecule/particle size (radius, r), mucin binding affinity, and half-lives were used to evaluate the impact of drug-specific factors on spatial distribution in mucus. Mucin concentration and muco-ciliary clearance were evaluated as biological system-specific factors. We then demonstrated how the spatial PK model can be used to predict antimicrobial drug effects of imipenem against the pathogen Pseudomonas aeruginosa in mucus.

Results: Under intravenous PK profiles, molecular/particle size (r) was found to play a dominant role in mucus drug diffusion, while drug-mucin interactions and muco-ciliary clearance showed a minor impact. Small molecule drugs (r <1 nm) could readily penetrate mucus, whereas large molecules or particles (r >20 nm) showed differential spatial drug distribution. Our case study demonstrates that baseline spatial bacterial organization can impact the treatment outcome of imipenem against mucus-associated infections.

Conclusion: The developed spatial PK modeling framework enabled quantitative description of the spatial distribution of drugs in airway mucus and can be of relevance to guide optimization of treatment strategies.

Conflict of interest statement

Declarations. Conflict of Interest: Yuchen Guo, Jinqiu Yin, Sirin Yonucu, Catherijne A.J. Knibbe, Tingjie Guo and Coen van Hasselt declare that they have no potential conflicts of interest that might be relevant to the contents of this manuscript. Catherijne A. J. Knibbe is an Editorial Board member of Clinical Pharmacokinetics. Catherijne A. J. Knibbe was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Data Availability: Data sharing is not applicable to this article as no datasets are associated with this study. Ethics Approval: Not applicable. Code Availability: The code used in this study is available via the GitHub repository https://github.com/vanhasseltlab/spatialPK.git . Authors' Contributions: Conceptualization: J.G. Coen van Hasselt, Jinqiu Yin, Tingjie Guo; Methodology: Yuchen Guo, Tingjie Guo, Sirin Yonucu; Formal analysis and investigation: Yuchen Guo, Tingjie Guo; Writing – original draft preparation: Yuchen Guo; Writing – review and editing: Yuchen Guo, Catherijne A.J. Knibbe, Tingjie Guo, J.G. Coen van Hasselt; Funding acquisition: J.G. Coen van Hasselt; Supervision: J.G. Coen van Hasselt, Tingjie Guo.

- **64 references**

Editorial

Thorax

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. 2025 Oct 5:thorax-2025-224029.

doi: 10.1136/thorax-2025-224029. Online ahead of print.

Lung Research Grand Challenges: transforming respiratory research

Ellen J Forty [1], Samantha M Walker [2], Eric W F W Alton [3], Ian P Hall [4]

Affiliations Expand

- **PMID: 41047238**

- **DOI: 10.1136/thorax-2025-224029**

No abstract available

Keywords: Asthma; Bronchiectasis; COPD Pathology; Cystic Fibrosis; Idiopathic pulmonary fibrosis; Paediatric Lung Disaese; Respiratory Function Tests; Symptom Flare Up.

Conflict of interest statement

Competing interests: EA: royalties or licenses: royalties from Boehringer Ingelheim related to cystic fibrosis gene therapy programme. Consulting fees: Boehringer Ingelheim—payments made to EA and institution; AlveoGene—payments made to EA. Patents planned, issued or pending: multiple patents filed by Imperial College. Participation on a Data Safety Monitoring Board or Advisory Board: Boehringer Ingelheim Advisory Board—payments made to EA Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid. Founder Director, AlveoGene Stock or stock options AlveoGene shares. SW: leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid co-chair of Lung Research and Innovation Group (LRIG). IH: grants or contracts from any entity. NIHR Senior Investigator Award—research grant to institution. Support for attending meetings and/or travel: travel to AUKCAR meeting in Reading, 2024—Expenses covered by Asthma + Lung UK. Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid: co-chair of Lung Research and Innovation Group (LRIG). Consulting fees: advisory board for GSK.

Supplementary info

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JAMA

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. 2025 Oct 7;334(13):1210.

doi: 10.1001/jama.2025.11485.

What Is Bronchiectasis?

Kristin L Walter [1]

Affiliations Expand

- PMID: 40773212

- DOI: 10.1001/jama.2025.11485

No abstract available

Plain language summary

This JAMA Patient Page describes bronchiectasis symptoms, risk factors, diagnosis, and treatments.

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