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

1

Editorial

COPD

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. 2024 Dec;21(1):2358097.

doi: 10.1080/15412555.2024.2358097. Epub 2024 May 28.

## [Proposal for a 4-Level Classification System of Severe COPD Exacerbation According to Healthcare Resource Utilization](#)

[Georgios Hillas](#)<sup>1</sup>, [Stelios Loukides](#)<sup>2</sup>, [Athena Gogali](#)<sup>3</sup>, [Konstantinos Kostikas](#)<sup>3</sup>

Affiliations expand

- PMID: 38807506

- DOI: [10.1080/15412555.2024.2358097](https://doi.org/10.1080/15412555.2024.2358097)

*No abstract available*

SUPPLEMENTARY INFO

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Clin Chest Med

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. 2024 Jun;45(2):461-473.

doi: [10.1016/j.ccm.2023.08.016](https://doi.org/10.1016/j.ccm.2023.08.016). Epub 2023 Sep 15.

# Smoking-Related Interstitial Lung Disease and Emphysema

[Joanna G Escalon](#)<sup>1</sup>, [Francis Girvin](#)<sup>2</sup>

Affiliations expand

- PMID: 38816100
- DOI: [10.1016/j.ccm.2023.08.016](https://doi.org/10.1016/j.ccm.2023.08.016)

## Abstract

Diagnosis and treatment of patients with smoking-related lung diseases often requires multidisciplinary contributions to optimize care. Imaging plays a key role in characterizing the underlying disease, quantifying its severity, identifying potential complications, and directing management. The primary goal of this article is to provide an overview of the imaging findings and distinguishing features of smoking-related lung diseases, specifically, emphysema/chronic obstructive pulmonary disease, respiratory bronchiolitis-interstitial lung disease, smoking-related interstitial fibrosis, desquamative interstitial pneumonitis, combined pulmonary fibrosis and emphysema, pulmonary Langerhans cell histiocytosis, and E-cigarette or vaping related lung injury.

**Keywords:** Combined pulmonary fibrosis and emphysema; Computed tomography; Desquamative interstitial pneumonia; Emphysema; Interstitial lung disease; Langerhans cell histiocytosis; Smoking; Smoking-related interstitial fibrosis.

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## Conflict of interest statement

Disclosure The authors have nothing to disclose.

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. 2024 Apr 29:10:100281.

doi: 10.1016/j.bjao.2024.100281. eCollection 2024 Jun.

# Effects of a lower versus a higher oxygenation target in intensive care unit patients with chronic obstructive pulmonary disease and acute hypoxaemic respiratory failure: a subgroup analysis of a randomised clinical trial

[Maria B Nielsen](#)<sup>1,2</sup>, [Thomas L Klitgaard](#)<sup>1</sup>, [Ulla M Weinreich](#)<sup>2,3,4</sup>, [Frederik M Nielsen](#)<sup>1,2</sup>, [Anders Perner](#)<sup>5,6</sup>, [Olav L Schjørring](#)<sup>1,2</sup>, [Bodil S Rasmussen](#)<sup>1,2</sup>

Affiliations expand

- PMID: 38711834
- PMCID: [PMC11070685](#)
- DOI: [10.1016/j.bjao.2024.100281](#)

## Abstract

**Background:** Oxygen supplementation is ubiquitous in intensive care unit (ICU) patients with chronic obstructive pulmonary disease (COPD) and acute hypoxaemia, but the optimal oxygenation target has not been established.

**Methods:** This was a pre-planned subgroup analysis of the Handling Oxygenation Targets in the ICU (HOT-ICU) trial, which allocated patients with acute hypoxaemia to a lower oxygenation target (partial pressure of arterial oxygen [ $P_{aO_2}$ ] of 8 kPa) vs a higher target ( $P_{aO_2}$  of 12 kPa) during ICU admission, for up to 90 days; the allocation was stratified for presence or absence of COPD. Here, we report key outcomes for patients with COPD.

**Results:** The HOT-ICU trial enrolled 2928 patients of whom 563 had COPD; 277 were allocated to the lower and 286 to the higher oxygenation group. After allocation, the median  $P_{aO_2}$  was 9.1 kPa (inter-quartile range 8.7-9.9) in the lower group vs 12.1 kPa (11.2-12.9) in the higher group. Data for arterial carbon dioxide ( $P_{aCO_2}$ ) were available for 497 patients (88%) with no between-group difference in time-weighted average;

median  $Paco_2$  6.0 kPa (5.2-7.2) in the lower group vs 6.2 kPa (5.4-7.3) in the higher group. At 90 days, 122/277 patients (44%) in the lower oxygenation group had died vs 132/285 patients (46%) in the higher (relative risk 0.98; 95% confidence interval 0.82-1.17;  $P=0.67$ ). No statistically significant differences were found in any secondary outcome.

**Conclusions:** In ICU patients with COPD and acute hypoxaemia, a lower vs a higher oxygenation target did not reduce mortality. There were no between-group differences in  $Paco_2$  or in secondary outcomes.

**Clinical trial registration:** [NCT03174002](#), EudraCT number 2017-000632-34.

**Keywords:** chronic obstructive pulmonary disease; critical care; hyperoxia; hypoxia; intensive care units; oxygen inhalation therapy.

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- [27 references](#)
- [3 figures](#)

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[Review](#)

Sleep Med Clin

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. 2024 Jun;19(2):371-378.

doi: 10.1016/j.jsmc.2024.02.013.

# Dyspnea and Quality of Life Improvements with Management of Comorbid Obstructive Sleep Apnea in Chronic Lung Disease

[Kori Ascher](#)<sup>1</sup>, [Shirin Shafazand](#)<sup>2</sup>

Affiliations expand

- PMID: 38692759
- DOI: [10.1016/j.jsmc.2024.02.013](https://doi.org/10.1016/j.jsmc.2024.02.013)

## Abstract

Obstructive sleep apnea (OSA) has emerged as a significant and prevalent comorbidity associated with chronic lung diseases, including chronic obstructive pulmonary disease, asthma, and interstitial lung diseases. These overlap syndromes are associated with worse patient-reported outcomes (sleep quality, quality of life measures, mental health) than each condition independently. Observational studies suggest that patients with overlap syndrome who are adherent to positive airway pressure therapy report improved quality of life, sleep quality, depression, and daytime symptoms. Screening for and management of OSA in patients with overlap syndrome should emphasize the interconnected nature of these 2 conditions and the positive impact that OSA management can have on patients' well-being and overall health.

**Keywords:** Asthma; COPD; Health-related quality of life; Interstitial lung disease; OSA; Overlap syndrome; Patient-reported health outcomes; Positive airway pressure therapy.

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Sleep Med Clin



. 2024 Jun;19(2):357-369.

doi: 10.1016/j.jsmc.2024.02.014. Epub 2024 Mar 15.

# Targeting Hypercapnia in Chronic Lung Disease and Obesity Hypoventilation: Benefits and Challenges

[Lee K Brown](#)<sup>1</sup>

Affiliations expand

- PMID: 38692758
- DOI: [10.1016/j.jsmc.2024.02.014](https://doi.org/10.1016/j.jsmc.2024.02.014)

## Abstract

Hypoventilation is a complication that is not uncommon in chronic obstructive pulmonary disease and calls for both medical treatment of the underlying disease and, frequently, noninvasive ventilation either during exacerbations requiring hospitalization or in a chronic state in the patient at home. Obesity hypoventilation syndrome by definition is associated with ventilatory failure and hypercapnia. It may or may not be accompanied by obstructive sleep apnea, which when detected becomes an additional target for positive airway pressure treatment. Intensive research has not completely resolved the best choice of treatment, and the simplest modality, continuous positive airway pressure, may still be entertained.

**Keywords:** Continuous positive airway pressure; Hypercapnia; Noninvasive ventilation; Obesity hypoventilation syndrome; Pulmonary Disease, Chronic Obstructive; Respiratory insufficiency; Sleep apnea.

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## Conflict of interest statement

Disclosure Dr L.K. Brown coedits the Sleep and Respiratory Neurobiology section of Current Opinion in Pulmonary Medicine and is a coauthor of an article on positive airway pressure treatment for OSA in UpToDate. Dr L.K. Brown is a member of the Council of the New Mexico Medical Society and serves on the Board of Trustees of the Greater Albuquerque Medical Association. He chairs the Polysomnography Practice Advisory Committee of the New Mexico Medical Board and chairs the New Mexico Advisory Board for Respiratory Care. Dr L.K. Brown chairs the Board of Directors of GAMA-PAC, the political action committee of the Greater Albuquerque Medical Association.

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[Review](#)

Sleep Med Clin

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. 2024 Jun;19(2):275-282.

doi: 10.1016/j.jsmc.2024.02.007. Epub 2024 Mar 5.

# Obstructive Sleep Apnea Effects on Chronic Airway Disease Exacerbations – Missed Opportunities for Improving Outcomes in Chronic Obstructive Pulmonary Disease and Asthma

[Marta Marin-Oto<sup>1</sup>](#), [Jose M Marin<sup>2</sup>](#)

Affiliations expand

- PMID: 38692752
- DOI: [10.1016/j.jsmc.2024.02.007](https://doi.org/10.1016/j.jsmc.2024.02.007)

## Abstract

In patients with chronic obstructive pulmonary disease (COPD) and asthma, exacerbations determine the natural history of both diseases. Patients with both respiratory diseases who suffer from obstructive sleep apnea (OSA) as a comorbidity (overlap syndromes) have a higher risk of exacerbations and hospitalization. In cases of OSA/COPD and OSA/asthma, continuous positive airway pressure treatment is indicated. Adequate adherence to therapy appears to reduce exacerbations and their severity, especially in OSA/COPD overlap. However, there is a lack of randomized trials that definitively demonstrate this evidence.

**Keywords:** Asthma; Asthma exacerbation; Chronic obstructive pulmonary disease; Chronic obstructive pulmonary disease exacerbation; Obstructive sleep apnea; Overlap syndrome; Sleep.

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## Conflict of interest statement

Disclosure Both authors report no conflicts of interest.

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Sleep Med Clin

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. 2024 Jun;19(2):253-260.

doi: 10.1016/j.jsmc.2024.02.005. Epub 2024 Mar 12.

# [Does Obstructive Sleep Apnea Lead to Progression of Chronic Obstructive Pulmonary Disease](#)

[Walter T McNicholas](#)<sup>1</sup>

Affiliations expand

- PMID: 38692750
- DOI: [10.1016/j.jsmc.2024.02.005](https://doi.org/10.1016/j.jsmc.2024.02.005)

## Abstract

Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) have important bidirectional relationships that influence the pathophysiology of each disorder. The slim hyperinflated "pink puffer" phenotype of COPD protects against OSA, whereas the heavier "blue bloater" phenotype predisposes to OSA by fluid retention. OSA may aggravate COPD by promoting airway inflammation. COPD-OSA overlap patients have lower quality of life and are at higher risk of cardiovascular comorbidity than either

disorder alone due to greater nocturnal oxygen desaturation and sympathetic activation. Management of OSA with positive airway pressure improves COPD outcomes that include lower exacerbation rates compared to untreated patients.

**Keywords:** Cardiovascular comorbidity; Chronic obstructive pulmonary disease; Obstructive sleep apnea; Outcomes; Overlap syndrome; Sleep disorders.

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## Conflict of interest statement

Disclosure The author has nothing to disclose.

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. 2024 Jun;19(2):239-251.

doi: 10.1016/j.jsmc.2024.02.004. Epub 2024 Mar 12.

# Chronic Cough and Obstructive Sleep Apnea

[Krishna M Sundar](#)<sup>1</sup>, [Amanda Carole Stark](#)<sup>2</sup>, [Peter Dicpinigaitis](#)<sup>3</sup>

Affiliations expand

- PMID: 38692749
- DOI: [10.1016/j.jsmc.2024.02.004](https://doi.org/10.1016/j.jsmc.2024.02.004)

## Abstract

Chronic cough, defined as a cough lasting more than 8 weeks, is a common medical condition occurring in 5% to 10% of the population. Its overlap with another highly prevalent disorder, obstructive sleep apnea (OSA), is therefore not surprising. The relationship between chronic cough and OSA extends beyond this overlap with higher prevalence of OSA in patients with chronic cough than in the general population. The use of continuous positive airway pressure can result in improvement in chronic cough although further studies are needed to understand which patients will experience benefit in their cough from the treatment of comorbid OSA.

**Keywords:** Cough; Cough hypersensitivity syndrome; Gastroesophageal reflux; Obstructive; Sleep apnea.

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## Conflict of interest statement

Disclosures K.M. Sundar has served as consultant in the past for Merck Inc. He is a cofounder of Hypnoscore LLC (software for population management of sleep apnea) in conjunction with the University of Utah Technology Commercialization Office. A.C. Stark has no conflicts to disclose. P. Dicipinigaitis serves as a consultant to Bellus, Chiesi, GSK, Merck, Trevi.

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Sleep Med Clin



. 2024 Jun;19(2):219-228.

doi: 10.1016/j.jsmc.2024.02.002. Epub 2024 Mar 7.

# Effects of Obstructive Sleep Apnea on Airway Immunity and Susceptibility to Respiratory Infections

[Samuel Epstein](#)<sup>1</sup>, [Dale Jun](#)<sup>1</sup>, [Jane C Deng](#)<sup>2</sup>, [Michelle Zeidler](#)<sup>3</sup>

Affiliations expand

- PMID: 38692747
- DOI: [10.1016/j.jsmc.2024.02.002](https://doi.org/10.1016/j.jsmc.2024.02.002)

## Abstract

Obstructive sleep apnea is a prevalent sleep disorder characterized by recurrent episodes of partial or complete upper airway collapse during sleep, leading to disrupted breathing patterns and intermittent hypoxia. OSA results in systemic inflammation but also directly affects the upper and lower airways leading to upregulation of inflammatory pathways and alterations of the local microbiome. These changes result in increased susceptibility to respiratory infections such as influenza, COVID-19, and bacterial pneumonia. This relationship is more complex and bidirectional in individuals with chronic lung disease such as chronic obstructive lung disease, interstitial lung disease and bronchiectasis.

**Keywords:** Airway immunity; Airway inflammation; Intermittent hypoxia; Lower airway; Obstructive sleep apnea; Respiratory infection; Upper airway.

Published by Elsevier Inc.

# Conflict of interest statement

Disclosure The authors have no disclosures.

SUPPLEMENTARY INFO

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Sleep Med Clin



. 2024 Jun;19(2):211-218.

doi: 10.1016/j.jsmc.2024.02.001. Epub 2024 Mar 8.

## [Mechanical Interactions Between the Upper Airway and the Lungs that Affect the Propensity to Obstructive Sleep Apnea in Health and Chronic Lung Disease](#)

[Bernie Y Sunwoo](#)<sup>1</sup>, [Atul Malhotra](#)<sup>2</sup>

Affiliations expand

- PMID: 38692746
- DOI: [10.1016/j.jsmc.2024.02.001](https://doi.org/10.1016/j.jsmc.2024.02.001)

## Abstract

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive narrowing and collapse of the upper airways during sleep. It is caused by multiple anatomic and nonanatomic factors but end-expiratory lung volume (EELV) is an important factor as increased EELV can stabilize the upper airway via caudal traction forces. EELV is impacted by changes in sleep stages, body position, weight, and chronic lung diseases, and this article reviews the mechanical interactions between the lungs and upper airway that affect the propensity to OSA. In doing so, it highlights the need for additional research in this area.

**Keywords:** Chronic lung disease; End-expiratory lung volume; Obstructive sleep apnea; Overlap syndrome; Pharyngeal critical closing pressure.

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Editorial

Lung

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. 2024 Jun;202(3):233-234.

doi: 10.1007/s00408-024-00693-3. Epub 2024 Apr 27.

# Elastolysis in COPD: a Target for Therapy

[Gerard M Turino](#)<sup>1</sup>, [Jerome O Cantor](#)<sup>2</sup>

Affiliations expand

- PMID: 38676772
- DOI: [10.1007/s00408-024-00693-3](https://doi.org/10.1007/s00408-024-00693-3)

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- [18 references](#)

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Adv Ther

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. 2024 Jun;41(6):2151-2167.

# Implications of Cardiopulmonary Risk for the Management of COPD: A Narrative Review

[Dave Singh](#)<sup>1</sup>, [MeiLan K Han](#)<sup>2</sup>, [Nathaniel M Hawkins](#)<sup>3</sup>, [John R Hurst](#)<sup>4</sup>, [Janwillem W H Kocks](#)<sup>5,6,7,8</sup>, [Neil Skolnik](#)<sup>9</sup>, [Daiana Stolz](#)<sup>10</sup>, [Jad El Khoury](#)<sup>11</sup>, [Chris P Gale](#)<sup>12,13,14</sup>

Affiliations expand

- PMID: 38664329
- PMCID: [PMC11133105](#)
- DOI: [10.1007/s12325-024-02855-4](#)

## Abstract

Chronic obstructive pulmonary disease (COPD) constitutes a major global health burden and is the third leading cause of death worldwide. A high proportion of patients with COPD have cardiovascular disease, but there is also evidence that COPD is a risk factor for adverse outcomes in cardiovascular disease. Patients with COPD frequently die of respiratory and cardiovascular causes, yet the identification and management of cardiopulmonary risk remain suboptimal owing to limited awareness and clinical intervention. Acute exacerbations punctuate the progression of COPD in many patients, reducing lung function and increasing the risk of subsequent exacerbations and cardiovascular events that may lead to early death. This narrative review defines and summarises the principles of COPD-associated cardiopulmonary risk, and examines respiratory interventions currently available to modify this risk, as well as providing expert opinion on future approaches to addressing cardiopulmonary risk.

**Keywords:** Cardiopulmonary risk; Cardiovascular disease; Chronic obstructive pulmonary disease; Exacerbation; Inhaled therapy; Mortality.

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## Conflict of interest statement

Dave Singh has received consultancy fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, EpiEndo, Genentech, GlaxoSmithKline, Glenmark, Gossamer Bio, Kinaset Therapeutics, Menarini, Novartis, Orion, Pulmatrix, Sanofi, Teva, Theravance Biopharma and Verona Pharma. MeiLan K. Han reports personal fees from Aerogen, Altesa BioPharma, Amgen, Apreo Health, AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, DevPro, Genentech, GlaxoSmithKline, Integrity, Novartis, Teva, MDBriefCase, Medscape, Medwiz, Merck, Mylan, NACE, Polarian, Pulmonx, Regeneron, Roche, RS BioTherapeutics, Sanofi, UpToDate and Verona Pharma; has received either in-kind research support or funds paid to the institution from the American Lung Association, AstraZeneca, Biodesix, Boehringer Ingelheim, the COPD Foundation, Gala Therapeutics, the National Institutes of Health, Novartis, Nuaira, Sanofi and Sunovion; has participated in data safety monitoring boards for Medtronic and Novartis with funds paid to the institution; and has received stock options from Altesa BioPharma and Meissa Vaccines. Nathaniel M. Hawkins reports grants, speaker bureau, advisory board and consultancy honoraria from pharmaceutical companies including AstraZeneca, Bayer, Boehringer Ingelheim, Novartis and Servier. John R. Hurst has received speaker/consultancy fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Takeda. Janwillem W.H. Kocks reports grants, personal fees and non-financial support from AstraZeneca; grants, personal fees and non-financial support from Boehringer Ingelheim; grants and personal fees from Chiesi; grants, personal fees and non-financial support from GlaxoSmithKline; non-financial support from Mundi Pharma; grants and personal fees from Teva; personal fees from MSD; personal fees from Covis Pharma; personal fees from ALK-Abelló; and grants from Valneva outside the submitted work; holds < 5% shares of Lothar Medtec GmbH and 72.5% of shares in the General Practitioners Research Institute. Neil Skolnik has received speaker/consultancy fees from Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Idorsia, Lilly, Merck, Novartis, Sanofi, Sanofi Pasteur and Teva; and research funding from AstraZeneca, Bayer, GlaxoSmithKline, Novo Nordisk and Sanofi. Daiana Stolz is the current GOLD representative for Switzerland and has received speaker/consultancy fees from Almirall, AstraZeneca, Bayer, Boehringer Ingelheim, CSL Behring, GlaxoSmithKline, MSD, Novartis, Sanofi and Vifor; and research grants from AstraZeneca and Curetis. Jad El Khoury is an employee of AstraZeneca and holds shares and stock options in the company. Chris P. Gale has received speaker fees from AstraZeneca, Medisetter, Menarini, Novartis, Raisio Group, Wondr Medical, Zydu; advisory board and consultancy honoraria from AI Nexus, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cardiomatics, Chiesi, Daiichi Sankyo, General Practitioners Research Institute, iRhythm, Menarini, Novartis, Organon, Phoenix Group; research grants from Abbott Diabetes, Bristol Myers Squibb, the British Heart Foundation, Horizon 2020, and the National Institute for Health and Care Research.

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- [1 figure](#)

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Respir Med



. 2024 Jun;227:107633.

doi: 10.1016/j.rmed.2024.107633. Epub 2024 Apr 15.

# [Sex differences and determinants of anxiety symptoms in patients with COPD initiating pulmonary rehabilitation](#)

[A M Yohannes](#)<sup>1</sup>, [R Casaburi](#)<sup>2</sup>, [S Dryden](#)<sup>3</sup>, [N A Hanania](#)<sup>4</sup>

Affiliations expand

- PMID: 38631527
- DOI: [10.1016/j.rmed.2024.107633](https://doi.org/10.1016/j.rmed.2024.107633)

## Abstract

**Background:** Anxiety is common in patients with chronic obstructive pulmonary disease (COPD). However, there is little evidence available regarding gender differences, and severity of dyspnea in relation to anxiety in patients with COPD.

**Aims:** We examined gender differences and the association of dyspnea with anxiety in a cohort of patients with COPD prior to entering a pulmonary rehabilitation (PR) program.

**Method:** We analyzed data from a prospective cohort of COPD patients who attended PR from 2013 to 2019 in Lytham, Lancashire, UK. Patients were aged 40 years or older with a post-bronchodilation forced expiratory volume in 1 s (FEV<sub>1</sub>) less than 80 % of the predicted normal value and FEV<sub>1</sub>/FVC (forced vital capacity) ratio less than 0.7. We assessed quality of life (QoL) using the Saint George's Respiratory Questionnaire (SGRQ), anxiety using the Anxiety Inventory for Respiratory disease (AIR), dyspnea using the modified Medical Research Council (mMRC) scale, and exercise capacity using the Incremental Shuttle Walk Test (ISWT).

**Results:** Nine hundred ninety-three patients with COPD (mean age = 71 years, FEV<sub>1</sub>/FVC = 58 % predicted, 51 % male) entered the PR program. Of these, 348 (35 %) had anxiety symptoms (AIR ≥8); of these 165 (47 %) were male and 183 (53 %) female, ( $\chi^2 = 3.33$ ,  $p = 0.06$ ). On logistic multivariate analysis, the following variables were independently associated with elevated anxiety: younger age ( $p < 0.001$ ), female sex ( $p = 0.03$ ), higher SGRQ-total score ( $p < 0.001$ ) and high FEV<sub>1</sub>/FVC ( $p < 0.002$ ). Dyspnea was associated with anxiety  $r = 0.25$ ,  $p < 0.001$ .

**Conclusion:** Over a third of COPD patients had clinically relevant anxiety symptoms with a higher prevalence in women than men. Anxiety was associated with younger age, female gender, and impaired QoL. Early recognition and treatment of anxiety in patients with COPD is worthy of consideration for those attending PR, especially women.

**Keywords:** Anxiety; COPD; Dyspnea; Female gender; Pulmonary rehabilitation.

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## Conflict of interest statement

Declaration of competing interest We declare that we have no conflict of interest in relation to this manuscript. Dr. Hanania, and Dr. Yohannes, as we are the editorial members of the Respiratory Medicine journal and recused for conflict of interest from handling this manuscript. If you need further information, please do not hesitate to contact me.

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Sleep Med

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. 2024 Jun;118:32-38.

doi: 10.1016/j.sleep.2024.03.041. Epub 2024 Apr 4.

# Prevalence and predictors of restless legs syndrome among patients having stable chronic obstructive pulmonary disease

[Sabbu Maharjan](#)<sup>1</sup>, [Ruchi Dua](#)<sup>2</sup>, [Lokesh Kumar Saini](#)<sup>3</sup>, [Niraj Kumar](#)<sup>4</sup>, [Ravi Gupta](#)<sup>1</sup>

Affiliations expand

- PMID: 38588638
- DOI: [10.1016/j.sleep.2024.03.041](https://doi.org/10.1016/j.sleep.2024.03.041)

## Abstract

**Background:** Patients having COPD share some factors, e.g., chronic hypoxemia, anemia of chronic disease and nicotine use, which are also the risk factors for RLS hence predispose them to experience RLS in higher than general population. There are limited studies with methodological constraints evaluating the prevalence and/or correlates of RLS among patients with COPD.

**Methods:** Consecutive adult patients of either gender, having stable COPD as per GOLD guidelines 2021, were assessed for RLS using IRLSSG (2014) criteria (excluding RLS mimics) and the severity of RLS was determined in participants having RLS. Phenomenology of RLS, past medical history and laboratory parameters were gathered. Insomnia and depression were assessed using the insomnia severity index and PHQ-9, respectively.

**Results:** Participants' (N = 210) mean age was  $63.02 \pm 8.19$  years, and 83.8% of subjects were men. 12.9% of participants were found to have RLS. Among those having RLS, nearly half (51.9%) had moderate symptoms, and 18.5% experienced severe symptoms. RLS was more prevalent among younger, females, those having severe COPD, participants having exacerbation of COPD in the previous year, lower post-bronchodilator FEV1, higher dyspnea and COPD assessment test score. Multivariate analysis showed that younger age, female gender, lower post-bronchodilator FEV1, lower FEV1/FVC ratio and higher serum creatinine increased the odds of having RLS. Depressive symptoms were more frequent in participants having RLS.

**Conclusions:** The present study found that the prevalence of RLS among patients with stable COPD was higher than the general population. Female gender, younger age, higher airflow limitation and higher serum creatinine (though in the physiological range) increase the odds of having RLS. Stable patients with COPD having these characteristics must be screened for RLS.

**Keywords:** COPD; Depression; RLS; Sleep; Sleep-quality.

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## 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.

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Randomized Controlled Trial



# Self-management intervention for patients following hospitalization for acute exacerbation of chronic obstructive pulmonary disease (AECOPD): A pilot randomized controlled trial

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Affiliations expand

- PMID: 38566419
- DOI: [10.1111/nhs.13114](https://doi.org/10.1111/nhs.13114)

## Abstract

The purpose of this study was to evaluate the handoff guidance (HG) self-management intervention for multimorbid chronic obstructive pulmonary disease (COPD) patients following hospitalization for acute exacerbation of COPD (AECOPD) using HG self-management intervention compared to a control group on COPD self-management outcomes (self-care, self-efficacy, health engagement) and assess feasibility, acceptability, and healthcare utilization. A randomized pilot study used a 2-group with repeated measures design. Adults with COPD who had been hospitalized for AECOPD were recruited. After discharge, the HG self-management intervention employed health coaching delivered at: 1-3, 10-12, and 20-22 days after hospital discharge. Follow-up data collected was collected at 1-3, 10-12, 20-22, 30, 60, and 90 days after hospital discharge. A total of 29 subjects participated, with a mean age of 66 (+8.7) years old, the majority were females (n = 18). Intervention participants reported the acceptability of the HG self-management intervention. Participants in both groups continued to report COPD

symptoms after discharge, which decreased over time, although not significantly different by group. The use of COPD maintenance, monitoring, and management behaviors was higher in the treatment group, although not significantly different.

**Keywords:** acute exacerbation of COPD (AECOPD) self-management; chronic obstructive lung disease (COPD); nurse-led intervention.

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- [37 references](#)

#### SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and funding [expand](#)

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Review

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. 2024 Jun;21(3):163-173.

doi: 10.1007/s11897-024-00660-2. Epub 2024 Mar 28.

# [Chronic Obstructive Pulmonary Disease in Heart Failure: Challenges in Diagnosis and Treatment for HFpEF and HFrEF](#)

Affiliations expand

- PMID: 38546964
- DOI: [10.1007/s11897-024-00660-2](https://doi.org/10.1007/s11897-024-00660-2)

## Abstract

**Purpose of review:** Chronic obstructive pulmonary disease (COPD) is common in heart failure (HF), and it has a significant impact on the prognosis and quality of life of patients. Additionally, COPD is independently associated with lower adherence to first-line HF therapies. In this review, we outline the challenges of identifying and managing HF with preserved (HFpEF) and reduced (HFrEF) ejection fraction with coexisting COPD.

**Recent findings:** Spirometry is necessary for COPD diagnosis and prognosis but is underused in HF. Therefore, misdiagnosis is a concern. Also, disease-modifying drugs for HF and COPD are usually safe but underprescribed when HF and COPD coexist. Patients with HF-COPD are poorly enrolled in clinical trials. Guidelines recommend that HF treatment should be offered regardless of COPD presence, but modern registries show that undertreatment persists. Treatment gaps could be attenuated by ensuring an accurate and earlier COPD diagnosis in patients with HF, clarifying the concerns related to pharmacotherapy safety, and increasing the use of non-pharmacologic treatments. Acknowledging the uncertainties, this review aims to provide key clinical resources to support better physician-patient co-decision-making and improve collaboration between health professionals.

**Keywords:** Betablockers; Bronchodilators; Lung disease; Obstructive deficit; Rehabilitation; Ventricular dysfunction.

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- [59 references](#)

SUPPLEMENTARY INFO

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Meta-Analysis

Ital J Dermatol Venerol



. 2024 Jun;159(3):329-335.

doi: 10.23736/S2784-8671.24.07641-2. Epub 2024 Mar 19.

# [The association between psoriasis and chronic obstructive pulmonary disease: a systematic review and meta-analysis](#)

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Affiliations expand

- PMID: 38502534
- DOI: [10.23736/S2784-8671.24.07641-2](https://doi.org/10.23736/S2784-8671.24.07641-2)

## Abstract

**Introduction:** Psoriasis is a chronic T-cell-mediated inflammatory and proliferative skin disease. Chronic obstructive pulmonary disease (COPD) is an inflammatory disease of the airways. COPD has been studied as a comorbidity of psoriasis, but the association needs further study, hence the objective of this study.

**Evidence acquisition:** A systematic review was performed using the database PubMed and 155 records were found including the ones found through references. Seven records were found eligible for this study including six observational studies and one experimental

study with a total of 229,075 participants. The odds ratio of COPD in patients with psoriasis and healthy subjects was analysed using a random effects model.

**Evidence synthesis:** The pooled data showed a significant association (OR=1.77, 95% CI [1.32; 2.39]) between psoriasis and COPD with high inter-study heterogeneity ( $I^2=96\%$ ). Sub-analyses of the different types of studies (cohort study: OR=2.53 [2.43; 2.63], case-control study: OR=1.6 [0.03; 100.96] and cross-sectional study: OR=1.57 [0.58; 4.22]) and smoking status (OR=1.7 [0.69; 4.14]) were also performed to further examine the association.

**Conclusions:** There is a significant association between psoriasis and COPD, but the underlying mechanism and how smoking status affects the results remain unclear and need further study. Physicians should be aware of the risk and its seriousness to provide better and more targeted treatment.

#### SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Respir Crit Care Med

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. 2024 Jun 1;209(11):1394-1396.

doi: 10.1164/rccm.202309-1699LE.

## [Risk of Cardiovascular Events after Acute Exacerbations of Chronic Obstructive Pulmonary Disease in](#)

# Patients Receiving Long-Term Low-Dose Azithromycin

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Affiliations expand

- PMID: 38502239
- DOI: [10.1164/rccm.202309-1699LE](https://doi.org/10.1164/rccm.202309-1699LE)

*No abstract available*

- [Cited by 1 article](#)

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Publication types, MeSH terms, Substances expand

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Review

Paediatr Respir Rev

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. 2024 Jun;50:2-22.

doi: 10.1016/j.prrv.2024.02.002. Epub 2024 Feb 16.

# Expiratory airflow limitation in adults born extremely preterm: A systematic review and meta-analysis

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Affiliations expand

- PMID: 38490917
- DOI: [10.1016/j.prrv.2024.02.002](https://doi.org/10.1016/j.prrv.2024.02.002)

**Free article**

## Abstract

Extreme preterm (EP) birth, denoting delivery before the onset of the third trimester, interrupts intrauterine development and causes significant early-life pulmonary trauma, thereby posing a lifelong risk to respiratory health. We conducted a systematic review and meta-analysis to investigate adult lung function following EP birth (gestational age <28 weeks); comparing forced expiratory volume in first second (FEV<sub>1</sub>), forced vital capacity (FVC), and FEV<sub>1</sub>/FVC to reference values. Subgroup differences were explored based on timing of birth relative to surfactant use (1991) and bronchopulmonary dysplasia (BPD) status. Systematic searches were performed in Medline, EMBASE, Web of Science and Cochrane Central. Quality assessments were carried out using a modified Newcastle-Ottawa Scale for cohort studies. Sixteen studies encompassing 1036 EP-born adults were included, with 14 studies (n = 787) reporting data as %predicted, and 11 (n = 879) as z-score (not mutually exclusive). Overall mean [95 % confidence interval (CI)] %FEV<sub>1</sub> was 85.30 (82.51; 88.09), %FVC was 94.33 (91.74; 96.91), and FEV<sub>1</sub>/FVC was 79.54 (77.71 to 81.38), all three with high heterogeneity. Overall mean (95 %CI) zFEV<sub>1</sub> was -1.05 (-1.21; -0.90) and zFVC was -0.45 (-0.59; -0.31), both with moderate heterogeneity. Subgroup analyses revealed no difference in FEV<sub>1</sub> before versus after widespread use of surfactant, but more impairments after neonatal BPD. This meta-analysis revealed significant airflow limitation in EP-born adults, mostly explained by those with neonatal BPD. FEV<sub>1</sub> was more reduced than FVC, and FEV<sub>1</sub>/FVC was at the lower limit of normal. Although at a group level, most adult EP-born individuals do not meet COPD criteria, these findings are concerning.

**Keywords:** Adult; Extremely low birth weight; Extremely premature; FEV(1); Lung function; Respiratory function.

## 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.

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Publication types, MeSH terms, Substancesexpand

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Observational Study

Am J Med

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. 2024 Jun;137(6):538-544.e1.

doi: 10.1016/j.amjmed.2024.02.034. Epub 2024 Mar 12.

# Smoking and Respiratory Diseases in Patients with Coronary Microvascular Dysfunction

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Affiliations expand

- PMID: 38485108

- DOI: [10.1016/j.amjmed.2024.02.034](https://doi.org/10.1016/j.amjmed.2024.02.034)

## Abstract

**Background:** Coronary microvascular disease (CMD) is common in patients with and without obstructive coronary artery disease, and is associated with adverse clinical outcomes. Respiratory-related variables are associated with pulmonary and systemic microvascular dysfunction, while evidence about their relationship with CMD is limited. We aim to evaluate respiratory-related variables as risk factors of CMD.

**Methods:** This is an observational, single-center study enrolling consecutive patients undergoing invasive evaluation of coronary microvascular function in the catheterization laboratory. Patients with evidence of obstructive coronary artery disease or with missing data were excluded. Associations between respiratory-related variables and indices of CMD were assessed using univariate and multivariate regression models.

**Results:** Overall, 266 patients (mean age  $67 \pm 11$  years, 59% females) were included in the current analysis. Of those, 155 (58%) had evidence of CMD. Among the respiratory variables, independent predictors of CMD were current smoking (adjusted odds ratio [AOR] 2.5; 95% confidence interval [CI], 1.2-5;  $P = .01$ ) and obstructive sleep apnea (AOR 5.7; 95% CI, 1.2-26;  $P = .03$ ), while chronic obstructive pulmonary disease was not. Among ever-smokers, higher smoking pack-years was an independent risk factor for CMD (median 35 vs 25 pack-years, AOR 1.09; 95% CI, 1.04-1.13;  $P < .01$ ), and was associated with higher rates of pathologic index of microcirculatory resistance and resistive reserve ratio.

**Conclusion:** In patients undergoing invasive coronary microvascular evaluation, current smoking and obstructive sleep apnea are independently associated with CMD. Among smokers, higher pack-years is a strong predictor for CMD. Our findings should raise awareness for prevention and possible treatment options.

**Keywords:** COPD; Interventional cardiology; MINOCA; Pulmonary; Risk Factors; Smoking.

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SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Med Sci

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. 2024 Jun;367(6):375-381.

doi: 10.1016/j.amjms.2024.03.014. Epub 2024 Mar 11.

# [The clinical and hemodynamic characteristics of pulmonary hypertension in patients with OSA-COPD overlap syndrome](#)

[Bing Zhu Hu](#)<sup>1</sup>, [Cheng Jiang](#)<sup>1</sup>, [Yong Jie Ding](#)<sup>2</sup>, [Wei Qin](#)<sup>1</sup>, [Wei Yu](#)<sup>1</sup>, [Yi Shi](#)<sup>1</sup>, [Fa Jiu Li](#)<sup>1</sup>, [Cheng Hong Li](#)<sup>1</sup>, [Qing Yun Li](#)<sup>3</sup>

Affiliations [expand](#)

- PMID: 38467374
- DOI: [10.1016/j.amjms.2024.03.014](https://doi.org/10.1016/j.amjms.2024.03.014)

## Abstract

**Background:** Our study aimed to assess the clinical and hemodynamic characteristics of pulmonary hypertension (PH) in patients with overlapping obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD), referred to OSA-COPD overlap syndrome (OS).

**Methods:** We enrolled a total of 116 patients with OS, COPD, or OSA who underwent right heart catheterization (RHC) due to suspected PH. We conducted a retrospective analysis of the clinical and hemodynamic characteristics of these patients.

**Results:** Among the three groups (OS group, n = 26; COPD group, n = 36; OSA group, n = 54), the prevalence of PH was higher in the OS group (n = 17, 65.4%) compared to OSA group (n = 26, 48.1%) and COPD group (n = 20, 55.6 %). Among three groups with PH, the superior vena cava pressure (CVP) and right ventricular pressure (RAP) were higher in the OS group than in the OSA group (P < 0.05). Patients in the OS and COPD groups had higher pulmonary artery wedge pressure (PAWP) than in the OSA group (14.88 ± 4.79 mmHg, 13.45 ± 3.68 mmHg vs. 11.00 ± 3.51 mmHg, respectively, P < 0.05). OS patients with PH exhibited higher respiratory event index (REI), time spent with SpO<sub>2</sub> <90%, oxygen desaturation index (ODI), minimal SpO<sub>2</sub> (MinSpO<sub>2</sub>) and mean SpO<sub>2</sub> (MSPo<sub>2</sub>) compared to OS patients without PH. After adjusting for potential covariates, we found that MinSpO<sub>2</sub> (OR 0.937, 95 % CI 0.882-0.994, P = 0.032), MSPo<sub>2</sub> (OR 0.805, 95% CI 0.682-0.949, P = 0.010), time spent with SpO<sub>2</sub> <90% (OR 1.422, 95% CI 1.137-1.780, P = 0.002), and FEV1 % pred (OR 0.977, 95 % CI 0.962-0.993, P = 0.005) were related to the development of PH.

**Conclusions:** Patients with OS showed higher prevalence of PH, along with higher PAWP, CVP and RAP. Worse nocturnal hypoxemia was found in OS patients with PH.

**Keywords:** Nocturnal hypoxemia; OSA-COPD overlap syndrome; Pulmonary hypertension; RHC.

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## Conflict of interest statement

Conflict of interest The authors declare that they have no conflict of interest.

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Publication types, MeSH termsexpand

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Randomized Controlled Trial



# Impacts of a health literacy-informed intervention in people with chronic obstructive pulmonary disease (COPD) on hospitalization, health literacy, self-management, quality of life, and health costs - A randomized controlled trial

[Christine R Borge](#)<sup>1</sup>, [Marie H Larsen](#)<sup>2</sup>, [Richard H Osborne](#)<sup>3</sup>, [Eline Aas](#)<sup>4</sup>, [Ingrid Tryland Kolle](#)<sup>5</sup>, [Rikke Reinertsen](#)<sup>5</sup>, [Martha P Lein](#)<sup>5</sup>, [Maria Thörn](#)<sup>5</sup>, [Ragnhild Mørch Lind](#)<sup>5</sup>, [Marie Groth](#)<sup>5</sup>, [Oda Strand](#)<sup>5</sup>, [Marit Helen Andersen](#)<sup>6</sup>, [Torbjørn Moum](#)<sup>7</sup>, [Eivind Engebretsen](#)<sup>8</sup>, [Astrid K Wahl](#)<sup>8</sup>

Affiliations expand

- PMID: 38458089
- DOI: [10.1016/j.pec.2024.108220](https://doi.org/10.1016/j.pec.2024.108220)

## Abstract

**Objective:** To compare the effect of motivational interviewing (MI) and tailored health literacy (HL) follow-up with usual care on hospitalization, costs, HL, self-management, Quality of life (QOL), and psychological stress in people with chronic obstructive pulmonary disease (COPD).

**Methods:** A RCT was undertaken in Norway between March 2018-December 2020 (n = 127). The control group (CG, n = 63) received usual care. The intervention group (IG, n = 64) received tailored HL follow-up from MI-trained COPD nurses with home visits for eight weeks and phone calls for four months after hospitalization. Primary outcomes were

hospitalization at eight weeks, six months, and one year from baseline. The trial was registered with ClinicalTrials.gov ([NCT03216603](https://clinicaltrials.gov/ct2/show/study/NCT03216603)) and analysed per protocol.

**Results:** Compared with the IG, the CG had 2.8 higher odds (95% CI [1.3 to 5.8]) of hospitalization and higher hospital health costs (MD=€ -6230, 95% CI [-6510 to -5951]) and lower QALYs (MD=0.1, 95% CI [0.10 to 0.11]) that gives an ICER = - 62,300. The IG reported higher QOL, self-management, and HL (p = 0.02- to <0.01).

**Conclusion:** MI-trained COPD nurses using tailored HL follow-up is cost-effective, reduces hospitalization, and increases QOL, HL, and self-care in COPD.

**Practice implication:** Tailored HL follow-up is beneficial for individuals with COPD and the healthcare system.

**Keywords:** COPD; Chronic diseases; Community health care service; Health literacy; Health literacy intervention; Quality of life; Self-management; Tailored follow-up.

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## 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: Christine R. Borge reports financial support was provided by DAM funding. Christine R. Borge reports financial support was provided by HSØ collaboration funds. Christine R. Borge reports financial support was provided by Lovisenberg Diaconal Hospital, municipality Grunerløkka, Gamle Oslo, St.Hanshaugen, Sagene and the University of Oslo. Christine R. Borge reports financial support was provided by Kirsten Rønnings Legat. Richard Osborne reports financial support was provided by National Health and Medical Research Council.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

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Respirology

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. 2024 Jun;29(6):443-444.

doi: 10.1111/resp.14699. Epub 2024 Mar 4.

# Use of spirometry to detect airflow obstruction

[Chi Chiu Leung](#)<sup>1</sup>

Affiliations expand

- PMID: 38438271
- DOI: [10.1111/resp.14699](https://doi.org/10.1111/resp.14699)

## Free article

*No abstract available*

**Keywords:** airflow obstruction; forced expiratory ratio; mortality; spirometry.

- [11 references](#)

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Respirology



. 2024 Jun;29(6):471-478.

doi: 10.1111/resp.14683. Epub 2024 Feb 25.

# Smoking, respiratory symptoms, lung function and life expectancy: A longitudinal study of ageing

[Kate Petrie](#)<sup>1</sup>, [Michael J Abramson](#)<sup>2</sup>, [Johnson George](#)<sup>1,2</sup>

Affiliations expand

- PMID: 38403987
- DOI: [10.1111/resp.14683](https://doi.org/10.1111/resp.14683)

## Abstract

**Background and objective:** Prognostic indices have been developed to predict various outcomes, including mortality. These indices and hazard ratios may be difficult for patients to understand. We investigated the association between smoking, respiratory symptoms and lung function with remaining life expectancy (LE) in older adults.

**Methods:** Data were from the 2004/05 English Longitudinal Study of Ageing (ELSA) (n = 8930), participants aged  $\geq 50$ -years, with mortality data until 2012. Respiratory symptoms included were chronic phlegm and shortness of breath (SOB). The association between smoking, respiratory symptoms and FEV<sub>1</sub>/FVC, and remaining LE was estimated using a parametric survival function and adjusted for covariates including age at baseline and sex.

**Results:** The extent to which symptoms and FEV<sub>1</sub>/FVC predicted differences in remaining LE varied by smoking. Compared to asymptomatic never smokers with normal lung function (the reference group), in never smokers, only those with SOB had a significant reduction in remaining LE. In former and current smokers, those with respiratory symptoms had significantly lower remaining LE compared to the reference group if they had FEV<sub>1</sub>/FVC

<0.70 compared to those with FEV<sub>1</sub>/FVC ≥0.70. Males aged 50-years, current smokers with SOB and FEV<sub>1</sub>/FVC <0.70, had a remaining LE of 19.2 (95%CI: 16.5-22.2) years, a decrease of 8.1 (5.3-10.8) years, compared to the reference group.

**Conclusion:** Smoking, respiratory symptoms and FEV<sub>1</sub>/FVC are strongly associated with remaining LE in older people. The use of remaining LE to communicate mortality risk to patients needs further investigation.

**Keywords:** COPD; chronic obstructive pulmonary disease; life expectancy; mortality risk; respiratory symptoms; smoking; spirometry.

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Comparative Study

Eur J Clin Pharmacol

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. 2024 Jun;80(6):847-853.

doi: 10.1007/s00228-024-03637-1. Epub 2024 Feb 23.

## Long-acting B-2 agonists (LABA) or long-acting muscarinic antagonists

# (LAMA): which one may be the first option in group A COPD patients?

[Onur Turan](#)<sup>1</sup>, [Nalan Ogan](#)<sup>2</sup>, [Fulsen Bozkus](#)<sup>3</sup>, [Nurhan Sarioğlu](#)<sup>4</sup>, [Pakize Ayşe Turan](#)<sup>5</sup>, [Celal Satıcı](#)<sup>6</sup>

Affiliations expand

- PMID: 38396308
- DOI: [10.1007/s00228-024-03637-1](https://doi.org/10.1007/s00228-024-03637-1)

## Abstract

**Introduction:** Long-acting muscarinic antagonists (LAMA) or beta-2 agonists (LABA) have been recommended for symptom control in group A COPD patients as a first-line bronchodilator treatment in GOLD guidelines. However, there is no mention of priority/superiority between the two treatment options. We aimed to compare the effectiveness of these treatments in this group.

**Methods:** The study cohort was formed of all subjects from six pulmonology clinics with an initial diagnosis of COPD who were new users of a LAMA or LABA from January 2020 to December 2021. Seventy-six group A COPD patients, in whom LABA or LAMA therapy had been started in the last 1 month as a first-line treatment, were included in our study. Participants were evaluated with spirometry, COPD Assessment Test (CAT), mMRC scale, and St. George Respiratory Questionnaire (SGRQ) for three times (baseline, 6-12<sup>th</sup> months).

**Results:** There were 76 group A COPD patients with LAMA (67.1%) and LABA (32.9%). The number of patients who improved in CAT score at the end of the first year was significantly higher in patients using LAMA than those using LABA ( $p = 0.022$ ); the improvement at minimum clinically important difference (MCID) in CAT score of LAMA group at 1<sup>st</sup> year was also significant ( $p = 0.044$ ). SGRQ total and impact scores were found to be statistically lower at 1<sup>st</sup> year compared to baseline in patients using LAMA ( $p = 0.010$  and  $0.006$ , respectively). Significant improvement was detected in CAT and SGRQ scores at the 6<sup>th</sup> month visit in the LAMA group having emphysema ( $p = 0.032$  and  $0.002$ , respectively).

**Conclusion:** According to significant improvements in CAT and SGRQ score, LAMA may be preferred over LABA as a bronchodilator agent in group A COPD patients, especially in emphysema-dominant phenotype.

**Keywords:** COPD; Group A; Long-acting beta-2 agonists (LABA); Long-acting muscarinic antagonists (LAMA); Treatment.

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Editorial

Palliat Support Care

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. 2024 Jun;22(3):429-431.

doi: 10.1017/S1478951524000063.

# [COPD patients' accessibility to palliative care: Current challenges and opportunities for improvement](#)

[Barbara Gonçalves](#)<sup>1,2</sup>, [Eileen Harkess-Murphy](#)<sup>3</sup>, [Audrey Cund](#)<sup>4</sup>, [Caroline Sime](#)<sup>5</sup>, [Joanne Lusher](#)<sup>6</sup>

Affiliations expand

- PMID: 38264901

- DOI: [10.1017/S1478951524000063](https://doi.org/10.1017/S1478951524000063)

No abstract available

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Publication types, MeSH termsexpand

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Am J Respir Crit Care Med

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. 2024 Jun 1;209(11):1314-1327.

doi: 10.1164/rccm.202307-1184OC.

# [Physiological Characterization of Preserved Ratio Impaired Spirometry in the CanCOLD Study: Implications for Exertional Dyspnea and Exercise Intolerance](#)

[Devin B Phillips](#)<sup>1,2,3</sup>, [Matthew D James](#)<sup>3</sup>, [Sandra G Vincent](#)<sup>3</sup>, [Amany F Elbehairy](#)<sup>4,5</sup>, [J Alberto Neder](#)<sup>3</sup>, [Miranda Kirby](#)<sup>6</sup>, [Josuel Ora](#)<sup>7</sup>, [Andrew G Day](#)<sup>8</sup>, [Wan C Tan](#)<sup>9</sup>, [Jean Bourbeau](#)<sup>10,11</sup>, [Denis E O'Donnell](#)<sup>3</sup>; [CanCOLD Collaborative Research Group and the Canadian Respiratory Research Network](#)

Collaborators, Affiliations expand

- PMID: 38170674

- DOI: [10.1164/rccm.202307-1184OC](https://doi.org/10.1164/rccm.202307-1184OC)

## Abstract

**Rationale:** It is increasingly recognized that adults with preserved ratio impaired spirometry (PRISm) are prone to increased morbidity. However, the underlying pathophysiological mechanisms are unknown. **Objectives:** Evaluate the mechanisms of increased dyspnea and reduced exercise capacity in PRISm. **Methods:** We completed a cross-sectional analysis of the CanCOLD (Canadian Cohort Obstructive Lung Disease) population-based study. We compared physiological responses in 59 participants meeting PRISm spirometric criteria (post-bronchodilator  $FEV_1 < 80\%$  predicted and  $FEV_1/FVC \geq 0.7$ ), 264 control participants, and 170 ever-smokers with chronic obstructive pulmonary disease (COPD), at rest and during cardiopulmonary exercise testing. **Measurements and Main Results:** Individuals with PRISm had lower total lung, vital, and inspiratory capacities than healthy controls (all  $P < 0.05$ ) and minimal small airway, pulmonary gas exchange, and radiographic parenchymal lung abnormalities. Compared with healthy controls, individuals with PRISm had higher dyspnea/[Formula: see text] $o_2$  ratio at peak exercise ( $4.0 \pm 2.2$  vs.  $2.9 \pm 1.9$  Borg units/L/min;  $P < 0.001$ ) and lower [Formula: see text] $o_{2peak}$  ( $74 \pm 22\%$  predicted vs.  $96 \pm 25\%$  predicted;  $P < 0.001$ ). At standardized submaximal work rates, individuals with PRISm had greater  $V_t$ /inspiratory capacity ( $V_t\%IC$ ;  $P < 0.001$ ), reflecting inspiratory mechanical constraint. In contrast to participants with PRISm, those with COPD had characteristic small airways dysfunction, dynamic hyperinflation, and pulmonary gas exchange abnormalities. Despite these physiological differences among the three groups, the relationship between increasing dyspnea and  $V_t\%IC$  during cardiopulmonary exercise testing was similar. Resting IC significantly correlated with [Formula: see text] $o_{2peak}$  ( $r = 0.65$ ;  $P < 0.001$ ) in the entire sample, even after adjusting for airflow limitation, gas trapping, and diffusing capacity. **Conclusions:** In individuals with PRISm, lower exercise capacity and higher exertional dyspnea than healthy controls were mainly explained by lower resting lung volumes and earlier onset of dynamic inspiratory mechanical constraints at relatively low work rates. Clinical trial registered with [www.clinicaltrials.gov](http://www.clinicaltrials.gov) ([NCT00920348](https://clinicaltrials.gov/ct2/show/study/NCT00920348)).

**Keywords:** dyspnea; exercise capacity; preserved ratio impaired spirometry; pulmonary function; spirometry.

## Comment in

- [Should the Term "PRISm" Be Restricted to Use in Evaluating Smokers?](#)  
Casaburi R, Crapo JD. *Am J Respir Crit Care Med*. 2024 Jun 1;209(11):1289-1291. doi: [10.1164/rccm.202401-0042ED](https://doi.org/10.1164/rccm.202401-0042ED). PMID: 38324051 No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Associated data, Grants and funding expand

FULL TEXT LINKS



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J Pharm Pract



. 2024 Jun;37(3):677-682.

doi: 10.1177/08971900231168927. Epub 2023 Mar 30.

# [Outcomes of a Pharmacy-Driven Inpatient Chronic Obstructive Pulmonary Disease \(COPD\) Transitions of Care \(TOC\) Management Process](#)

[Aaron Roberts](#)<sup>1</sup>, [Meredith Hope Ball](#)<sup>2</sup>, [Austin Clark Bentley](#)<sup>1</sup>, [Aubrie Rafferty](#)<sup>3</sup>

Affiliations expand

- PMID: 36996030
- PMCID: [PMC11041072](#)
- DOI: [10.1177/08971900231168927](#)

## Abstract

**Background:** Current data shows 30% of patients hospitalized for Chronic Obstructive Pulmonary Disease (COPD) exacerbation are readmitted within 30 days. Medication management during transitions of care (TOC) has shown impact on clinical outcomes, however there is insufficient data to suggest how pharmacy TOC services might benefit this patient population. **Objective:** Evaluate the effects of pharmacy-driven COPD TOC services on hospital re-presentation rates. **Methods:** A single-center retrospective chart review conducted of patients hospitalized for a COPD exacerbation. A comprehensive admission-to-discharge TOC service was provided by early immersion pharmacy students, advanced immersion pharmacy students, and an attending pharmacist in a layered learning model. The primary outcome was 30-day re-presentation rate. Secondary outcomes were 90-day re-presentation rate, volume of interventions made and description of the service. **Results:** From 1/1/2019 to 12/31/2019, there were 2422 patients admitted for COPD exacerbation management and 756 patients received at least one intervention from the COPD TOC service. 30% needed a change to inhaler therapy. The provider accepted 57.8% of the recommended changes, and 36% and 33% of eligible patients received an inhaler technique education and bedside delivery of the new inhaler, respectively. Outcomes in the 30-day re-presentation and 90-day censored re-presentation rates for the intervention and control group were 28.5% vs 25.5% ( $P = .12$ ) and 46.7% vs 42.9%, respectively. **Conclusion:** This study did not find a significant change in 30-day re-presentation rate with a pharmacy-driven COPD TOC service. It did find that a significant number of patients admitted with COPD exacerbation may need an inhaler change, and demonstrates the utility of this kind of TOC service for identifying and correcting medication-related problems unique to this disease state. There were opportunities for improvement in percent of patients receiving the full intended intervention.

**Keywords:** COPD; layered learning; transitions of care.

## Conflict of interest statement

DisclosuresThe authors have no financial conflicts or other competing interests to disclose. This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

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J Pharm Pract

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. 2024 Jun;37(3):607-611.

doi: 10.1177/08971900221150286. Epub 2023 Jan 4.

# Impact of Clinical Pharmacist Practitioner Management of Chronic Obstructive Pulmonary Disease in the Ambulatory Care Setting

[Alexa M Haddon](#)<sup>1</sup>, [Kylee R Gross](#)<sup>1</sup>, [Cassandra J Mozes](#)<sup>2</sup>

Affiliations expand

- PMID: 36599814
- DOI: [10.1177/08971900221150286](https://doi.org/10.1177/08971900221150286)

## Abstract

**Objectives:** To evaluate the impact of clinical pharmacist practitioner (CPP) management on potentially inappropriate use of inhaled corticosteroids (ICS) in the ambulatory care setting. **Design:** Multicenter, prospective quality assurance/improvement (QA/QI) project. **Setting:** Erie Veterans Affairs Medical Center (VAMC) and surrounding Ashtabula, Crawford, and Venango County Community-Based Outpatient Clinics (CBOCs). **Participants:** Thirty-five participants with chronic obstructive pulmonary disease (COPD) who met inclusion criteria were included in the project. **Interventions:** Participants were contacted to schedule an initial sixty-minute telephone visit with a CPP. Exacerbation history, rescue inhaler use, and symptom burden were assessed using the COPD Assessment Test (CAT) and Modified Medical Research Council Breathlessness Scale (mMRC) scales. Medication regimens were optimized based on guideline

recommendations with an emphasis on appropriate use of ICS. Participants were scheduled for follow-up telephone visits with the CPP every 4 weeks. **Main Outcome Measures:** The primary project outcome was potentially inappropriate use of ICS without a long-acting muscarinic antagonist (LAMA)/long-acting beta agonist (LABA). Secondary project outcomes included ICS de-escalation, vaccinations, and smoking cessation. **Results:** The primary outcome of reducing use of ICS without a LAMA/LABA was achieved in thirty-one (88.6%) participants. ICS de-escalation was achieved in twenty-three (65.7%) participants. Rates of recommended vaccinations and smoking cessation with nicotine replacement therapy increased as a result of pharmacist intervention. **Conclusion:** Pharmacist management of COPD in the ambulatory care setting was associated with a decrease in potentially inappropriate use of ICS and an increase in preventative care measures.

**Keywords:** ambulatory care; chronic obstructive pulmonary disease; de-escalation; inhaled corticosteroids; pharmacist.

## Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Intern Emerg Med

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. 2024 May 31.

doi: 10.1007/s11739-024-03653-0. Online ahead of print.

# Low-dose azithromycin prophylaxis in patients with atrial fibrillation and chronic obstructive pulmonary disease

[Tommaso Bucci](#)<sup>1,2</sup>, [Dennis Wat](#)<sup>1,3</sup>, [Sarah Sibley](#)<sup>3</sup>, [Dan Wootton](#)<sup>4,5</sup>, [David Green](#)<sup>3</sup>, [Pasquale Pignatelli](#)<sup>2</sup>, [Gregory Y H Lip](#)<sup>6,7</sup>, [Freddy Frost](#)<sup>1,3</sup>

Affiliations expand

- PMID: 38819711
- DOI: [10.1007/s11739-024-03653-0](https://doi.org/10.1007/s11739-024-03653-0)

## Abstract

Low-dose azithromycin prophylaxis is associated with improved outcomes in people suffering frequent exacerbations of chronic obstructive pulmonary disease (COPD), but the use of macrolides in patients with cardiovascular disease has been debated. To investigate the risk of adverse events after COPD exacerbations in patients with atrial fibrillation (AF) treated with azithromycin prophylaxis. Retrospective cohort study within the TriNetX Platform, including AF patients with COPD exacerbations. Risks of primary and secondary outcomes were recorded up to 30 days post-COPD exacerbations and compared between azithromycin users and azithromycin non-users. The primary outcomes were the risks for a composite of (1) cardiovascular (all-cause death, heart failure, ventricular arrhythmias, ischemic stroke, myocardial infarction, and cardiac arrest), and (2) hemorrhagic events (intracranial hemorrhage (ICH), and gastro-intestinal bleeding). Cox-regression analyses compared outcomes between groups after propensity score matching (PSM). After PSM, azithromycin users (n = 2434, 71 ± 10 years, 49% females) were associated with a lower 30-day risk of post-exacerbation cardiovascular (HR 0.67, 95% CI 0.61-0.73) and hemorrhagic composite outcome (HR 0.45, 95% CI 0.32-0.64) compared to azithromycin non-users (n = 2434, 72 ± 11 years, 51% females). The beneficial effect was consistent for each secondary outcomes, except ICH. On sensitivity analyses, the reduced risk of adverse events in azithromycin users was irrespective of smoking status, exacerbation severity, and type of oral anticoagulation. Azithromycin prophylaxis is associated with a lower risk of all-cause death, thrombotic and hemorrhagic events in AF patients with COPD. The possible role of azithromycin prophylaxis as part of the integrated care management of AF patients with COPD needs further study.

**Keywords:** Atrial fibrillation; Azithromycin; COPD; Cardiovascular events; Macrolides.

- [29 references](#)

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J Am Heart Assoc



. 2024 May 31:e033882.

doi: 10.1161/JAHA.123.033882. Online ahead of print.

# [Chronic Obstructive Pulmonary Disease Exacerbations Increase the Risk of Subsequent Cardiovascular Events: A Longitudinal Analysis of the COPDGene Study](#)

[Han-Mo Yang](#)<sup>1,2,3</sup>, [Min Hyung Ryu](#)<sup>1,2</sup>, [Vincent J Carey](#)<sup>1,2</sup>, [Gregory L Kinney](#)<sup>4</sup>, [John E Hokanson](#)<sup>4</sup>, [Mark T Dransfield](#)<sup>5</sup>, [Craig P Hersh](#)<sup>1,6,2</sup>, [Edwin K Silverman](#)<sup>1,6,2</sup>; [COPDGene Investigators](#) †

Collaborators, Affiliations expand

- PMID: 38818936
- DOI: [10.1161/JAHA.123.033882](https://doi.org/10.1161/JAHA.123.033882)

## Abstract

**Background:** Cardiovascular disease (CVD) is the most important comorbidity in patients with chronic obstructive pulmonary disease (COPD). COPD exacerbations not only contribute to COPD progression but may also elevate the risk of CVD. This study aimed to determine whether COPD exacerbations increase the risk of subsequent CVD events using up to 15 years of prospective longitudinal follow-up data from the COPDGene (Genetic Epidemiology of Chronic Obstructive Pulmonary Disease) study.

**Methods and results:** The COPDGene study is a large, multicenter, longitudinal investigation of COPD, including subjects at enrollment aged 45 to 80 years with a minimum of 10 pack-years of smoking history. Cox proportional hazards models and Kaplan-Meier survival curves were used to assess the risk of a composite end point of CVD based on the COPD exacerbation rate. Frequent exacerbators exhibited a higher cumulative incidence of composite CVD end points than infrequent exacerbators, irrespective of the presence of CVD at baseline. After adjusting for covariates, frequent exacerbators still maintained higher hazard ratios (HRs) than the infrequent exacerbator group (without CVD: HR, 1.81 [95% CI, 1.47-2.22]; with CVD: HR, 1.92 [95% CI, 1.51-2.44]). This observation remained consistently significant in moderate to severe COPD subjects and the preserved ratio impaired spirometry population. In the mild COPD population, frequent exacerbators showed a trend toward more CVD events.

**Conclusions:** COPD exacerbations are associated with an increased risk of subsequent cardiovascular events in subjects with and without preexisting CVD. Patients with COPD experiencing frequent exacerbations may necessitate careful monitoring and additional management for subsequent potential CVD.

**Registration:** URL: <https://www.clinicaltrials.gov>; Unique identifier: [NCT00608764](https://www.clinicaltrials.gov/ct2/show/study/NCT00608764).

**Keywords:** COPD exacerbation; cardiovascular events; chronic obstructive pulmonary disease; clinical epidemiology; preserved ratio impaired spirometry.

SUPPLEMENTARY INFO

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# Defining the role of exertional hypoxemia and pulmonary vasoconstriction on lung function decline, morbidity, and mortality in patients with chronic obstructive lung disease – the PROSA study: rationale and study design

[Rainer Böger](#)<sup>1,2</sup>, [Juliane Hannemann](#)<sup>3,4</sup>

Affiliations expand

- PMID: 38816826
- DOI: [10.1186/s12890-024-03074-x](https://doi.org/10.1186/s12890-024-03074-x)

## Abstract

**Background:** Chronic obstructive lung disease (COPD) has diverse molecular pathomechanisms and clinical courses which, however, are not fully mirrored by current therapy. Intermittent hypoxemia is a driver of lung function decline and poor outcome, e.g., in patients with concomitant obstructive sleep apnea. Transient hypoxemia during physical exercise has been suggested to act in a similar manner. The PROSA study is designed to prospectively assess whether the clinical course of COPD patients with or without exertional desaturation differs, and to address potential pathophysiological mechanisms and biomarkers.

**Methods:** 148 COPD patients (GOLD stage 2-3, groups B or C) will undergo exercise testing with continuous pulse oximetry. They will be followed for 36 months by spirometry, echocardiography, endothelial function testing, and biomarker analyses. Exercise testing

will be performed by comparing the 6-min walk test (6MWT), bicycle ergometry, and a 15-sec breath-hold test. Exertional desaturation will be defined as  $SpO_2 < 90\%$  or  $\Delta SpO_2 \geq 4\%$  during the 6MWT. The primary endpoint will be the rate of decline of FEV1(LLN) between COPD patients with and without exertional desaturation.

**Discussion:** The PROSA Study is an investigator-initiated prospective study that was designed to prove or dismiss the hypothesis that COPD patients with exertional desaturation have a significantly more rapid rate of decline of lung function as compared to non-desaturators. A 20% difference in the primary endpoint was considered clinically significant; it can be detected with a power of 90%. If the primary endpoint will be met, exercise testing with continuous pulse oximetry can be used as a ubiquitously available, easy screening tool to prospectively assess the risk of rapid lung function decline in COPD patients at an early disease stage. This will allow to introduce personalized, risk-adapted therapy to improve COPD outcome in the long run. PROSA is exclusively funded by public funds provided by the European Research Council through an ERC Advanced Grant. Patient recruitment is ongoing; the PROSA results are expected to be available in 2028.

**Trial registration:** The PROSA Study has been prospectively registered at [clinicaltrials.gov](https://clinicaltrials.gov) (register no. [NCT06265623](https://clinicaltrials.gov/ct2/show/study/NCT06265623), dated 09.02.2024).

**Keywords:** 6-minute walk test; Chronic obstructive lung disease; Endothelium; Exercise testing; Exertional desaturation; Outcome; Prospective study.

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- [43 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

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[Review](#)



. 2024 May 30.

doi: 10.1080/14740338.2024.2362817. Online ahead of print.

# An overview of the efficacy and safety of $\beta_2$ -Adrenoceptor antagonists for the treatment of chronic obstructive pulmonary disease

[Maria Gabriella Matera](#)<sup>1</sup>, [Paola Rogliani](#)<sup>2</sup>, [Luigino Calzetta](#)<sup>3</sup>, [Mario Cazzola](#)<sup>2</sup>

Affiliations expand

- PMID: 38813912
- DOI: [10.1080/14740338.2024.2362817](https://doi.org/10.1080/14740338.2024.2362817)

## Abstract

**Introduction:** The safety of  $\beta_2$ -AR antagonists in the treatment of patients with COPD continues to be a topic of research and discussion within the medical community. Emerging evidence suggests potentially benefits in the management of this complex respiratory condition. However, antagonists display a minimal preference for  $\beta_2$ -AR over  $\beta_1$ -AR present a complex therapeutic challenge in COPD management, necessitating an understanding of small differences in their pharmacological profiles and clinical implications.

**Areas covered:** An overview of the mechanisms of action of  $\beta_2$ -AR antagonists and their potential impact on respiratory function, their pharmacological interactions, clinical implications, and future perspectives in COPD.

**Expert opinion:**  $\beta$ -Blockers have the potential to become a versatile class of therapeutic agents with benefits beyond their original cardiovascular use. However, the one-size-fits-all approach of prescribing  $\beta$ -blockers regardless of their receptor selectivity to COPD patients with concomitant heart disease may not be appropriate. Instead, it is advisable to develop an individualized treatment strategy based on a thorough assessment of the patient's

overall health. Further research efforts should focus on elucidating the optimal use  $\beta_2$ -AR antagonists in COPD, balancing cardiovascular benefits with potential respiratory risks to enhance outcomes and quality of life for individuals living with this debilitating respiratory condition.

**Keywords:** cardiovascular diseases; chronic obstructive pulmonary disease; interactions; lung function; risk assessment; B-adrenoceptors;  $\beta_2$ -adrenoceptor antagonists.

SUPPLEMENTARY INFO

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Heliyon



. 2024 May 14;10(10):e31201.

doi: 10.1016/j.heliyon.2024.e31201. eCollection 2024 May 30.

# [Exacerbation predictive modelling using real-world data from the myCOPD app](#)

[Henry M G Glyde](#)<sup>1</sup>, [Alison M Blythin](#)<sup>2</sup>, [Tom M A Wilkinson](#)<sup>3</sup>, [Ian T Nabney](#)<sup>4</sup>, [James W Dodd](#)<sup>5</sup>

Affiliations [expand](#)

- PMID: 38803869

- PMID: [PMC11128912](#)
- DOI: [10.1016/j.heliyon.2024.e31201](#)

## Abstract

**Background:** Acute exacerbations of COPD (AECOPD) are episodes of breathlessness, cough and sputum which are associated with the risk of hospitalisation, progressive lung function decline and death. They are often missed or diagnosed late. Accurate timely intervention can improve these poor outcomes. Digital tools can be used to capture symptoms and other clinical data in COPD. This study aims to apply machine learning to the largest available real-world digital dataset to develop AECOPD Prediction tools which could be used to support early intervention and improve clinical outcomes.

**Objective:** To create and validate a machine learning predictive model that forecasts exacerbations of COPD 1-8 days in advance. The model is based on routine patient-entered data from myCOPD self-management app.

**Method:** Adaptations of the AdaBoost algorithm were employed as machine learning approaches. The dataset included 506 patients users between 2017 and 2021. 55,066 app records were available for stable COPD event labels and 1263 records of AECOPD event labels. The data used for training the model included COPD assessment test (CAT) scores, symptom scores, smoking history, and previous exacerbation frequency. All exacerbation records used in the model were confined to the 1-8 days preceding a self-reported exacerbation event.

**Results:** The EasyEnsemble Classifier resulted in a Sensitivity of 67.0 % and a Specificity of 65 % with a positive predictive value (PPV) of 5.0 % and a negative predictive value (NPV) of 98.9 %. An AdaBoost model with a cost-sensitive decision tree resulted in a Sensitivity of 35.0 % and a Specificity of 89.0 % with a PPV of 7.08 % and NPV of 98.3 %.

**Conclusion:** This preliminary analysis demonstrates that machine learning approaches to real-world data from a widely deployed digital therapeutic has the potential to predict AECOPD and can be used to confidently exclude the risk of exacerbations of COPD within the next 8 days.

**Keywords:** Chronic obstructive pulmonary disease (COPD); Machine learning; Prediction models; mHealth.

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## Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Tom Wilkinson reports a relationship with my mhealth ltd that includes: board membership. Alison Blythin reports a relationship with my mhealth ltd that includes: employment. 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.

- [25 references](#)
- [6 figures](#)

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. 2024 May 9;10(10):e30920.

doi: 10.1016/j.heliyon.2024.e30920. eCollection 2024 May 30.

# [Clinical factors associated with smoking cessation among smokers with Chronic Obstructive Pulmonary Disease by sex: Longitudinal analyses from French smoking cessation services](#)

[Ingrid Allagbé](#)<sup>1,2</sup>, [Roche Nicolas](#)<sup>3</sup>, [Guillaume Airagnes](#)<sup>1,4</sup>, [Limosin Frédéric](#)<sup>5,6,7</sup>, [Abdel-Ali Boussadi](#)<sup>8,9</sup>, [Anne-Laurence Le Faou](#)<sup>1,3,2</sup>

Affiliations expand

- PMID: 38770314
- PMCID: [PMC11103529](#)
- DOI: [10.1016/j.heliyon.2024.e30920](#)

## Abstract

**Background:** Smoking is responsible for 80 % of cases of Chronic Obstructive Pulmonary Disease (COPD), while the prognosis is improved by smoking cessation (SC). We examined clinical factors associated with SC among smokers with COPD comparing women and men.

**Methods:** The study comprised a cohort of 1470 smokers who visited a SC service and completed at least 28-day of follow-up visits. The outcome was smoking status at follow-up (abstinence, reduction, no change). Abstinence was defined as continuous abstinence for at least 28 days, validated by the measurement of expired Carbon Monoxide. Reduction was defined as a halving of the baseline tobacco consumption.

**Results:** The average age of the population was 53 ( $\pm 11$ ) years and 58.2 % were women. Men were 2 years younger than women and consulted more likely after a hospital contact, whereas women consulted on their own initiative. Women more often had a depression history, whereas men had medical comorbidities and co-addictions. There was no significant difference by sex regarding the abstinence rate (41.0 % in women vs 40.7 in men,  $p > 0.9$ ). The factors significantly associated with higher abstinence rates in both sexes were: at least one previous quit attempt and number of follow-up visits  $\geq 4$ . The factors negatively associated with quitting in women were diabetes, intake of mood stabilizers and consuming more than 10 cigarettes per day while having a chronic bronchitis, taking antidepressants and having consumed cannabis in the last 30 days hampered SC in men.

**Conclusions:** Concerning factors associated with SC, few differences were found between female and male smokers suffering from COPD. However, due to the different medical and smoking behavior characteristics according to sex, it might be important to take these differences into account in order to provide tailored SC management.

**Keywords:** COPD; Nicotine replacement therapy; Smoking cessation; Smoking cessation services; Tobacco; Varenicline.

## Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Allagbé Ingrid: Pfizer grant for research and communication on CDTnet data. Roche Nicolas: Reports grants and personal fees from Boehringer Ingelheim, Pfizer and Novartis, personal fees from Teva, GSK, AstraZeneca, Chiesi, Mundipharma, Cipla, Sanofi, Sandoz, 3 M, Zambon, outside the submitted work. Airagnes Guillaume: received fees from Lundbeck, Pierre Fabre and Pfizer, unrelated to the article. Limosin Frédéric: received fees from Lundbeck, unrelated to the article. Le Faou Anne-Laurence: conference fees in a conference organized by Pfizer in 2021, unrelated to the article. 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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. 2024 May 30;63(5):2301037.

doi: 10.1183/13993003.01037-2023. Print 2024 May.

## [The association of blood eosinophil counts and FEV<sub>1</sub> decline: a cohort study](#)

[Yun Soo Hong](#)<sup>1,2,3</sup>, [Hye Yun Park](#)<sup>4,3</sup>, [Seungho Ryu](#)<sup>5,6,7</sup>, [Sun Hye Shin](#)<sup>4</sup>, [Di Zhao](#)<sup>2,7</sup>, [Dave Singh](#)<sup>8</sup>, [Eliseo Guallar](#)<sup>2,7</sup>, [Juhee Cho](#)<sup>2,7</sup>, [Yoosoo Chang](#)<sup>9,6,7,10</sup>, [Seong Yong Lim](#)<sup>11,10</sup>

Affiliations [expand](#)

- PMID: 38636990

- DOI: [10.1183/13993003.01037-2023](https://doi.org/10.1183/13993003.01037-2023)

## Abstract

**Background:** Accelerated lung function decline is characteristic of COPD. However, the association between blood eosinophil counts and lung function decline, accounting for current smoking status, in young individuals without prevalent lung disease is not fully understood.

**Methods:** This is a cohort study of 629 784 Korean adults without COPD or a history of asthma at baseline who participated in health screening examinations including spirometry and differential white blood cell counts. We used a linear mixed-effects model to estimate the annual change in forced expiratory volume in 1 s (FEV<sub>1</sub>) (mL) by baseline blood eosinophil count, adjusting for covariates including smoking status. In addition, we performed a stratified analysis by baseline and time-varying smoking status.

**Results:** During a mean follow-up of 6.5 years (maximum 17.8 years), the annual change in FEV<sub>1</sub> (95% CI) in participants with eosinophil counts <100, 100-199, 200-299, 300-499 and ≥500 cells·μL<sup>-1</sup> in the fully adjusted model were -23.3 (-23.9--22.7) mL, -24.3 (-24.9--23.7) mL, -24.8 (-25.5--24.2) mL, -25.5 (-26.2--24.8) mL and -26.8 (-27.7--25.9) mL, respectively. When stratified by smoking status, participants with higher eosinophil count had a faster decline in FEV<sub>1</sub> than those with lower eosinophil count in both never- and ever-smokers, which persisted when time-varying smoking status was used.

**Conclusions:** Higher blood eosinophil counts were associated with a faster lung function decline among healthy individuals without lung disease, independent of smoking status. The findings suggest that higher blood eosinophil counts contribute to the risk of faster lung function decline, particularly among younger adults without a history of lung disease.

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## Conflict of interest statement

Conflict of interest: D. Singh reports personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Menarini, Mundipharma, Novartis, Peptinnovate, Pfizer, Pulmatrix, Theravance and Verona, outside the submitted work. The remaining authors declare no competing interests.

## Comment in

- [Blood eosinophils and lung function loss: from passive prediction to active prevention?](#)  
Ramakrishnan S, Montgomery B, Pavord ID. Eur Respir J. 2024 May 30;63(5):2400812. doi: 10.1183/13993003.00812-2024. Print 2024 May. PMID: 38816039 No abstract available.

#### SUPPLEMENTARY INFO

MeSH termsexpand

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Respir Med



. 2024 May 29:107683.

doi: 10.1016/j.rmed.2024.107683. Online ahead of print.

## [Patients with bronchiectasis have a lower combined risk of cardiovascular risk factors and cardiovascular comorbidity compared to patients with COPD](#)

[Martina Lo Casto](#)<sup>1</sup>, [Stefania Marino](#)<sup>1</sup>, [Marta M Zammuto](#)<sup>1</sup>, [Alessandra Tomasello](#)<sup>1</sup>, [Alida Benfante](#)<sup>1</sup>, [Nicola Scichilone](#)<sup>1</sup>, [Salvatore Battaglia](#)<sup>2</sup>

Affiliations expand

- PMID: 38821218

- DOI: [10.1016/j.rmed.2024.107683](https://doi.org/10.1016/j.rmed.2024.107683)

## Abstract

**Introduction and objectives:** Chronic respiratory diseases are associated with an increased risk of cardiovascular diseases (CVD); however, it is unknown whether some respiratory diseases are at higher risk than others. In this perspective, head-to-head studies comparing bronchiectasis and chronic obstructive pulmonary disease (COPD) are encouraged. We explored whether the prevalence of cardiovascular risk factors (diabetes mellitus and hyperlipidemia) and cardiovascular comorbidity (systemic hypertension, ischemic heart diseases, cardiac arrhythmia, stroke) are different in these two diseases.

**Methods:** The present retrospective case-control study aimed to compare patients with bronchiectasis with age and sex-matched individuals with COPD. A total of 63 patients with bronchiectasis and 63 with COPD were retained for analysis.

**Results:** Patients with bronchiectasis had a lower risk of systemic hypertension (OR 0.42 (C.I. 0.20 to 0.87)) and diabetes mellitus (OR 0.28 (C.I. 0.09 to 0.81)). In contrast, ischemic heart diseases, cardiac arrhythmia, stroke, and hyperlipidemia did not differ between the two groups. Logistic regression analysis showed that age, male sex, and COPD remain independent risk factors for having at least one condition of a composite index including the above-mentioned CVD and CV risk factors. In detail, a patient with COPD has a risk of 4.648 times (C.I. 1.48 to 15.78) for having at least one CVD compared with a patient with bronchiectasis.

**Conclusions:** The current findings suggest that subjects with bronchiectasis may experience lower cardiovascular risk than those with COPD. Larger studies are needed to confirm this preliminary observation and its clinical implications.

**Keywords:** Bronchiectasis; COPD; cardiovascular diseases; comorbidity.

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## 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.

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Respir Res



. 2024 May 29;25(1):227.

doi: 10.1186/s12931-024-02769-3.

# [Expression of glucocorticoid receptor and HDACs in airway smooth muscle cells is associated with response to steroids in COPD](#)

[Liang Zhou](#)<sup>1</sup>, [Michael Roth](#)<sup>1</sup>, [Eleni Papakonstantinou](#)<sup>1,2,3,4</sup>, [Michael Tamm](#)<sup>1,2</sup>, [Daiana Stolz](#)<sup>5,6,7,8</sup>

Affiliations [expand](#)

- PMID: 38812021
- PMCID: [PMC11137987](#)
- DOI: [10.1186/s12931-024-02769-3](#)

## Abstract

**Background:** Steroid insensitivity in Chronic Obstructive Pulmonary Disease (COPD) presents a problem for controlling the chronic inflammation of the airways. The glucocorticoid receptor (GR) mediates the intracellular signaling of inhaled corticosteroids (ICS) by interacting with transcription factors and histone deacetylases (HDACs). The aim of this study was to assess if COPD patients' response to ICS in vivo, may be associated with

the expression of GR, the complex of GR with transcription factors, and the expression of various HDACs in vitro.

**Methods:** Primary airway smooth muscle cells (ASMC) were established from endobronchial biopsies obtained from patients with asthma (n = 10), patients with COPD (n = 10) and subjects that underwent diagnostic bronchoscopy without pathological findings and served as controls (n = 6). ASMC were also established from 18 COPD patients, 10 responders and 8 non-responders to ICS, who participated in the HISTORIC study, an investigator-initiated and driven clinical trial that proved the hypothesis that COPD patients with high ASMC in their endobronchial biopsies respond better to ICS than patients with low ASMC. Expression of GR and its isoforms GR $\alpha$  and GR $\beta$  and HDACs was investigated in primary ASMC in the absence or in the presence of dexamethasone (10<sup>-8</sup>M) by western blotting. The complex formation of GR with transcription factors was assessed by co-immunoprecipitation.

**Results:** Expression of GR and its isoform GR $\alpha$  but not GR $\beta$  was significantly reduced in ASMC from COPD patients as compared to controls. There were no significant differences in the expression of GR, GR $\alpha$  and GR $\beta$  between responders and non-responders to ICS. However, treatment with dexamethasone upregulated the expression of total GR (p = 0.004) and GR $\alpha$  (p = 0.005) after 30 min in responders but not in non-responders. The formation of the complex GR-c-Jun was increased 60 min after treatment with dexamethasone only in responders who exhibited significantly lower expression of HDAC3 (p = 0.005) and HDAC5 (p < 0.0001) as compared to non-responders.

**Conclusions:** These data suggest that ASMC from COPD patients who do not respond to treatment with ICS, are characterized by reduced GR-c-Jun complex formation and increased expression of HDAC3 and HDAC5.

**Trial registration:** ISRCTN11017699 (Registration date: 15/11/2016).

**Keywords:** Airway smooth muscle cells; Chronic obstructive pulmonary disease; Glucocorticoid receptor; Glucocorticoid sensitivity; Histone deacetylases.

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## Conflict of interest statement

The authors declare no competing interests.

- [61 references](#)
- [7 figures](#)

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Randomized Controlled Trial

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. 2024 May 29;25(1):228.

doi: 10.1186/s12931-024-02854-7.

# [Nebulised interferon beta-1a \(SNG001\) in the treatment of viral exacerbations of COPD](#)

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Affiliations expand

- PMID: 38811970
- PMCID: [PMC11138078](#)
- DOI: [10.1186/s12931-024-02854-7](#)

# Abstract

**Background:** Respiratory viral infections are major drivers of chronic obstructive pulmonary disease (COPD) exacerbations. Interferon- $\beta$  is naturally produced in response to viral infection, limiting replication. This exploratory study aimed to demonstrate proof-of-mechanism, and evaluate the efficacy and safety of inhaled recombinant interferon- $\beta$ 1a (SNG001) in COPD. Part 1 assessed the effects of SNG001 on induced sputum antiviral interferon-stimulated gene expression, sputum differential cell count, and respiratory function. Part 2 compared SNG001 and placebo on clinical efficacy, sputum and serum biomarkers, and viral clearance.

**Methods:** In Part 1, patients (N = 13) with stable COPD were randomised 4:1 to SNG001 or placebo once-daily for three days. In Part 2, patients (N = 109) with worsening symptoms and a positive respiratory viral test were randomised 1:1 to SNG001 or placebo once-daily for 14 days in two Groups: A (no moderate exacerbation); B (moderate COPD exacerbation [i.e., acute worsening of respiratory symptoms treated with antibiotics and/or oral corticosteroids]).

**Results:** In Part 1, SNG001 upregulated sputum interferon gene expression. In Part 2, there were minimal SNG001-placebo differences in the efficacy endpoints; however, whereas gene expression was initially upregulated by viral infection, then declined on placebo, levels were maintained with SNG001. Furthermore, the proportion of patients with detectable rhinovirus (the most common virus) on Day 7 was lower with SNG001. In Group B, serum C-reactive protein and the proportion of patients with purulent sputum increased with placebo (suggesting bacterial infection), but not with SNG001. The overall adverse event incidence was similar with both treatments.

**Conclusions:** Overall, SNG001 was well-tolerated in patients with COPD, and upregulated lung antiviral defences to accelerate viral clearance. These findings warrant further investigation in a larger study.

**Trial registration:** EU clinical trials register (2017-003679-75), 6 October 2017.

**Keywords:** Biomarkers; Chronic obstructive pulmonary disease; Interferons; Symptom flare up.

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## Conflict of interest statement

In addition to writing support, the authors have the following conflicts of interest to declare.

PDM is an employee of Synairgen Research plc, the parent company of Synairgen Research Ltd (and such costs are met by Synairgen Research Ltd), the sponsor of this trial, and owns shares and has options on shares in Synairgen plc.

JLB is an employee of Synairgen Research Ltd, the sponsor of this trial, and has options on shares in Synairgen plc.

VJT is an employee of Synairgen Research Ltd, the sponsor of this trial, and owns shares and has options on shares in Synairgen plc.

TNB provided statistical support, programming and consultancy to Synairgen Research Ltd via a contract with his employer, Veramed Ltd.

CN has no other conflicts of interest to disclose.

MM provided consulting services to Synairgen Research Ltd, the sponsor of this trial, with all payments made to tranScrip Ltd.

MGC declares grants and funding to his institution from AstraZeneca for investigator-sponsored and AstraZeneca-sponsored studies, to his institution from Phillips Research for collaborative research, and to him and his institution from the National Institute for Health and Care Research, consulting fees from Synairgen PLC, AstraZeneca, and Chiesi, honoraria for lectures/educational meetings from AstraZeneca, Chiesi, Boehringer Ingelheim, GlaxoSmithKline, and Pfizer, and support to attend congresses from AstraZeneca and Chiesi, all outside the scope of this manuscript.

DS declares the receipt of consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Synairgen, Teva, Theravance, and Verona, all outside the scope of this manuscript.

RC declares an AstraZeneca grant for an investigator-led study within a Medical Research Council project, payment or honoraria for lectures from GlaxoSmithKline, AstraZeneca, Teva, Chiesi, Sanofi, and Novartis, support for attending conferences from Chiesi, Sanofi, and GlaxoSmithKline, and participation in advisory boards for GlaxoSmithKline, AstraZeneca, and Celltrion, all outside the scope of this manuscript.

BL reports investigator fees and fees for the conduct of the current study. Outside the scope of this manuscript, he has no other conflicts of interest to disclose.

KL is an employee of Synairgen Research Ltd, the sponsor of this trial, and has options on shares in Synairgen plc.

SR is an employee of Synairgen Research Ltd, the sponsor of this trial, and has options on shares in Synairgen plc.

SD is an employee of Synairgen Research Ltd, the sponsor of this trial, and owns shares and has options on shares in Synairgen plc.

FJG declares the receipt of consulting fees paid to tranScrip Ltd from Synairgen Research plc, the sponsor of this trial, and participation in a Data Safety Monitoring Board for Synairgen. She is also president of the Faculty of Pharmaceutical Medicine of three UK Royal College of Physicians.

STH received payments as non-executive director of, and owns shares in, Synairgen plc, the parent company of the sponsor of this trial.

RD declares the receipt of consulting fees and payment for participation in a Data Safety Monitoring Board or Advisory Board from Synairgen Research Ltd, the sponsor of this trial. RD owns shares in Synairgen plc, the parent company of the sponsor of this trial. Outside the trial, he declares payment or honoraria from Regeneron, GlaxoSmithKline and Kymab.

TMAW received research funding and consultancy fees from Synairgen Research Ltd, the sponsor of this trial. Outside the trial, he declares research grants from the National Institute for Health and Care Research, Medical Research Council, Bergenbio, AstraZeneca, UCB and Janssen, consultancy fees from AstraZeneca, Valneva, Olam Pharma, Janssen and My mHealth, lecture fees from AstraZeneca, Boehringer Ingelheim and Roche, participation on a Data Safety Monitoring Board for Valneva, and that he holds stock in My mHealth.

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. 2024 May 29:2400172.

doi: 10.1183/13993003.00172-2024. Online ahead of print.

## [Inhaled Treprostinil in Pulmonary Hypertension Associated with COPD: PERFECT study results](#)

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- PMID: 38811045
- DOI: [10.1183/13993003.00172-2024](https://doi.org/10.1183/13993003.00172-2024)

## Abstract

**Introduction:** Pulmonary hypertension accompanying chronic obstructive pulmonary disease (PH-COPD) is associated with worse outcomes than COPD alone. There are currently no approved therapies to treat PH-COPD. The PERFECT study ([NCT03496623](https://clinicaltrials.gov/ct2/show/study/NCT03496623)) evaluated the safety and efficacy of inhaled treprostinil (iTRE) in this patient population.

**Methods:** Patients with PH-COPD (mean pulmonary artery pressures  $\geq 30$  mmHg and pulmonary vascular resistances  $\geq 4$  Wood units) were enrolled in a multicentre, randomised (1:1), double-blind, placebo-controlled, 12-week, crossover study. A contingent parallel design was also prespecified and implemented, based on a blinded interim analysis of missing data. Patients received treatment with iTRE up to 12 breaths (72  $\mu$ g) 4 times daily or placebo. The primary efficacy end point was change in peak 6-minute walk distance (6 MWD) at Week 12.

**Results:** In total, 76 patients were randomised, 64 in the original crossover design and 12 in the contingent parallel design; 66 patients received iTRE and 58 received placebo. The study was terminated early at the recommendation of the Data and Safety Monitoring Committee based on the totality of evidence that iTRE increased the risk of serious adverse events and suggestive evidence of an increased risk of mortality. The change in 6MWD was numerically worse with iTRE exposure than with placebo exposure.

**Conclusions:** The risk-benefit observations associated with iTRE in patients with PH-COPD did not support continuation of the PERFECT study. The results of this study do not support iTRE as a viable treatment option in patients with PH-COPD.

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. 2024 May 29:2400163.

doi: 10.1183/13993003.00163-2024. Online ahead of print.

# ChatGPT versus Bing: Clinicians Assessment of the Accuracy of AI Platforms in Responding to COPD Questions

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- PMID: 38811043
- DOI: [10.1183/13993003.00163-2024](https://doi.org/10.1183/13993003.00163-2024)

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. 2024 May 29;11(3):247-260.

doi: 10.15326/jcopdf.2024.0527.

# The COPD Foundation on Its Twentieth Anniversary

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- PMID: 38809791
- DOI: [10.15326/jcopdf.2024.0527](https://doi.org/10.15326/jcopdf.2024.0527)

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**Keywords:** COPD Foundation; COPD education; COPD programs; patient advocacy.

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. 2024 May 29;11(3):261-269.

doi: 10.15326/jcopdf.2023.0477.

# COPD: Iron Deficiency and Clinical Characteristics in Patients With and Without Chronic Respiratory Failure

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- PMID: 38575374
- DOI: [10.15326/jcopdf.2023.0477](https://doi.org/10.15326/jcopdf.2023.0477)

**Free article**

## Abstract

**Background:** The prevalence of iron deficiency in patients with chronic obstructive pulmonary disease (COPD) varies in previous studies. We aimed to assess its prevalence according to 3 well-known criteria for iron deficiency, its associations with clinical characteristics of COPD, and mortality.

**Methods:** In a cohort study consisting of 84 COPD patients, of which 21 had chronic respiratory failure, and 59 were non-COPD controls, ferritin, transferrin saturation (TSat), and mortality across 6.5 years were assessed. Associations between clinical characteristics and iron deficiency were examined by logistic regression, while associations with mortality were assessed in mixed effects Cox regression analyses.

**Results:** The prevalence of iron deficiency in the study population was 10%-43% according to diagnostic criteria, and was consistently higher in individuals with COPD, peaking at 71% in participants with chronic respiratory failure. Ferritin < cutoff was significantly associated with forced expiratory volume in 1 second (FEV<sub>1</sub>) (odds ratio [OR] 0.33 per liter increase), smoking (OR 3.2), and cardiovascular disease (OR 4.7). TSat < 20% was associated with body mass index (BMI) (OR 1.1 per kg/m<sup>2</sup> increase) and hemoglobin (OR 0.65 per g/dL increase). The combined criterion of low ferritin and TSat was only associated with FEV<sub>1</sub> (OR 0.39 per liter increase). Mortality was not significantly associated with iron deficiency (hazard ratio [HR] 1.2-1.8).

**Conclusion:** The prevalence of iron deficiency in the study population increased with increasing severity of COPD. Iron deficiency, defined by ferritin < cutoff, was associated with bronchial obstruction, current smoking, and cardiovascular disease, while TSat < 20% was associated with reduced levels of hemoglobin and increased BMI. Iron deficiency was not associated with increased mortality.

**Keywords:** COPD; anemia; chronic respiratory failure; iron deficiency; polycythemia.

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. 2024 May 29;11(3):326-330.

doi: 10.15326/jcopdf.2024.0496.

## [From Invisibility to Inclusion: A Call to Action to Address COPD Disparities in the Lesbian, Gay, Bisexual, Transgender, and Queer+ Community](#)

[Ninand T Maniar](#)<sup>1,2</sup>, [M Bradley Drummond](#)<sup>3</sup>

Affiliations expand

- PMID: 38563736
- DOI: [10.15326/jcopdf.2024.0496](https://doi.org/10.15326/jcopdf.2024.0496)

**Free article**

## Abstract

COPD is a significant cause of morbidity and mortality both in the United States and worldwide. Lesbian, gay, bisexual, transgender, or queer + (LGBTQ+) individuals (the plus sign indicates inclusion of people who are questioning, intersex, asexual, or who hold other gender/sex/romantic identities not specifically identified) have a higher rate of tobacco smoking, predisposing them to an increased risk of developing COPD. Despite this risk, the burden of COPD in LGBTQ+ individuals is not known. Moreover, there is limited focus on efforts to identify and reduce disease risk in this population. In this perspective, we present the results of a focused literature review of COPD in LGBTQ+ populations. We found only 8 studies that reported the prevalence of COPD in different subgroups of the LGBTQ+ population. All studies found an increased prevalence of COPD in the studied LGBTQ+ sub-groups compared to their heterosexual and/or cisgender counterparts. We propose a 3-pronged call to action to improve the care of LGBTQ+ people with COPD. First, we must improve awareness and education about COPD in the LGBTQ+ community through the effective development and dissemination of educational resources to LGBTQ+ people and their health care providers. Second, we call for prevention and intervention efforts through targeted tobacco cessation initiatives and case-finding via screening spirometry among symptomatic LGBTQ+ smokers. Finally, well-designed cohort studies are required to better characterize the COPD burden among LGBTQ+ populations. With targeted approaches in these 3 areas, we can improve the health of this vulnerable population, historically marginalized by current COPD research efforts.

**Keywords:** chronic obstructive; health equity; pulmonary disease; sexual and gender minorities.

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Respir Med



. 2024 May 28:107682.

doi: 10.1016/j.rmed.2024.107682. Online ahead of print.

# Correlation of fractional exhaled nitric oxide (FeNO) and clinical outcomes in patients with chronic obstructive pulmonary disease: A prospective cohort study

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- PMID: 38815659
- DOI: [10.1016/j.rmed.2024.107682](https://doi.org/10.1016/j.rmed.2024.107682)

## Abstract

**Background:** Fractional exhaled nitric oxide (FeNO) is an acceptable and noninvasive marker for defining eosinophilic airway inflammation. Further study is necessary to clarify the role of FeNO in patients with chronic obstructive pulmonary disease (COPD). This study aimed to determine the association between FeNO levels and clinical outcomes.

**Methods:** A prospective observational study was conducted at Songklanagarind Hospital from October 2020 to November 2022. FeNO testing and spirometry were performed at the initial visit and 12-month follow-up. Exacerbation, hospitalization, lung function decline, and all-cause mortality were analyzed to determine the association between FeNO levels and clinical outcomes.

**Results:** A total of 60 patients with COPD were enrolled, 88.3% of whom were male, with a mean age of 71.3±9.5 years. There were 18 patients (30%) in the high FeNO group (≥25 ppb) and 42 patients (70%) in the low (<25 ppb) FeNO group. The mean blood eosinophil count (BEC) was significantly higher in the high FeNO group (p<0.001). After a 12-month follow-up period, high FeNO group had higher exacerbation events (HR of 1.26, 95% confidence interval (CI), 1.10-1.97, p 0.025). Hospitalization and mortality rates were significantly higher in the high FeNO group. Regardless of the inhaled corticosteroids used, patients with high BEC and FeNO levels tended to have a greater risk of exacerbation.

**Conclusion:** In patients with COPD, FeNO levels are strongly correlated with BEC. Poor clinical outcomes were reported in patients with high FeNO levels. FeNO may be a useful biomarker for predicting clinical outcomes in patients with COPD.

**Keywords:** blood eosinophil; chronic obstructive pulmonary disease; exacerbation; fractional exhaled nitric oxide; hospitalization; mortality.

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## Conflict of interest statement

Declaration of Competing Interest: None.

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. 2024 May 28:107680.

doi: 10.1016/j.rmed.2024.107680. Online ahead of print.

# Risk of pharmacological treatment of anxiety and depression after admission for acute exacerbation of chronic obstructive pulmonary disease

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Affiliations expand

- PMID: 38815658
- DOI: [10.1016/j.rmed.2024.107680](https://doi.org/10.1016/j.rmed.2024.107680)

## Abstract

**Background:** Anxiety and depression are very common in patients with COPD and may lead to lower quality of life and higher risk of exacerbations and mortality. This study aimed to examine the incidence of anxiety and depression within one year after admission with acute exacerbation in COPD (AECOPD). The secondary aim was to examine the characteristics of the patients who develop anxiety and depression.

**Methods:** This retrospective cohort study used the Danish National Patient Registry. Patients aged 40-90 years admitted for COPD between 01.01.99 and 31.12.18 were included. Patients with mental disorders within 10 years before admission were excluded. Age, sex, educational level, inhaled medication, and comorbidities were evaluated. Anxiety or depression were defined by redemption of anxiolytics or antidepressants within one year after admission.

**Results:** We included 97,929 patients. Anxiolytics and antidepressants were redeemed by 4 and 5% of patients respectively. Higher age, male sex, treatment with short acting  $\beta$ 2-agonists and short acting muscarinic antagonists, cancer and heart failure were positively associated to risk of anxiety or depression, while diabetes and treatment with triple inhalation therapy showed an inverse association.

**Conclusion:** Respectively four and five per cent of patients redeemed anxiolytics and antidepressants within the first year after their first severe AECOPD. Several patient characteristics were significantly associated to risk of anxiety or depression. The results from this study support that there is a risk of anxiety and depression after AECOPD in addition to the known risk of preexisting anxiety and depression.

**Keywords:** Anxiety; Chronic obstructive pulmonary disease; Epidemiology; comorbidities; depression.

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## Conflict of interest statement

Declaration of Competing Interest There is no conflict of interest.

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. 2024 May 28:12:2050313X241256862.

doi: 10.1177/2050313X241256862. eCollection 2024.

# [Acute ischemic colitis complicating an exacerbation of chronic obstructive pulmonary disease: A case report of gut-lung crosstalk](#)

[Zakhama Mejda](#)<sup>1</sup>, [Nciri Alaa](#)<sup>1</sup>, [Bellalah Ahlem](#)<sup>2</sup>, [Loghmari Mohamed Hichem](#)<sup>1</sup>, [Guediche Arwa](#)<sup>1</sup>, [Jemni Imen](#)<sup>1</sup>, [Nabil Ben Chaabene](#)<sup>1</sup>, [Zakhama Abdelfattah](#)<sup>2</sup>, [Safer Leila](#)<sup>2</sup>

Affiliations expand

- PMID: 38812834
- PMCID: [PMC11135070](#)
- DOI: [10.1177/2050313X241256862](#)

## Abstract

Acute ischemic colitis is a pathology as frequent as it is serious and requires urgent management. It's often occurring in a context of particular thromboembolic or hypovolemic risk, but certain clinical situations are not commonly known to provide mesenteric ischemia. Herein, we report the case of a 47-year-old man who presented with a severe acute colitis occurring in the course of acute exacerbation of a chronic obstructive pulmonary diseases with maintained stability of hemodynamic state. The diagnosis of acute ischemic colitis complicating an exacerbation of chronic obstructive pulmonary diseases was made. A clinical and biological improvement quickly marked the patient's condition after the management of the respiratory problem.

**Keywords:** Mesenteric ischemia; chronic obstructive pulmonary disease; corticosteroids; exacerbation; ischemic colitis.

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## Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

- [13 references](#)
- [2 figures](#)

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BMC Public Health



. 2024 May 28;24(1):1423.

doi: 10.1186/s12889-024-18911-1.

# [Epidemiological characteristics of asthma-COPD overlap, its association with all-cause mortality, and the mediating role of depressive symptoms: evidence from NHANES 2005–2018](#)

[Meng Zhu](#) <sup>#1,2</sup>, [An Chen](#) <sup>#3,4</sup>

Affiliations [expand](#)

- PMID: 38807148
- PMCID: [PMC11134654](#)
- DOI: [10.1186/s12889-024-18911-1](#)

## Abstract

**Background:** Asthma-COPD overlap (ACO) is a distinct and intricate respiratory condition that requires specific attention and management. The objective of this cohort study was to examine the epidemiological characteristics of ACO, explore the association between ACO and all-cause mortality, and investigate the potential mediating role of depressive symptoms in this association.

**Methods:** This retrospective cohort study used data from the National Health and Nutrition Examination Survey (NHANES) 2005-2018 and National Death Index (NDI) 2019. A total of 22,745 participants were included: 705 with ACO, 2352 with asthma-only, 853 with COPD-only, and 18,835 without asthma or COPD. The non-ACO group (N = 22,040) referred to the individuals without ACO. Statistical tests were employed to assess differences in some characteristics between the ACO group and the other groups. Cox proportional hazards models were applied to evaluate the relationship between ACO and all-cause mortality, estimating hazard ratios (HR) with 95% confidence intervals. Mediation analysis was conducted to investigate the potential mediating effects of depressive symptoms on the association of ACO with all-cause mortality.

**Results:** The prevalence of ACO was 3.10% in our study population. Compared to the non-ACO participants, the ACO participants exhibited significantly different characteristics, including higher age, a lower family income-to-poverty ratio, a higher body mass index, higher rates of comorbidities i.e., hypertension, diabetes, hyperlipidemia, cardiovascular disease, and cancer, poorer dietary habits, and a higher rate of depressive disorders. Compared to the participants without ACO, the participants with ACO exhibited a significant increase in all-cause mortality (HR = 1.908, 95%CI 1.578-1.307,  $p < 0.001$ ). The proportions mediated by depressive symptoms for ACO -associated all-cause mortality were 8.13% (CI: 4.22%-14.00%,  $p < 0.001$ ).

**Conclusions:** This study revealed a strong relationship between ACO and all-cause mortality and uncovered a potential psychological mechanism underlying this relationship. Our study indicates the possible necessity of offering comprehensive care to ACO patients, encompassing early detection, lifestyle guidance, and mental health support. Nevertheless, due to the limitations in the study design and the dataset, the results should be interpreted with caution.

**Keywords:** All-cause mortality; Asthma-COPD overlap; Depressive symptoms; Mediation analysis.

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## Conflict of interest statement

The authors declare no competing interests.

- [79 references](#)
- [1 figure](#)

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Multicenter Study

BMJ Open

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. 2024 May 28;14(5):e080518.

doi: 10.1136/bmjopen-2023-080518.

# [Design of the multicentre randomised controlled BENTO trial to demonstrate patient-relevant benefit of bronchoscopic lung volume reduction using thermal vapour ablation in the German healthcare system for patients with upper lobe emphysema: a study protocol](#)

[Konstantina Kontogianni](#)<sup>1,2</sup>, [Kaid Darwiche](#)<sup>3</sup>, [Ralf Harto Huebner](#)<sup>4</sup>, [Fathema Hassinger](#)<sup>5</sup>, [Thomas Riemer](#)<sup>5</sup>, [Felix Jf Herth](#)<sup>6,2</sup>, [Judith Brock](#)<sup>6,2</sup>

Affiliations [expand](#)

- PMID: 38806430

- PMID: [PMC11138281](#)
- DOI: [10.1136/bmjopen-2023-080518](#)

## Abstract

**Introduction:** Application of vapour ablation as a novel approach to lung volume reduction has positive effects in patients with severe emphysema. The BENTO study is a randomised, controlled, open, multicentre trial, to assess the effects of bronchoscopic thermal vapour ablation (BTVA) in the German healthcare system.

**Methods and analysis:** Patients with bilateral heterogeneous emphysema of the upper lobes in Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 3/4 will be enrolled in this trial and will receive either standard medical management alone (according to GOLD guidelines) or BTVA treatment with the InterVapor system together with standard medical management. Patients will be randomised in a 2:1 ratio (treatment group:control group). A total of 224 patients will be enrolled at 15 study sites. The primary endpoint is the change in patient-reported disease-specific quality of life, as measured by the St George's Respiratory Questionnaire for chronic obstructive pulmonary disease patients between randomisation and the 9-month follow-up visit. Secondary endpoints include adverse events, mortality, vital status, changes in lung function parameters, exercise capacity and other efficacy measures at 3, 9 and 12 months. The BENTO trial was commissioned by the German Federal Joint Committee, to demonstrate that this approach is an efficient and safe treatment option in the German healthcare system.

**Ethics and dissemination:** The protocol has been approved by the lead ethics committee in Germany (Ethics Committee of the Medical Faculty of Heidelberg) and until present also by the following ethics committees: Ethics Committee of the Medical Faculty of Duisburg-Essen, Ethics Committee of the Medical Faculty of Martin-Luther-University Halle-Wittenberg, Ethics Committee of the State Medical Association of Hessen, Ethics Commission of the State Office for Health and Social Affairs of the State of Berlin, Ethics Committee of the Medical Faculty of Greifswald. The results will be published in a peer-reviewed journal.

**Trial registration number:** [NCT05717192](#).

**Keywords:** Bronchoscopy; Emphysema; Thoracic medicine.

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## Conflict of interest statement

Competing interests: KK reports honoraria for lectures, presentations or educational events from AstraZeneca, streamed up and Berlin Chemie, lecturing honoraria with payments made to the institution from and CSL Behring and Olympus Medical and support for attending meetings and travel from Boston Scientific and AstraZeneca, all outside the submitted work. KD reports consulting fees from Bess, Lys Medical and PulmonX, honoraria or payment for lectures and presentations from Bess, Boston Scientific, Böhringer I., Broncus Medical, Fujifilm, FreeFlow, Lys Medical, Morair, Medtech, Medtronic, Olympus, Storz, PulmonX and participation on a Data Safety Monitoring Board or Advisory Board for FujiFilm, Bess, Lys Medical. RHH reports payment or honoraria for lectures and presentations from PulmonX. FH reports salary payments from IHF Ludwigshafen. TR reports salary payments from IHF Ludwigshafen. FJFH reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Pulmonx and Uptake Medical. JB reports grants or contracts from Gräfin Beatrice von Hardenberg Stiftung, consulting fees from Intuitive Surgical, Boehringer Ingelheim, Astra Zeneca and payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Astra Zeneca, Boehringer Ingelheim, Berlin Chemie, Olympus and streamed up.

- [13 references](#)
- [1 figure](#)

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. 2024 May 28;69(6):713-723.

doi: 10.4187/respcare.11656.

# Barriers to Pulmonary Rehabilitation

[Carolyn L Rochester](#)<sup>1</sup>

Affiliations expand

- PMID: 38806224
- DOI: [10.4187/respcare.11656](https://doi.org/10.4187/respcare.11656)

## Abstract

Pulmonary rehabilitation (PR) is one of the most effective therapies for chronic respiratory diseases, yet it is significantly underutilized. There are several patient-related, geographic, societal, and health system-related barriers to PR. People with chronic respiratory disease face a collectively high burden of treatments including health care provider visits, medications, oxygen and other durable medical equipment, and providers' recommendation to undertake PR may be considered an added burden more than a likely benefit. Transportation difficulties, lack of insurance coverage, competing time priorities, low knowledge of PR, lack of perceived likely benefit, comorbidities, and other factors also pose obstacles to participation in PR for patients. Geographic availability of PR is heterogenous; in the United States, out-patient center-based PR programs are often not available within close proximity to patients' residence, posing barriers to patients' access to it. PR programs are lacking altogether in many areas; rural areas are particularly affected. Existing PR programs are often poorly funded and underresourced. Socioeconomic and racial disparities also influence patients' likelihood of receiving PR. Also, health care professionals (HCPs) often do not refer their patients with chronic respiratory disease to PR, owing to a lack of knowledge and awareness of its content and benefits, patient candidacy, or of the referral process. A limited number of multidisciplinary HCPs trained in PR likely also contributes to limited access to PR for patients. Collectively, these multifaceted barriers to PR create unacceptable health care disparities. Strategies to address barriers to PR are urgently needed in order to enable individuals who need to receive it.

**Keywords:** access; barriers; chronic respiratory diseases; geographic; health-system; patient; pulmonary rehabilitation.

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## Conflict of interest statement

Dr Rochester discloses relationships with Boehringer Ingelheim, GSK, and AstraZeneca.

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Editorial

Respirology

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. 2024 May 28.

doi: 10.1111/resp.14758. Online ahead of print.

# Treatable traits—Where we are, where we are headed

[Vanessa Marie McDonald](#)<sup>1,2,3</sup>, [Peter Gerard Gibson](#)<sup>1,2,3</sup>

Affiliations expand

- PMID: 38804093
- DOI: [10.1111/resp.14758](https://doi.org/10.1111/resp.14758)

*No abstract available*

**Keywords:** COPD; asthma; management.

- [22 references](#)

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Review

Respir Care

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. 2024 May 28;69(6):724-739.

doi: 10.4187/respcare.11609.

# [Maintenance Pulmonary Rehabilitation: An Update and Future Directions](#)

[Marilyn L Moy](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 38744473
- DOI: [10.4187/respcare.11609](https://doi.org/10.4187/respcare.11609)

## Abstract

The Global Initiative for Chronic Obstructive Lung Disease guidelines recommend pulmonary rehabilitation (PR) for individuals with COPD to improve exercise capacity and health-related quality of life (HRQOL) and reduce symptoms of dyspnea. For cost-effectiveness in COPD care, PR is second only to smoking cessation. However, PR programs typically last 9-12 weeks. The benefits of PR in terms of exercise capacity and HRQOL often decrease toward pre-PR levels as early as 3-6 months after completing PR if patients do not continue to engage in exercise. This review will (1) briefly summarize the efficacy data that informed the 2023 American Thoracic Society (ATS) clinical practice guidelines for maintenance PR, (2) discuss exercise components of maintenance PR studied since 2020 when the last papers were included in the ATS guidelines, (3) explore future directions for delivery of maintenance PR using technology-mediated models, and (4) examine the need for behavior change techniques informed by theoretical models that underpin long-term behavior change. This review will focus on persons with COPD who have completed an out-patient core initial PR program as most of the data on maintenance PR have been published in this patient population. Core PR typically implies a facility-based initial intensive structured program. All patients who complete a core initial PR program should be counseled by PR staff at the discharge visit to engage in ongoing exercise. This usual care is equally as important as referral to a formal PR maintenance program. It is critical to emphasize that usual care after core initial PR means all patients should be supported to participate in regular ongoing exercise, regardless of whether supervised maintenance PR is available. Currently, the optimal frequency, exercise and/or physical activity content, and delivery mode for maintenance PR in persons with COPD and other chronic respiratory diseases remain unknown. Patient safety and degree of in-person supervision required due to the severity of the underlying lung disease need to be considered. Future research of maintenance PR should be underpinned by behavior change techniques. Finally, in the setting of finite resources, balancing the competing priorities of core initial programs with those of maintenance PR programs needs to be achieved.

**Keywords:** behavior change; delivery mode; efficacy; exercise; maintenance pulmonary rehabilitation; usual care.

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## Conflict of interest statement

Dr Moy has disclosed no conflicts of interest.

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. 2024 May 28;69(6):740-754.

doi: 10.4187/respcare.11699.

# [Pulmonary Rehabilitation Reimbursement Challenges](#)

[Chris Garvey](#)<sup>1</sup>

Affiliations expand

- PMID: 38688548
- DOI: [10.4187/respcare.11699](https://doi.org/10.4187/respcare.11699)

## Abstract

Pulmonary rehabilitation (PR) is a highly effective intervention for persons with chronic respiratory diseases, resulting in improvement in exercise capacity, dyspnea, health-related quality of life, mood, reduced hospitalization, and improved survival and cost savings post-COPD hospitalization. Despite demonstrated effectiveness, PR is underutilized in part due to lack of awareness, limited access, and inadequate PR reimbursement. Poor payment is a long-standing barrier to PR's financial stability and access. Addressing PR payment, access, and utilization is a complex challenge and requires strategic, collaborative long-term approaches to meaningful solutions. Strategies to overcome payment disparities begin with legislative approaches to address limitations of Centers for Medicare and Medicaid Services coverage. Additional priorities include permanent approval for remote physician

and advanced practice provider (APP) PR supervision, PR referrals by APPs, telerehabilitation using two-way audio/video technology, and elimination of the PR lifetime maximum limit of 72 h or units/patient. Methods are needed to effectively link appropriate PR prescribing and encouragement with primary care providers, hospitalists, case managers, and hospital navigators to optimize PR referrals. There is an important need to address inadequate PR access in rural settings. Potential opportunities to improve PR referrals and access include exploration of PR synergies with value-based care models that emphasize high-quality care and cost savings. Development and use of effective PR provider tools and resources may help address the above challenges as well as financially benefit PR programs.

**Keywords:** Medicare; access; awareness; exercise; insurance; payment; pulmonary rehabilitation; reimbursement.

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## Conflict of interest statement

Ms Garvey discloses a relationship with Boehringer Ingelheim.

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. 2024 May 28;69(6):755-762.

# Point: Center-Based Pulmonary Rehabilitation Is the Standard

[Richard Casaburi](#)<sup>1</sup>

Affiliations expand

- PMID: 38531638
- DOI: [10.4187/respcare.11785](https://doi.org/10.4187/respcare.11785)

## Abstract

Currently, a major pulmonary rehabilitation focus is on expanding access. At-home rehabilitation is being explored as an in-center pulmonary rehabilitation alternative. It has been asserted that in-home pulmonary rehabilitation confers similar benefits to in-center pulmonary rehabilitation. An extensive database documents that in-center pulmonary rehabilitation confers a range of patient-relevant benefits. Recently, evidence has been presented that in-center pulmonary rehabilitation improves survival, perhaps the most important benefit of all. It can be argued that improvements in physical fitness, assessed as exercise capacity, are mechanistically related to survival improvements. Therefore, in-home rehabilitation must demonstrate exercise capacity improvements similar to those regularly seen in-center to be considered equivalent. A literature search identified 11 studies that compared in-home with in-center pulmonary rehabilitation for COPD that recorded exercise tolerance outcomes. Despite being described as in-home programs, almost all featured prefatory in-center evaluation; some featured in-home visits by rehabilitation professionals. In 6 of the 11 studies, only walking exercise was prescribed. Only 3 included 2-way audio/visual patient-therapist contact. With regard to exercise outcomes; in 3, there was greater in-center group improvement; in 4, outcomes were similar; and, in 4, the in-center group failed to demonstrate clinically important exercise outcome increases; decidedly mixed results. Importantly, in 8 of 11 studies, the 6-min walk test was an exercise outcome. It is argued that the 6-min walk test does not generally elicit physiologically maximum responses and cannot be used to assess exercise capacity improvements. Of the 4 studies that used other exercise outcomes, in 2, exercise endurance increase was similar between in-home and in-center groups; in the other 2, the in-center group had superior improvements. Mixed results indeed! In conclusion, there is insufficient evidence to conclude that in-home pulmonary rehabilitation yields improvements equivalent to center-based programs in physical function, the outcome likely driving long-term prognosis. Moreover, it needs to be established which of the wide variety of in-home program designs now being offered should be promoted.

**Keywords:** 6- min walk test; COPD; Pulmonary rehabilitation; center-based; exercise capacity; home-based; physical fitness.

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## Conflict of interest statement

Dr Casaburi discloses relationships with Inogen, Boehringer-Ingelheim, Glaxo SmithKline, and Regeneron.

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. 2024 May 28;69(6):686-696.

doi: 10.4187/respcare.11541.

# [Review of the Evidence for Pulmonary Rehabilitation in COPD: Clinical Benefits and Cost-Effectiveness](#)

[Courtney E Lamberton](#)<sup>1</sup>, [Christopher L Mosher](#)<sup>2</sup>

Affiliations expand

- PMID: 38503466
- DOI: [10.4187/respcare.11541](https://doi.org/10.4187/respcare.11541)

## Abstract

COPD is a common and lethal chronic condition, recognized as a leading cause of death worldwide. COPD is associated with significant morbidity and disability, particularly among older adults. The disease course is marked by periods of stability and disease exacerbations defined by worsening respiratory status resulting in a high burden of health care utilization and an increased risk of mortality. Treatment is focused on pharmacologic therapies, but these are not completely effective. Pulmonary rehabilitation (PR) represents a key medical intervention for patients with chronic respiratory diseases, including COPD. PR provides individualized and progressive exercise training, education, and self-management strategies through a comprehensive and multidisciplinary program. PR has been associated with improvement in exercise capacity, health-related quality of life, and dyspnea in patients living with COPD. Moreover, PR has been associated with improvements in hospital readmission and 1-y survival. In addition to the clinical benefits, PR is estimated to be a cost-effective medical intervention. Despite these benefits, participation in PR remains low. We will review the evidence for PR in each of these benefit domains among patients with stable COPD and in those recovering from a COPD exacerbation.

**Keywords:** COPD; COPD exacerbation; hospitalization; mortality; pulmonary rehabilitation.

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## Conflict of interest statement

Dr Mosher discloses relationships with the Patient-Centered Outcomes Research Institute, American Lung Association, AstraZeneca, National Institutes of Health, COPD Foundation, and Wellinks. Dr Lamberton has disclosed no conflicts of interest.

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. 2024 May 28;69(6):640-650.

doi: 10.4187/respcare.11705.

# [Pulmonary Rehabilitation: Mechanisms of Functional Loss and Benefits of Exercise](#)

[Linda Nici](#)<sup>1</sup>

Affiliations expand

- PMID: 38503465
- DOI: [10.4187/respcare.11705](https://doi.org/10.4187/respcare.11705)

## Abstract

Exercise limitation is a characteristic feature of chronic respiratory diseases such as COPD and is associated with poor outcomes including decreased functional status and health-related quality of life and increased mortality. The mechanisms responsible for exercise limitation are complex and include ventilatory limitation, cardiovascular impairment, and skeletal muscle dysfunction. In addition, comorbidities such as cardiovascular disease are common in this population and can further impact exercise capacity. Exercise training, a core component of pulmonary rehabilitation, improves exercise capacity by addressing many of these mechanisms that, in turn, can potentially slow the decline of lung function, reduce the frequency of exacerbations, and decrease mortality. This article will discuss the mechanisms of exercise limitation in individuals with chronic respiratory disease, primarily

focusing on COPD, and provide an overview of exercise training and its benefits in this patient population.

**Keywords:** exercise limitation; exercise training; physical activity; pulmonary rehabilitation; skeletal muscles; ventilatory muscles.

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## Conflict of interest statement

Dr Nici has disclosed no conflicts of interest.

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. 2024 May 28;63(5):2400150.

doi: 10.1183/13993003.00150-2024. Print 2024 May.

# Type 2 airway inflammation in COPD

[Francesca Polverino](#)<sup>1</sup>, [Don D Sin](#)<sup>2</sup>

Affiliations expand

- PMID: 38485148

- DOI: [10.1183/13993003.00150-2024](https://doi.org/10.1183/13993003.00150-2024)

## Abstract

Globally, nearly 400 million persons have COPD, and COPD is one of the leading causes of hospitalisation and mortality across the world. While it has been long-recognised that COPD is an inflammatory lung disease, dissimilar to asthma, type 2 inflammation was thought to play a minor role. However, recent studies suggest that in approximately one third of patients with COPD, type 2 inflammation may be an important driver of disease and a potential therapeutic target. Importantly, the immune cells and molecules involved in COPD-related type 2 immunity may be significantly different from those observed in severe asthma. Here, we identify the important molecules and effector immune cells involved in type 2 airway inflammation in COPD, discuss the recent therapeutic trial results of biologicals that have targeted these pathways and explore the future of therapeutic development of type 2 immune modulators in COPD.

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## Conflict of interest statement

Conflict of interest: F. Polverino reports support for the present manuscript from NHLBI HL149744 and Baylor College of Medicine funds outside the submitted work, grants from Victory Houston and Boehringer Ingelheim, and consulting fees from Sanofi-Regeneron, Verona Pharma and Genentech for advisory board participation; in addition, F. Polverino has received travel support to attend ATS Meeting 2023 and is a European Respiratory Journal Section Editor and RCMB programme committee chair. D.D. Sin reports support for the present manuscript as Canada Research Chair, grants from Nextone and lecture honoraria from AZ, GSK and BI; in addition, D.D. Sin is European Respiratory Journal Deputy Chief Editor and the chair of a data and safety monitoring board for an NHLBI-funded clinical trial.

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

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. 2024 May 15;8(3):253-262.

doi: 10.1016/j.mayocpiqo.2024.04.001. eCollection 2024 Jun.

## Phenotypic Clusters and Multimorbidity in Hypermobile Ehlers- Danlos Syndrome

[Taylor Petrucci](#)<sup>1</sup>, [S Jade Barclay](#)<sup>2</sup>, [Cortney Gensemer](#)<sup>1,3</sup>, [Jordan Morningstar](#)<sup>1</sup>, [Victoria Daylor](#)<sup>1</sup>, [Kathryn Byerly](#)<sup>1</sup>, [Erika Bistran](#)<sup>1</sup>, [Molly Griggs](#)<sup>1</sup>, [James M Elliot](#)<sup>2</sup>, [Teresa Kelechi](#)<sup>4</sup>, [Shannon Phillips](#)<sup>4</sup>, [Michelle Nichols](#)<sup>4</sup>, [Steven Shapiro](#)<sup>5</sup>, [Sunil Patel](#)<sup>3</sup>, [Nabila Bouatia-Naji](#)<sup>6</sup>, [Russell A Norris](#)<sup>1,3</sup>

Affiliations expand

- PMID: 38779137
- PMCID: [PMC11109295](#)
- DOI: [10.1016/j.mayocpiqo.2024.04.001](#)

## Abstract

**Objective:** To perform a retrospective clinical study in order to investigate phenotypic penetrance within a large registry of patients with hypermobile Ehlers-Danlos syndrome (hEDS) to enhance diagnostic and treatment guidelines by understanding associated comorbidities and improving accuracy in diagnosis.

**Patients and methods:** From May 1, 2021 to July 31, 2023, 2149 clinically diagnosed patients with hEDS completed a self-reported survey focusing on diagnostic and comorbid conditions prevalence. K-means clustering was applied to analyze survey responses, which were then compared across gender groups to identify variations and gain clinical insights.

**Results:** Analysis of clinical manifestations in this cross-sectional cohort revealed insights into multimorbidity patterns across organ systems, identifying 3 distinct patient groups. Differences among these phenotypic clusters provided insights into diversity within the population with hEDS and indicated that Beighton scores are unreliable for multimorbidity phenotyping.

**Conclusion:** Clinical data on the phenotypic presentation and prevalence of comorbidities in patients with hEDS have historically been limited. This study provides comprehensive data sets on phenotypic presentation and comorbidity prevalence in patients with hEDS, highlighting factors often overlooked in diagnosis. The identification of distinct patient groups emphasizes variations in hEDS manifestations beyond current guidelines and emphasizes the necessity of comprehensive multidisciplinary care for those with hEDS.

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## Conflict of interest statement

The authors report no competing interests.

- [18 references](#)
- [4 figures](#)

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. 2024 Jun;11(6):399-400.

doi: 10.1016/S2215-0366(24)00129-9. Epub 2024 Apr 17.

# The challenges at the core of multimorbidity research

[Oleguer Plana-Ripoll](#)<sup>1</sup>, [Danni Chen](#)<sup>2</sup>, [Lisbeth Mølgaard Laustsen](#)<sup>2</sup>, [Natalie C Momen](#)<sup>3</sup>

Affiliations expand

- PMID: 38642561
- DOI: [10.1016/S2215-0366\(24\)00129-9](https://doi.org/10.1016/S2215-0366(24)00129-9)

*No abstract available*

## Conflict of interest statement

OP-R has received funding from Lundbeck Foundation (Fellowship number R345-2020-1588) and Independent Research Fund Denmark (grant numbers 1030-00085B and 2066-00009B). All other authors report no competing interests.

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. 2024 Jun;11(6):431-442.

doi: 10.1016/S2215-0366(24)00091-9. Epub 2024 Apr 17.

# Prevalence of multimorbidity in people with and without severe mental illness: a systematic review and meta-analysis

[Sean Halstead](#)<sup>1</sup>, [Chester Cao](#)<sup>2</sup>, [Grímur Høgnason Mohr](#)<sup>3</sup>, [Bjørn H Ebdrup](#)<sup>4</sup>, [Toby Pillinger](#)<sup>5</sup>, [Robert A McCutcheon](#)<sup>6</sup>, [Joseph Firth](#)<sup>7</sup>, [Dan Siskind](#)<sup>8</sup>, [Nicola Warren](#)<sup>8</sup>

Affiliations expand

- PMID: 38642560
- DOI: [10.1016/S2215-0366\(24\)00091-9](https://doi.org/10.1016/S2215-0366(24)00091-9)

## Abstract

**Background:** People with severe mental illness, such as schizophrenia-spectrum disorder and bipolar disorder, face poorer health outcomes from multiple chronic illnesses. Physical multimorbidity, the coexistence of two or more chronic physical conditions, and psychiatric multimorbidity, the coexistence of three or more psychiatric disorders, are both emerging concepts useful in conceptualising disease burden. However, the prevalence of physical and psychiatric multimorbidity in this cohort is unknown. This study aimed to estimate the absolute prevalence of both physical and psychiatric multimorbidity in people with severe mental illness, and also compare the odds of physical multimorbidity prevalence against people without severe mental illness.

**Methods:** We searched CINAHL, EMBASE, PubMed, and PsycINFO from inception until Feb 15, 2024, for observational studies that measured multimorbidity prevalence. To be included, studies had to have an observational study design, be conducted in an adult population (mean age  $\geq 18$  years) diagnosed with either schizophrenia-spectrum disorder or bipolar disorder, and include a measurement of occurrence of either physical multimorbidity ( $\geq 2$  physical health conditions) or psychiatric multimorbidity ( $\geq 3$  psychiatric conditions total, including the severe mental illness). From control studies, a random-effects meta-analysis compared odds of physical multimorbidity between people with and without severe mental illness. Absolute prevalence of physical and psychiatric multimorbidity in people with severe mental illness was also calculated. Sensitivity and

meta-regression analyses tested an array of demographic, diagnostic, and methodological variables.

**Findings:** From 11 144 citations we included 82 observational studies featuring 1 623 773 individuals with severe mental illness (specifically schizophrenia-spectrum disorder or bipolar disorder), of which 21 studies featured 13 235 882 control individuals without severe mental illness (descriptive data for the entire pooled cohorts were not available for numbers of males and females, age, and ethnicity). This study did not feature involvement of people with lived experience. The odds ratio (OR) of physical multimorbidity between people with and without severe mental illness was 2.40 (95% CI 1.57-3.65,  $k=11$ ,  $p=0.0009$ ). This ratio was higher in younger severe mental illness populations (mean age  $\leq 40$  years, OR 3.99, 95% CI 1.43-11.10) compared with older populations (mean age  $>40$  years, OR 1.55, 95% CI 0.96-2.51; subgroup differences  $p=0.0013$ ). For absolute prevalence, 25% of those with severe mental illness have physical multimorbidity (95% CI 0.19-0.32,  $k=29$ ) and 14% have psychiatric multimorbidity (95% CI 0.08-0.23,  $k=21$ ).

**Interpretation:** This is the first meta-analysis to estimate physical alongside psychiatric multimorbidity prevalence, showing that these are common in people with schizophrenia-spectrum disorder and bipolar disorder. The greater burden of physical multimorbidity in people with severe mental illness compared with those without is higher for younger cohorts, reflecting a need for earlier intervention. Our findings speak to the utility of multimorbidity for characterising the disease burden associated with severe mental illness, and the importance of facilitating integrated physical and mental health care.

**Funding:** None.

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## Conflict of interest statement

Declaration of interests SH is supported by an Australian Research Training Program scholarship. GHM has received salary via a grant from Independent Research Fund Denmark (case number 2096–00099B). BHE is part of the Advisory Board of Eli Lilly Denmark, Janssen-Cilag, Lundbeck Pharma, and Takeda Pharmaceutical Company; and has received lecture fees from Bristol-Myers Squibb, Boehringer Ingelheim, Otsuka Pharma Scandinavia, Eli Lilly Company, and Lundbeck Pharma. DS is supported by the National Health and Medical Research Council Investigator Fellowship GNT 1194635. NW has received speaker fees from Otsuka, Lundbeck, and Janssen. RAM has received speaker or consultancy fees from Karuna, Janssen, Boehringer Ingelheim, and Otsuka, and codirects a company that designs digital resources to support treatment of mental illness. TP has participated in educational speaker meetings organised by Lundbeck, Otsuka, Sunovion, Janssen, Schwabe Pharma, ROVI Biotech, and Recordati, he receives book royalties from Wiley Blackwell, and he codirects a company that designs digital resources to support treatment of mental illness. All other authors declare no competing interests.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Br J Psychiatry

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. 2024 Jun;224(6):237-244.

doi: 10.1192/bjp.2024.25.

# [Associations between multimorbidity and neuropathology in dementia: consideration of functional cognitive disorders, psychiatric illness and dementia mimics](#)

[Calum A Hamilton](#)<sup>1</sup>, [Fiona E Matthews](#)<sup>2</sup>, [Johannes Attems](#)<sup>1</sup>, [Paul C Donaghy](#)<sup>1</sup>, [Daniel Erskine](#)<sup>1</sup>, [John-Paul Taylor](#)<sup>1</sup>, [Alan J Thomas](#)<sup>1</sup>

Affiliations expand

- PMID: 38584319
- PMCID: [PMC7615979](#)

- DOI: [10.1192/bjp.2024.25](https://doi.org/10.1192/bjp.2024.25)

## Abstract

**Background:** Multimorbidity, the presence of two or more health conditions, has been identified as a possible risk factor for clinical dementia. It is unclear whether this is due to worsening brain health and underlying neuropathology, or other factors. In some cases, conditions may reflect the same disease process as dementia (e.g. Parkinson's disease, vascular disease), in others, conditions may reflect a prodromal stage of dementia (e.g. depression, anxiety and psychosis).

**Aims:** To assess whether multimorbidity in later life was associated with more severe dementia-related neuropathology at autopsy.

**Method:** We examined ante-mortem and autopsy data from 767 brain tissue donors from the UK, identifying physical multimorbidity in later life and specific brain-related conditions. We assessed associations between these purported risk factors and dementia-related neuropathological changes at autopsy (Alzheimer's-disease related neuropathology, Lewy body pathology, cerebrovascular disease and limbic-predominant age-related TDP-43 encephalopathy) with logistic models.

**Results:** Physical multimorbidity was not associated with greater dementia-related neuropathological changes. In the presence of physical multimorbidity, clinical dementia was less likely to be associated with Alzheimer's disease pathology. Conversely, conditions which may be clinical or prodromal manifestations of dementia-related neuropathology (Parkinson's disease, cerebrovascular disease, depression and other psychiatric conditions) were associated with dementia and neuropathological changes.

**Conclusions:** Physical multimorbidity alone is not associated with greater dementia-related neuropathological change; inappropriate inclusion of brain-related conditions in multimorbidity measures and misdiagnosis of neurodegenerative dementia may better explain increased rates of clinical dementia in multimorbidity.

**Keywords:** Multimorbidity; dementias/neurodegenerative diseases; depressive disorders; neuropathology; psychotic disorders/schizophrenia.

## Conflict of interest statement

### Declaration of Interests

CAH has received honoraria from Dementias Platform UK for presentations unrelated to this work, and a research project grant from the NIHR Newcastle Biomedical Research Centre.

FEM has nothing to disclose.

JA has nothing to disclose.

PCD has received research project grants from Alzheimer's Research UK, Alzheimer's Society, Lewy Body Society, Weston Brain Institute, and the Medical Research Council, and research honoraria from Neurology Academy unrelated to this work.

DE has received research grants from the Wellcome Trust, Lewy Body Society, and Alzheimer's Research UK.

JPT has received speaker fees from GE Healthcare and Bial, unrelated to this work. He has provided consultancy services to Sosei-Heptares and Kirin-Kyowa, unrelated to this work. He has received royalties from Oxford University Press and grants from the UK NIHR, Alzheimer's Research UK, UKRI, Alzheimer's Society and Lewy body Society.

AJT has received consultancy fees and support for investigator-led research from GE Healthcare unrelated to this work, and research grants from the Medical Research Council, Alzheimer's Society, Alzheimer's Brain Banks UK, Lewy Body Society, Alzheimer's Research UK, and NIHR Newcastle Biomedical Research Centre.

- [25 references](#)

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J Affect Disord

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. 2024 Jun 1:354:434-442.

doi: 10.1016/j.jad.2024.03.090. Epub 2024 Mar 18.

## [Inter- and intrapopulation differences in the association between physical](#)

# multimorbidity and depressive symptoms

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Affiliations expand

- PMID: 38508455
- DOI: [10.1016/j.jad.2024.03.090](https://doi.org/10.1016/j.jad.2024.03.090)

## Abstract

**Background:** The association between physical multimorbidity and depression differs by populations. However, no direct inter- or intrapopulation comparison of the association has been conducted. Thus, this study aims to estimate the association in China and the United States and reveal inter- and intrapopulation differences in the association.

**Methods:** Middle-aged and older adults from the China Health and Retirement Longitudinal Study and the Health and Retirement Study were included. Physical multimorbidity was defined as the simultaneous presence of two or more chronic physical conditions and depressive symptoms was measured by the Center for Epidemiologic Studies Depression Scale. Generalized estimating equation model and stratification multilevel method were the main statistical models.

**Results:** The presence of physical multimorbidity was associated with a higher risk of depression in both China (RR = 1.360 [95 % CI: 1.325-1.395]) and the US (RR = 1.613 [95 % CI: 1.529-1.701]). For individuals at a low risk of multimorbidity, multimorbidity was associated with 47.4 % (95 % CI: 1.377-1.579) and 71.1 % (95 % CI: 1.412-2.074) increases in the likelihood of depression in China and the US. The effect size was smaller for individuals at a moderate or high risk. However, the cross-national differences were greater for those with a high risk of multimorbidity.

**Limitations:** The self-report measures, attribution bias.

**Conclusions:** Compared to Chinese adults, the presence of physical multimorbidity led to an additional increase in depressive symptoms for American counterparts. The association was stronger for individuals at a low risk of multimorbidity, but cross-national differences were observed mostly among individuals at a high risk.

**Keywords:** China; Depressive symptoms; Interpopulation; Intrapopulation; Physical multimorbidity; The United States.

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## 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 article.

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MeSH termsexpand

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Randomized Controlled Trial

Int J Clin Pharm

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. 2024 Jun;46(3):656-664.

doi: 10.1007/s11096-024-01700-6. Epub 2024 Feb 17.

# Antipsychotic prescribing and drug-related readmissions in multimorbid older inpatients: a post-hoc analysis of the OPERAM population

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Affiliations expand

- PMID: 38367103
- DOI: [10.1007/s11096-024-01700-6](https://doi.org/10.1007/s11096-024-01700-6)

## Abstract

**Background:** Limited data are available on characteristics associated with antipsychotic use in multimorbid older adults.

**Aim:** Primary: to identify patient characteristics associated with antipsychotic prescribing in a multimorbid population of older inpatients with polypharmacy. Secondary: (1) to observe if antipsychotics use during an index hospitalisation was associated with a drug related admission (DRA) within one year, and (2) to describe these cases of antipsychotic-related readmissions.

**Method:** This was a secondary analysis of the OPERAM randomized controlled trial. Multivariate analysis assessed the association between characteristics and comorbidities with antipsychotic use. An expert team assessed DRA occurring during the one-year follow-up.

**Results:** Antipsychotics were prescribed to 5.5% (n = 110) patients upon admission while 7.7% (n = 154) inpatients received antipsychotics at any time (i.e. upon admission, during hospitalisation, and/or at discharge). The most frequently prescribed antipsychotics were quetiapine (n = 152), haloperidol (n = 48) and risperidone (n = 22). Antipsychotic prescribing was associated with dementia (OR = 3.7 95%CI[2.2;6.2]), psychosis (OR = 26.2 [7.4;92.8]), delirium (OR = 6.4 [3.8;10.8]), mood disorders (OR = 2.6 [1.6;4.1]),  $\geq 15$  drugs a day (OR = 1.7 [1.1;2.6]), functional dependency (Activities of Daily Living score < 50/100) (OR = 3.9 [2.5;6.1]) and < 2 units of alcohol per week (OR = 2.2 [1.4;3.6]). DRA occurred in 458 patients (22.8%) within one year. Antipsychotic prescribing at any time was not associated with DRA (OR = 1.0 [0.3;3.9]) however contributed to 8 DRAs, including 3 falls.

**Conclusion:** In this European multimorbid polymedicated older inpatients, antipsychotics were infrequently prescribed, most often at low dosage. Besides neuro-psychiatric symptoms, risk factors for in-hospital antipsychotic prescribing were lower functional status and polymedication.

**Keywords:** Antipsychotic agents; Drug-related admission; Multimorbidity; Older patients.

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- [42 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Geroscience

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. 2024 Jun;46(3):3419-3428.

doi: 10.1007/s11357-024-01087-2. Epub 2024 Feb 5.

# [Percutaneous biopsies of skeletal muscle and adipose tissue in individuals older than 70: methods and outcomes in the Study of Muscle, Mobility and Aging \(SOMMA\)](#)

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Affiliations expand

- PMID: 38315316
- PMCID: [PMC11009187](#)

- DOI: [10.1007/s11357-024-01087-2](https://doi.org/10.1007/s11357-024-01087-2)

## Abstract

Biopsies of muscle and adipose tissue (AT) are useful tools to gain insights into the aging processes in these tissues. However, they are invasive procedures and their risk/benefit profile in older adults can be altered by sarcopenia, frailty, poor healing, and multimorbidity. Their success rates, safety, and tolerability in a geriatric population have not been reported in detail. Investigators in the Study of Muscle, Mobility, and Aging (SOMMA) performed biopsies of muscle and AT in older adults and prospectively collected data on biopsy success rates, safety, and tolerability. We report here the methods and outcomes of these two procedures. In total, 861 participants (aged 70-94) underwent percutaneous biopsies of the Vastus lateralis muscle with a Bergstrom needle. A subset (n = 241) also underwent percutaneous biopsies of the abdominal subcutaneous AT with the tumescent liposuction technique. Success rate was assessed by the percentage of biopsies yielding adequate specimens for analyses; tolerability by pain scores; and safety by frequency of adverse events. All data were prospectively collected. The overall muscle biopsy success rate was 97.1% and was modestly lower in women. The AT biopsy success rate was 95.9% and slightly lower in men. Minimal or no pain was reported in 68% of muscle biopsies and in 83% of AT biopsies. Adverse events occurred in 2.67% of muscle biopsies and 4.15% of AT biopsies. None was serious. In older adults, percutaneous muscle biopsies and abdominal subcutaneous AT biopsies have an excellent safety profile, often achieve adequate tissue yields for analyses, and are well tolerated.

**Keywords:** Biopsy; Liposuction; Older adult; Procedures.

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## Conflict of interest statement

The authors declare no competing interests.

- [22 references](#)
- [3 figures](#)

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MeSH terms, Grants and funding [expand](#)

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Observational Study

BMC Geriatr



. 2024 May 30;24(1):475.

doi: 10.1186/s12877-024-04925-2.

# [Trajectories of chronic multimorbidity patterns in older patients: MTOP study](#)

[Marina Lleal](#)<sup>1,2,3</sup>, [Montserrat Baré](#)<sup>4</sup>, [Susana Herranz](#)<sup>5</sup>, [Josefina Orús](#)<sup>6</sup>, [Ricard Comet](#)<sup>5</sup>, [Rosa Jordana](#)<sup>7</sup>, [Marisa Baré](#)<sup>8,9,10</sup>

Affiliations expand

- PMID: 38816787
- DOI: [10.1186/s12877-024-04925-2](https://doi.org/10.1186/s12877-024-04925-2)

## Abstract

**Background:** Multimorbidity is associated with negative results and poses difficulties in clinical management. New methodological approaches are emerging based on the hypothesis that chronic conditions are non-randomly associated forming multimorbidity patterns. However, there are few longitudinal studies of these patterns, which could allow for better preventive strategies and healthcare planning. The objective of the MTOP (Multimorbidity Trajectories in Older Patients) study is to identify patterns of chronic multimorbidity in a cohort of older patients and their progression and trajectories in the previous 10 years.

**Methods:** A retrospective, observational study with a cohort of 3988 patients aged > 65 was conducted, including suspected and confirmed COVID-19 patients in the reference area of Parc Taulí University Hospital. Real-world data on socio-demographic and diagnostic variables were retrieved. Multimorbidity patterns of chronic conditions were identified with fuzzy c-means cluster analysis. Trajectories of each patient were established along three time points (baseline, 5 years before, 10 years before). Descriptive statistics were performed together with a stratification by sex and age group.

**Results:** 3988 patients aged over 65 were included (58.9% females). Patients with  $\geq 2$  chronic conditions changed from 73.6 to 98.3% in the 10-year range of the study. Six clusters of chronic multimorbidity were identified 10 years before baseline, whereas five clusters were identified at both 5 years before and at baseline. Three clusters were consistently identified in all time points (Metabolic and vascular disease, Musculoskeletal and chronic pain syndrome, Unspecific); three clusters were only present at the earliest time point (Male-predominant diseases, Minor conditions and sensory impairment, Lipid metabolism disorders) and two clusters emerged 5 years before baseline and remained (Heart diseases and Neurocognitive). Sex and age stratification showed different distribution in cluster prevalence and trajectories.

**Conclusions:** In a cohort of older patients, we were able to identify multimorbidity patterns of chronic conditions and describe their individual trajectories in the previous 10 years. Our results suggest that taking these trajectories into consideration might improve decisions in clinical management and healthcare planning.

**Trial registration number:** [NCT05717309](#).

**Keywords:** Ageing; Chronic conditions; Cluster analysis; Longitudinal study; Multimorbidity; Older patients; Trajectories.

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- [42 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated data, Grants and funding [expand](#)

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Commun Med (Lond)



. 2024 May 29;4(1):102.

doi: 10.1038/s43856-024-00529-4.

# Identifying multi-resolution clusters of diseases in ten million patients with multimorbidity in primary care in England

[Thomas Beaney](#)<sup>1,2</sup>, [Jonathan Clarke](#)<sup>3</sup>, [David Salman](#)<sup>4,5</sup>, [Thomas Woodcock](#)<sup>4</sup>, [Azeem Majeed](#)<sup>4</sup>, [Paul Aylin](#)<sup>4</sup>, [Mauricio Barahona](#)<sup>3</sup>

Affiliations expand

- PMID: 38811835
- PMCID: [PMC11137021](#)
- DOI: [10.1038/s43856-024-00529-4](#)

## Abstract

**Background:** Identifying clusters of diseases may aid understanding of shared aetiology, management of co-morbidities, and the discovery of new disease associations. Our study aims to identify disease clusters using a large set of long-term conditions and comparing methods that use the co-occurrence of diseases versus methods that use the sequence of disease development in a person over time.

**Methods:** We use electronic health records from over ten million people with multimorbidity registered to primary care in England. First, we extract data-driven representations of 212 diseases from patient records employing (i) co-occurrence-based methods and (ii) sequence-based natural language processing methods. Second, we apply

the graph-based Markov Multiscale Community Detection (MMCD) to identify clusters based on disease similarity at multiple resolutions. We evaluate the representations and clusters using a clinically curated set of 253 known disease association pairs, and qualitatively assess the interpretability of the clusters.

**Results:** Both co-occurrence and sequence-based algorithms generate interpretable disease representations, with the best performance from the skip-gram algorithm. MMCD outperforms k-means and hierarchical clustering in explaining known disease associations. We find that diseases display an almost-hierarchical structure across resolutions from closely to more loosely similar co-occurrence patterns and identify interpretable clusters corresponding to both established and novel patterns.

**Conclusions:** Our method provides a tool for clustering diseases at different levels of resolution from co-occurrence patterns in high-dimensional electronic health records, which could be used to facilitate discovery of associations between diseases in the future.

## Plain language summary

Having multiple long-term conditions is linked to worse health, poorer quality of life, and difficulties accessing healthcare. Identifying groups, or 'clusters' of diseases that are more likely to occur together in one person may help healthcare services to better meet the needs of those with multiple conditions. Our study aims to identify clusters of similar diseases, based not only on the diseases someone has now, but on the order in which they developed them. We compare a range of methods and find that our strategy performs best at explaining diseases that are already known to be linked, whilst also identifying new clusters of diseases. These methods could be used in future to better understand how diseases occur together, which could help the design of more efficient healthcare services.

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## Conflict of interest statement

The authors declare no competing interests.

- [74 references](#)
- [9 figures](#)

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BMJ Open



. 2024 May 28;14(5):e082825.

doi: 10.1136/bmjopen-2023-082825.

# [Structured medication reviews for adults with multimorbidity and polypharmacy in primary care: a systematic review protocol](#)

[Elena Lammila-Escalera](#)<sup>1</sup>, [Geva Greenfield](#)<sup>2</sup>, [Reham Aldakhil](#)<sup>2</sup>, [Hadar Zaman](#)<sup>3</sup>, [Ana Luisa Neves](#)<sup>2</sup>, [Azeem Majeed](#)<sup>2</sup>, [Benedict Wj Hayhoe](#)<sup>2</sup>

Affiliations expand

- PMID: 38806416
- PMCID: [PMC11138296](#)
- DOI: [10.1136/bmjopen-2023-082825](#)

## Abstract

**Introduction:** Polypharmacy is common among individuals with multimorbidity, often leading to inappropriate medication use and is associated with an increased risk of frailty, hospitalisation and mortality. Structured medication reviews (SMRs) have emerged as a promising method for optimising medication use. However, research examining their efficacy is limited. This review aims to evaluate the impact of SMRs on improving outcomes

for adults with multimorbidity and polypharmacy in primary care settings. Additionally, this review seeks to identify prevailing patterns and trends in the mode of delivery of SMRs.

**Methods and analysis:** A systematic review will be conducted using Ovid MEDLINE, Ovid EMBASE, Web of Science and CINAHL (1997-present). Primary outcomes will include medication-related measures such as dose, frequency and dosage form. Secondary outcomes under investigation will include physical, mental, functional and health service outcomes, as reported. Two independent reviewers will conduct the screening and data extraction, resolving disagreements through discussion. Once eligible studies are identified, the extracted data will be summarised in tabular format. The risk of bias in the articles will be assessed using either the Cochrane Risk of Bias 2 tool or the Newcastle-Ottawa scale, depending on the design of the studies retrieved. Subgroup analysis will be performed using demographic variables and modes of delivery where the data supports. If appropriate, a meta-analysis of the data extracted will be conducted to determine the impact of the SMRs on reported outcomes. If a meta-analysis is not possible due to heterogeneity, a narrative synthesis approach will be adopted.

**Ethics and dissemination:** This proposed review is exempt from ethical approval as it aims to collate and summarise peer-reviewed, published evidence. This protocol and the subsequent review will be disseminated in peer-reviewed journals, conferences and patient-led lay summaries.

**Prospero registration number:** CRD42023454965.

**Keywords:** CLINICAL PHARMACOLOGY; Patient-Centered Care; Systematic Review.

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## Conflict of interest statement

Competing interests: None declared.

- [52 references](#)

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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

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Clin Transl Allergy

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. 2024 Jun;14(6):e12358.

doi: 10.1002/ct2.12358.

## Relevance of individual bronchial symptoms for asthma diagnosis and control in patients with rhinitis: A MASK-air study

[Bernardo Sousa-Pinto](#)<sup>1,2</sup>, [Gilles Louis](#)<sup>3,4</sup>, [Rafael J Vieira](#)<sup>1,2</sup>, [Wienczyslawa Czarlewski](#)<sup>5,6</sup>, [Josep M Anto](#)<sup>7,8,9</sup>, [Rita Amaral](#)<sup>1,2</sup>, [Ana Sá-Sousa](#)<sup>1,2</sup>, [Luisa Brussino](#)<sup>10,11</sup>, [G Walter Canonica](#)<sup>12,13</sup>, [Claudia Chaves Loureiro](#)<sup>14,15</sup>, [Alvaro A Cruz](#)<sup>16</sup>, [Bilun Gemicioglu](#)<sup>17,18</sup>, [Tari Haahtela](#)<sup>19</sup>, [Maciej Kupczyk](#)<sup>20</sup>, [Violeta Kvedariene](#)<sup>21,22</sup>, [Desirée E Larenas-Linnemann](#)<sup>23</sup>, [Nhân Pham-Thi](#)<sup>24,25,26</sup>, [Francesca Puggioni](#)<sup>27</sup>, [Frederico S Regateiro](#)<sup>28,29,30,31</sup>, [Jan Romantowski](#)<sup>32</sup>, [Joaquin Sastre](#)<sup>33</sup>, [Nicola Scichilone](#)<sup>34</sup>, [Luis Taborda-Barata](#)<sup>31,35</sup>, [Maria Teresa Ventura](#)<sup>36,37</sup>, [Ioana Agache](#)<sup>38</sup>, [Anna Bedbrook](#)<sup>6,39</sup>, [Alida Benfante](#)<sup>34</sup>, [Karl C Bergmann](#)<sup>40,41</sup>, [Sinthia Bosnic-Anticevich](#)<sup>42,43</sup>, [Matteo Bonini](#)<sup>44,45</sup>, [Louis-Philippe Boulet](#)<sup>46</sup>, [Guy Brusselle](#)<sup>47</sup>, [Roland Buhl](#)<sup>48</sup>, [Lorenzo Cecchi](#)<sup>49</sup>, [Denis Charpin](#)<sup>50</sup>, [Elisio M Costa](#)<sup>51</sup>, [Stefano Del Giacco](#)<sup>52</sup>, [Marek Jutel](#)<sup>53,54</sup>, [Ludger Klimek](#)<sup>55,56</sup>, [Piotr Kuna](#)<sup>20</sup>, [Daniel Laune](#)<sup>57</sup>, [Mika Makela](#)<sup>19</sup>, [Mario Morais-Almeida](#)<sup>58</sup>, [Rachel Nadif](#)<sup>59,60</sup>, [Marek Niedozytko](#)<sup>31,32</sup>, [Nikolaos G Papadopoulos](#)<sup>61</sup>, [Alberto Papi](#)<sup>62</sup>, [Oliver Pfaar](#)<sup>63</sup>, [Daniela Rivero-Yeverino](#)<sup>64</sup>, [Nicolas Roche](#)<sup>60,65,66</sup>, [Boleslaw Samolinski](#)<sup>67</sup>, [Mohamed H Shamji](#)<sup>45,68</sup>, [Aziz Sheikh](#)<sup>69</sup>, [Charlotte Suppli Ulrik](#)<sup>70,71</sup>, [Omar S Usmani](#)<sup>45,71,72</sup>, [Arunas Valiulis](#)<sup>73,74</sup>, [Arzu Yorgancioglu](#)<sup>75</sup>, [Torsten Zuberbier](#)<sup>40,41</sup>, [Joao A Fonseca](#)<sup>1,2</sup>, [Benoit Pétré](#)<sup>3</sup>, [Renaud Louis](#)<sup>4,76</sup>, [Jean Bousquet](#)<sup>6,39,40,41,60</sup>, [MASK-air think tank](#)<sup>77</sup>

Affiliations expand

- PMID: 38804596
- DOI: [10.1002/ct2.12358](https://doi.org/10.1002/ct2.12358)

**Free article**

# Abstract

**Rationale:** It is unclear how each individual asthma symptom is associated with asthma diagnosis or control.

**Objectives:** To assess the performance of individual asthma symptoms in the identification of patients with asthma and their association with asthma control.

**Methods:** In this cross-sectional study, we assessed real-world data using the MASK-air® app. We compared the frequency of occurrence of five asthma symptoms (dyspnea, wheezing, chest tightness, fatigue and night symptoms, as assessed by the Control of Allergic Rhinitis and Asthma Test [CARAT] questionnaire) in patients with probable, possible or no current asthma. We calculated the sensitivity, specificity and predictive values of each symptom, and assessed the association between each symptom and asthma control (measured using the e-DASTHMA score). Results were validated in a sample of patients with a physician-established diagnosis of asthma.

**Measurement and main results:** We included 951 patients (2153 CARAT assessments), with 468 having probable asthma, 166 possible asthma and 317 no evidence of asthma. Wheezing displayed the highest specificity (90.5%) and positive predictive value (90.8%). In patients with probable asthma, dyspnea and chest tightness were more strongly associated with asthma control than other symptoms. Dyspnea was the symptom with the highest sensitivity (76.1%) and the one consistently associated with the control of asthma as assessed by e-DASTHMA. Consistent results were observed when assessing patients with a physician-made diagnosis of asthma.

**Conclusions:** Wheezing and chest tightness were the asthma symptoms with the highest specificity for asthma diagnosis, while dyspnea displayed the highest sensitivity and strongest association with asthma control.

**Keywords:** asthma; diagnosis; dyspnea; mHealth; wheezing.

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Multicenter Study

Hosp Pediatr



. 2024 Jun 1;14(6):e254-e259.

doi: 10.1542/hpeds.2023-007627.

# [Azithromycin for Pediatric Critical Asthma: A Multicenter Retrospective Cohort Study](#)

[Alexa R Roberts](#)<sup>1</sup>, [Nikhil Vallabhaneni](#)<sup>2</sup>, [Brett Russi](#)<sup>1</sup>, [Tisha L Spence](#)<sup>1</sup>, [Jennifer W Leiding](#)<sup>3</sup>, [Anthony A Sochet](#)<sup>1,2,4</sup>

Affiliations expand

- PMID: 38757173
- DOI: [10.1542/hpeds.2023-007627](https://doi.org/10.1542/hpeds.2023-007627)

## Abstract

**Objectives:** To characterize the prescribing trends and clinical outcomes related to azithromycin (AZI) among children hospitalized for critical asthma (CA).

**Methods:** We performed a multicenter, retrospective cohort study using the Pediatric Health Information Systems registry of children 3 to 17 years of age hospitalized in a PICU for CA from January 2011 to December 2022. We excluded for alternative indications for AZI (eg, atypical pneumonia, B. pertussis infection, acute otitis media, acute sinusitis,

pharyngitis/tonsillitis, and urethritis). The primary outcome was AZI prescribing rate by hospital and calendar year (trends assessed by Joinpoint regression). Cohorts with and without AZI exposure were further characterized by demographics, CA treatments, and inpatient outcomes using descriptive and comparative (ie,  $\chi^2$  and Wilcoxon rank tests) statistics.

**Results:** Of the 47 797 children studied, 9901 (20.7%) were prescribed AZI with a downward annual trend noted from 34.7% in 2011% to 12.4% in 2022 (-1.7% per year,  $R^2 = 0.91$ ). Median institutional AZI prescribing rate was 19.2% (interquartile range [IQR] 11.7%-28%; total range 5.6%-60%). Compared with children not prescribed AZI, those prescribed AZI were older (median 8.3 [IQR 5.7-11.6] vs 7.3 [4.9-10.8] years,  $P < .001$ ) and experienced a more severe clinical trajectory with greater rates of bilevel positive airway pressure ventilation (19.7% vs 12.6%,  $P < .001$ ), invasive ventilation (22.1% vs 13.5%,  $P < .001$ ), extracorporeal life support (0.8% vs 0.1%,  $P < .001$ ), and median length of stay (4 [IQR 3-6] vs 3 [IQR 2-4] days,  $P < .001$ ).

**Conclusions:** Between 2011 and 2022, 20.7% of children hospitalized for CA were prescribed AZI notwithstanding the absence of trial-derived efficacy or safety data for this indication and population.

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Editorial

Lancet Respir Med

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. 2024 Jun;12(6):419.

doi: 10.1016/S2213-2600(24)00149-8. Epub 2024 May 8.

# Tackling health disparities in asthma: a life-course challenge

[The Lancet Respiratory Medicine](#)

- PMID: 38734023
- DOI: [10.1016/S2213-2600\(24\)00149-8](https://doi.org/10.1016/S2213-2600(24)00149-8)

*No abstract available*

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Lung

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. 2024 Jun;202(3):275-280.

doi: 10.1007/s00408-024-00698-y. Epub 2024 May 11.

# Cough Response to High-Dose Inhaled Corticosteroids in Patients with

# Chronic Cough and Fractional Exhaled Nitric Oxide Levels $\geq$ 25 ppb: A Prospective Study

[Ji-Ho Lee](#)<sup>#1</sup>, [Sung-Yoon Kang](#)<sup>#2</sup>, [Iseul Yu](#)<sup>1</sup>, [Kyung Eun Park](#)<sup>3</sup>, [Ji-Yoon Oh](#)<sup>4</sup>, [Ji-Hyang Lee](#)<sup>4</sup>, [So-Young Park](#)<sup>5</sup>, [Min-Hye Kim](#)<sup>6</sup>, [Eun-Jung Jo](#)<sup>7</sup>, [Ji-Yong Moon](#)<sup>8</sup>, [Sae-Hoon Kim](#)<sup>9</sup>, [Sang-Hoon Kim](#)<sup>10</sup>, [Byung-Jae Lee](#)<sup>11</sup>, [Woo-Jung Song](#)<sup>12 13</sup>; [Korean Academy of Asthma Allergy, Clinical Immunology Working Group on Chronic Cough](#)

Affiliations expand

- PMID: 38733542
- DOI: [10.1007/s00408-024-00698-y](https://doi.org/10.1007/s00408-024-00698-y)

## Abstract

This study aimed to investigate the effects of high-dose inhaled corticosteroids (ICS) on chronic cough patients with elevated fractional exhaled nitric oxide (FeNO) levels. In a prospective study, adults with chronic cough and FeNO  $\geq$  25 ppb, without any other apparent etiology, received fluticasone furoate (200 mcg) for three weeks. Outcomes were evaluated using FeNO levels, cough severity, and Leicester Cough Questionnaire (LCQ) before and after treatment. Of the fifty participants (average age: 58.4 years; 58% female), the treatment responder rate ( $\geq$  1.3-point increase in LCQ) was 68%, with a significant improvement in cough and LCQ scores and FeNO levels post-treatment. However, improvements in cough did not significantly correlate with changes in FeNO levels. These findings support the guideline recommendations for a short-term ICS trial in adults with chronic cough and elevated FeNO levels, but the lack of correlations between FeNO levels and cough raises questions about their direct mechanistic link.

**Keywords:** Asthma; Corticosteroids; Cough; Eosinophilic bronchitis; Fractional exhaled nitric oxide.

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Pediatr Pulmonol

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. 2024 Jun;59(6):1569-1577.

doi: 10.1002/ppul.26907. Epub 2024 May 6.

# [Age-related effects of Mycoplasma pneumoniae infection and subsequent asthma exacerbation in children](#)

[Eun Kyo Ha](#)<sup>1</sup>, [Joo Ok Jin](#)<sup>1</sup>, [Ju Hee Kim](#)<sup>2</sup>, [Jeewon Shin](#)<sup>3</sup>, [Gi Chun Lee](#)<sup>4</sup>, [Hye Ryeong Cha](#)<sup>5</sup>, [Sun Hee Choi](#)<sup>6</sup>, [Man Yong Han](#)<sup>3</sup>

Affiliations expand

- PMID: 38708969
- DOI: [10.1002/ppul.26907](https://doi.org/10.1002/ppul.26907)

## Abstract

**Background:** Mycoplasma pneumoniae causes community-acquired pneumonia in children and increases asthma risk, but large studies are lacking.

**Objective:** To assess the link between M. pneumoniae infection and to asthma exacerbation, in children with allergies, and age of infection impact.

**Methods:** This retrospective cohort study analyzed medical records of South Korean children between January 2002 and December 2017. The study's exposure was hospitalization with an *M. pneumoniae*-related diagnosis, and the outcome was defined as asthma exacerbation, confirmed by hospitalization at least 6 months after *M. pneumoniae* infection, with alternative validation using asthma diagnosis and systemic steroid prescription records. Hazard ratios (HRs) for asthma exacerbation risk were estimated for the matched cohort using a Cox proportional hazards model stratified by allergic comorbidities. Time-dependent covariates and age-stratified exposure groups were used to calculate odds ratios.

**Results:** The study included 84,074 children with *M. pneumoniae* infection and 336,296 unexposed children. Follow-up for  $12.2 \pm 2.3$  years found the exposed group had a significant risk of asthma exacerbation (HR 2.86, 95% confidence interval [CI] 2.67-3.06) regardless of allergic comorbidities. The risk was highest (over threefold) in children infected between 24 and 71 months. Sensitivity analysis using an alternative definition of the outcome showed an HR of 1.38 (95% CI 1.35-1.42), further supporting the association between *M. pneumoniae* infection and asthma exacerbation.

**Conclusion:** *M. pneumoniae* infection was significantly associated with an increased risk of subsequent asthma exacerbation regardless of allergic comorbidities. Further research needed for understanding and confirmation.

**Keywords:** *Mycoplasma pneumoniae*; allergic rhinitis; asthma; atopic dermatitis; childhood; epidemiology; pneumonia.

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- [23 references](#)

SUPPLEMENTARY INFO

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Respir Med



. 2024 Jun;227:107652.

doi: 10.1016/j.rmed.2024.107652. Epub 2024 May 1.

# Are biologics effective on lung hyperinflation in patients with resistant asthma?

[Toshiro Goto](#)<sup>1</sup>, [Christian Gomez Hernandez](#)<sup>2</sup>, [Yasushi Tsujimoto](#)<sup>3</sup>, [Takashi Kitagawa](#)<sup>4</sup>

Affiliations expand

- PMID: 38697230
- DOI: [10.1016/j.rmed.2024.107652](https://doi.org/10.1016/j.rmed.2024.107652)

*No abstract available*

## Conflict of interest statement

Declaration of competing interest There are no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

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Sleep Med Clin



. 2024 Jun;19(2):371-378.

doi: 10.1016/j.jsmc.2024.02.013.

# Dyspnea and Quality of Life Improvements with Management of Comorbid Obstructive Sleep Apnea in Chronic Lung Disease

[Kori Ascher](#)<sup>1</sup>, [Shirin Shafazand](#)<sup>2</sup>

Affiliations expand

- PMID: 38692759
- DOI: [10.1016/j.jsmc.2024.02.013](https://doi.org/10.1016/j.jsmc.2024.02.013)

## Abstract

Obstructive sleep apnea (OSA) has emerged as a significant and prevalent comorbidity associated with chronic lung diseases, including chronic obstructive pulmonary disease, asthma, and interstitial lung diseases. These overlap syndromes are associated with worse patient-reported outcomes (sleep quality, quality of life measures, mental health) than each condition independently. Observational studies suggest that patients with overlap syndrome who are adherent to positive airway pressure therapy report improved quality of life, sleep quality, depression, and daytime symptoms. Screening for and management of OSA in patients with overlap syndrome should emphasize the interconnected nature of these 2 conditions and the positive impact that OSA management can have on patients' well-being and overall health.

**Keywords:** Asthma; COPD; Health-related quality of life; Interstitial lung disease; OSA; Overlap syndrome; Patient-reported health outcomes; Positive airway pressure therapy.

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Review

Sleep Med Clin



. 2024 Jun;19(2):275-282.

doi: 10.1016/j.jsmc.2024.02.007. Epub 2024 Mar 5.

# [Obstructive Sleep Apnea Effects on Chronic Airway Disease Exacerbations – Missed Opportunities for Improving Outcomes in Chronic Obstructive Pulmonary Disease and Asthma](#)

[Marta Marin-Oto](#)<sup>1</sup>, [Jose M Marin](#)<sup>2</sup>

Affiliations expand

- PMID: 38692752

- DOI: [10.1016/j.jsmc.2024.02.007](https://doi.org/10.1016/j.jsmc.2024.02.007)

## Abstract

In patients with chronic obstructive pulmonary disease (COPD) and asthma, exacerbations determine the natural history of both diseases. Patients with both respiratory diseases who suffer from obstructive sleep apnea (OSA) as a comorbidity (overlap syndromes) have a higher risk of exacerbations and hospitalization. In cases of OSA/COPD and OSA/asthma, continuous positive airway pressure treatment is indicated. Adequate adherence to therapy appears to reduce exacerbations and their severity, especially in OSA/COPD overlap. However, there is a lack of randomized trials that definitively demonstrate this evidence.

**Keywords:** Asthma; Asthma exacerbation; Chronic obstructive pulmonary disease; Chronic obstructive pulmonary disease exacerbation; Obstructive sleep apnea; Overlap syndrome; Sleep.

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## Conflict of interest statement

Disclosure Both authors report no conflicts of interest.

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Sleep Med Clin

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. 2024 Jun;19(2):261-274.

doi: 10.1016/j.jsmc.2024.02.006. Epub 2024 Mar 7.

# Contribution of Obstructive Sleep Apnea to Asthmatic Airway Inflammation and Impact of Its Treatment on the Course of Asthma

[Octavian C loachimescu](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 38692751
- DOI: [10.1016/j.jsmc.2024.02.006](https://doi.org/10.1016/j.jsmc.2024.02.006)

## Abstract

Asthma and obstructive sleep apnea (OSA) are very common respiratory disorders in the general population. Beyond their high prevalence, shared risk factors, and genetic linkages, bidirectional relationships between asthma and OSA exist, each disorder affecting the other's presence and severity. The author reviews here some of the salient links between constituents of the alternative overlap syndrome, that is, OSA comorbid with asthma, with an emphasis on the effects of OSA or its treatment on inflammation in asthma. In the directional relationship from OSA toward asthma, beyond direct influences, multiple factors and comorbidities seem to contribute.

**Keywords:** Alternative overlap syndrome; Asthma; Inflammation; Obstructive sleep apnea; Positive airway pressure; Sleep apnea.

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Editorial

Br J Gen Pract



. 2024 May 30;74(743):244-245.

doi: 10.3399/bjgp24X738201. Print 2024 Jun.

## [Asthma deaths in children in the UK: the last straw!](#)

[Mark L Levy](#)<sup>1</sup>, [Louise Fleming](#)<sup>2</sup>, [Andrew Bush](#)<sup>3</sup>

Affiliations expand

- PMID: 38684376
- PMID: [PMC11104359](#)
- DOI: [10.3399/bjgp24X738201](#)

*No abstract available*

### **Conflict of interest statement**

Mark L Levy has received payments from publishers Taylor & Francis and Class Publishing; consulting fees from Smart Respiratory, Respiro, Imperial College, AstraZeneca, Novartis, and TEVA; speaker/writing fees from Chiesi, AstraZeneca, and TEVA; honoraria for manuscript writing and educational events from Consorzio Futuro in Ricerca; fees for expert testimony from HM Coroner, Waltham Forrest, London; support to attend meetings

from TEVA; and has held leadership roles (unpaid) in Global Initiative on Asthma, NHS England, and UK All Party Parliamentary Advisory Group (Asthma). Louise Fleming reports consulting fees from AstraZeneca, Sanofi Regeneron, and GSK and honoraria for lectures from AstraZeneca and Novartis. All fees were paid directly to her institution. Andrew Bush reports no conflicts of interest.

- [16 references](#)

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Respir Med

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. 2024 Jun;227:107653.

doi: 10.1016/j.rmed.2024.107653. Epub 2024 Apr 26.

## [Are biologics effective on lung hyperinflation in patients with resistant asthma? A reply](#)

[Mario Cazzola](#)<sup>1</sup>, [Mauro Maniscalco](#)<sup>2</sup>

Affiliations expand

- PMID: 38679339

- DOI: [10.1016/j.rmed.2024.107653](https://doi.org/10.1016/j.rmed.2024.107653)

No abstract available

## 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.

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Respir Med

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. 2024 Jun;227:107655.

doi: 10.1016/j.rmed.2024.107655. Epub 2024 Apr 26.

# Navigating biologic therapies in elderly asthma

[Hyeln Ji](#)<sup>1</sup>, [Laren D Tan](#)<sup>2</sup>, [George W Hafzalla](#)<sup>1</sup>, [Nolan Nguyen](#)<sup>1</sup>, [Abdullah Alismail](#)<sup>3</sup>

Affiliations expand

- PMID: 38679338
- DOI: [10.1016/j.rmed.2024.107655](https://doi.org/10.1016/j.rmed.2024.107655)

## Abstract

The prevalence of asthma among the elderly population has witnessed a notable rise, presenting unique challenges in diagnosis and management. Biologic therapies, such as omalizumab, mepolizumab, reslizumab, benralizumab, dupilumab, and tezepelumab, have demonstrated efficacy in targeting specific pathways associated with severe asthma in elderly individuals. However, a significant research gap exists in the application of these therapies in elderly asthma patients. Despite the considerable size of the elderly asthma population and the social and economic burden that this specific demographic imposes on society, the available body of research catering to this group is limited. Notably, no RCTs have been expressly designed for the elderly across all asthma biologic therapies. Moreover, most RCTs have set upper age cutoffs, commonly 75 years old, and exclusion criteria for common comorbidities in the elderly, thus marginalizing this group from pivotal research. This underscores the crucial need for intentional inclusion of elderly participants in separately designed clinical trials and more researches, aiming to augment the generalizability of findings and enhance therapeutic outcomes. Given the distinct physiological changes associated with aging, there may be a concern regarding the efficacy and safety of biologic therapies in the elderly compared to non-elderly adults, posing a barrier to their use in this population. However, observational studies have shown similar benefits of these therapies in elderly individuals as seen in non-elderly adults. Other anticipated challenges related to initiating biologic therapy in elderly people with asthma including dosing consideration and monitoring strategies, which are important areas of investigation for optimizing asthma management will be discussed in this review. In summary, this review navigates the current landscape of biologic therapies for elderly asthma, offering valuable insights for various stakeholders, including researchers, healthcare providers, and policymakers, to advance asthma care in this vulnerable population. We propose that future research should concentrate on tailored, evidence-based approaches to address the undertreatment of elderly asthma patients.

**Keywords:** Asthma; Asthmatics; Biologics; Efficacy; Elderly; Safety.

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## Conflict of interest statement

Declaration of competing interest All authors have no conflict of interest to report.

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Review

Curr Opin Pediatr



. 2024 Jun 1;36(3):251-255.

doi: 10.1097/MOP.0000000000001351. Epub 2024 Apr 1.

# Revisiting dexamethasone use in the pediatric emergency department

[Rebecca Weinstein](#)<sup>1</sup>, [Catherine E Naber](#), [Kristina Brumme](#)

Affiliations expand

- PMID: 38655807
- DOI: [10.1097/MOP.0000000000001351](https://doi.org/10.1097/MOP.0000000000001351)

## Abstract

**Purpose of review:** Dexamethasone is an essential treatment for common pediatric inflammatory, airway, and respiratory conditions. We aim to provide up-to-date

recommendations for treatment of anaphylaxis, croup, coronavirus disease, multisystem inflammatory syndrome in children, and asthma with dexamethasone for use in the pediatric emergency department.

**Recent findings:** Literature largely continues to support the use of dexamethasone in most of the above conditions, however, recommendations for dosing and duration are evolving.

**Summary:** The findings discussed in this review will enable pediatric emergency medicine providers to use dexamethasone effectively as treatment of common pediatric conditions and minimize the occurrence of side-effects caused by gratuitous corticosteroid use.

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Respirology

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. 2024 Jun;29(6):455-457.

doi: 10.1111/resp.14729. Epub 2024 Apr 23.

## [Asthma-related death trends and biologics use for severe asthma in the super-aged society of Japan](#)

[Keiko Kan-O<sup>1</sup>](#)

Affiliations expand

- PMID: 38651273
- DOI: [10.1111/resp.14729](https://doi.org/10.1111/resp.14729)

**Free article**

*No abstract available*

**Keywords:** Japan; asthma-related deaths; biologics; severe asthma; super-aged society.

- [7 references](#)

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. 2024 Jun;227:107637.

doi: 10.1016/j.rmed.2024.107637. Epub 2024 Apr 16.

# [Asthma patients' and physicians' perspectives on the burden and management of asthma: Post-hoc](#)

# analysis of APPaRENT 1 and 2 to assess predictors of treatment adherence

[Giorgio Walter Canonica](#)<sup>1</sup>, [Christian Domingo](#)<sup>2</sup>, [Kim L Lavoie](#)<sup>3</sup>, [Amrit Kaliasethi](#)<sup>4</sup>, [Shireen Quli Khan](#)<sup>5</sup>, [Anurita Majumdar](#)<sup>6</sup>, [Sourabh Fulmali](#)<sup>7</sup>

Affiliations expand

- PMID: 38636683
- DOI: [10.1016/j.rmed.2024.107637](https://doi.org/10.1016/j.rmed.2024.107637)

**Free article**

## Abstract

**Introduction:** Patient adherence to maintenance medication is critical for improving clinical outcomes in asthma and is a recommended guiding factor for treatment strategy. Previously, the APPaRENT studies assessed patient and physician perspectives on asthma care; here, a post-hoc analysis aimed to identify patient factors associated with good adherence and treatment prescription patterns.

**Methods:** APPaRENT 1 and 2 were cross-sectional online surveys of 2866 adults with asthma and 1883 physicians across Argentina, Australia, Brazil, Canada, China, France, Italy, Mexico, and the Philippines in 2020-2021. Combined data assessed adherence to maintenance medication, treatment goals, use of asthma action plans, and physician treatment patterns and preferences. Multivariable logistic regression models assessed associations between patient characteristics and both treatment prescription (by physicians) and patient treatment adherence.

**Results:** Patient and physician assessments of treatment goals and adherence differed, as did reporting of short-acting  $\beta_2$ -agonist (SABA) prescriptions alongside maintenance and reliever therapy (MART). Older age and greater patient-reported severity and reliever use were associated with better adherence. Patient-reported prescription of SABA with MART was associated with household smoking, severe or poorly controlled asthma, and living in China or the Philippines.

**Conclusions:** Results revealed an important disconnect between patient and physician treatment goals and treatment adherence, suggesting that strategies for improving patient adherence to maintenance medication are needed, focusing on younger patients with milder disease. High reliever use despite good adherence may indicate poor disease control. Personalised care considering patient characteristics alongside physician training

in motivational communication and shared decision-making could improve patient management and outcomes.

**Keywords:** 3–6): Treatment adherence; Inhalation therapy; Patient engagement; Physician–patient relations.

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## Conflict of interest statement

Declaration of competing interest Giorgio Walter Canonica reports having received research grants as well as being a lecturer or having received advisory board fees from A. Menarini, Alk-Abello, Allergy Therapeutics, AstraZeneca, Chiesi Farmaceutici, Firma, Genentech, Guidotti-Malesci, GSK, Hal Allergy, Mylan, Novartis, Regeneron, Roche, Sanofi-Aventis, Sanofi-Genzyme, Stallergenes Greer, Valeas, and OM Pharma, outside the submitted work. Christian Domingo has received funding for travel or speaker fees from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis, Stallergenes, Takeda, and Pfizer, and declares no specific conflicts of interest to report regarding this paper. Kim L. Lavoie reports investigator-initiated research support and speaking fees from AbbVie, consulting fees and speaking fees from Astellas, Boehringer Ingelheim, GSK, X-Factor, Respiplus, and Novartis, consulting fees from Janssen, Sojecci Inc., and AstraZeneca, and speaking fees from Bayer and Mundipharma, outside the submitted work. Amrit Kaliasethi is an employee of Fishawack Communications Ltd, part of Avalere Health. Shireen Quli Khan, Anurita Majumdar, and Sourabh Fulmali are full-time employees of GSK and hold shares in GSK.

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Am J Ind Med

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. 2024 Jun;67(6):532-538.

doi: 10.1002/ajim.23585. Epub 2024 Apr 7.

# Work-related asthma prevalence among US employed adults

[Girija Syamlal](#)<sup>1</sup>, [Katelynn E Dodd](#)<sup>1</sup>, [Jacek M Mazurek](#)<sup>1</sup>

Affiliations expand

- PMID: 38583075
- DOI: [10.1002/ajim.23585](https://doi.org/10.1002/ajim.23585)

## Abstract

**Background:** Work-related asthma (WRA), a preventable occupational disease, can result in adverse health outcomes and employment disability, including decreased productivity, lost workdays, and job loss. Early identification of WRA cases and avoidance of further exposures is crucial for optimal management.

**Objective:** We estimate WRA prevalence among US workers by selected sociodemographic characteristics, industry, and occupation groups and assess the differences in adverse health outcomes, preventive care, and lost workdays between persons with WRA and those with non-WRA.

**Methods:** The 2020 National Health Interview Survey (NHIS) data for working adults aged  $\geq 18$  years employed in the 12 months before the survey were analyzed. Prevalence, and adjusted prevalence ratios with 95% confidence intervals were estimated using multivariate logistic regression.

**Results:** Of the estimated 170 million US adults working in the past year, 13.0 million (7.6%) had asthma. Among workers with asthma, an estimated 896,000 (6.9%) had WRA. WRA prevalence was highest among males, workers aged  $\geq 55$  years, those with no health insurance, those living in the Midwest, and those employed in the accommodation, food, and other services industry, and in production, installation, transportation, and material moving occupations. Workers with WRA were significantly more likely to use preventive medication and rescue inhalers, and to experience adverse health outcomes and lost workdays than workers with non-WRA.

**Conclusion:** Early identification of WRA cases, assessment of workplace exposures, and implementation of targeted interventions that consider the hierarchy of controls are critical to preventing future WRA cases and associated adverse health consequences.

**Keywords:** employment; industry and occupation; prevention; work-lost days; work-related asthma.

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Review

Curr Opin Allergy Clin Immunol

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. 2024 Jun 1;24(3):114-121.

doi: 10.1097/ACI.0000000000000987. Epub 2024 Apr 1.

## [Biological treatments in childhood asthma](#)

[Antonio Nieto-García<sup>1</sup>](#), [María Nieto-Cid<sup>2</sup>](#), [Ángel Mazón-Ramos<sup>3</sup>](#)

Affiliations expand

- PMID: 38567842
- DOI: [10.1097/ACI.0000000000000987](https://doi.org/10.1097/ACI.0000000000000987)

## Abstract

**Purpose of review:** The aim is to update the information currently available for the use of biologics in severe asthma in children, in order to facilitate their prescription as far as possible.

**Recent findings:** The appearance of biologics for the treatment of severe asthma has meant a revolutionary change in the therapeutic approach to this disease. Currently, five biologics have been approved for severe asthma in children and/or adolescents by the regulatory agencies: omalizumab, mepolizumab, benralizumab, dupilumab and tezepelumab. But despite their positive results in terms of efficacy, there are still relevant points of debate that should induce caution when selecting the most appropriate biologic in a child with severe asthma. Indeed, safety is essential and, for several of the existing treatments, the availability of medium-term to long-term data in this regard is scarce.

**Summary:** The use of biologics can facilitate the therapeutic paradigm shift from pleiotropic treatments to personalized medicine. However, the choice of the most appropriate biologics remains a pending issue. On the other hand, to the extent that several of the biologics have been available for a relatively short time, the most robust evidence in terms of efficacy and safety in children is that of omalizumab.

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Paediatr Respir Rev

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. 2024 Jun;50:38-40.

doi: 10.1016/j.prrv.2023.05.005. Epub 2024 Mar 29.

# Should an inhaled corticosteroid accompany each dose of fast-acting beta2-agonist for relief of asthma symptoms?

[Leslie Hendeles](#)<sup>1</sup>, [Miles Weinberger](#)<sup>2</sup>

Affiliations expand

- PMID: 38565492
- DOI: [10.1016/j.prrv.2023.05.005](https://doi.org/10.1016/j.prrv.2023.05.005)

*No abstract available*

**Keywords:** Asthma; Exacerbations; Inhaled corticosteroid; Rapid acting beta agonist; SMART.

## 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.

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Lancet Respir Med



. 2024 Jun;12(6):421-422.

doi: 10.1016/S2213-2600(24)00088-2. Epub 2024 Mar 22.

# Oral corticosteroids for acute preschool wheeze

[Heidi Makrinioti](#)<sup>1</sup>

Affiliations expand

- PMID: 38527488
- DOI: [10.1016/S2213-2600\(24\)00088-2](https://doi.org/10.1016/S2213-2600(24)00088-2)

*No abstract available*

## Conflict of interest statement

I declare no competing interests.

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Meta-Analysis

Lancet Respir Med



. 2024 Jun;12(6):444-456.

doi: 10.1016/S2213-2600(24)00041-9. Epub 2024 Mar 22.

# [Efficacy of oral corticosteroids for acute preschool wheeze: a systematic review and individual participant data meta-analysis of randomised clinical trials](#)

[Bohee Lee](#)<sup>1</sup>, [Steve Turner](#)<sup>2</sup>, [Meredith Borland](#)<sup>3</sup>, [Péter Csonka](#)<sup>4</sup>, [Jonathan Grigg](#)<sup>5</sup>, [Theresa W Guilbert](#)<sup>6</sup>, [Tuomas Jartti](#)<sup>7</sup>, [Abraham Oommen](#)<sup>8</sup>, [Jonathan Twynam-Perkins](#)<sup>9</sup>, [Steff Lewis](#)<sup>10</sup>, [Steve Cunningham](#)<sup>11</sup>

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- PMID: 38527486
- DOI: [10.1016/S2213-2600\(24\)00041-9](https://doi.org/10.1016/S2213-2600(24)00041-9)

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## Abstract

**Background:** Oral corticosteroids are commonly used for acute preschool wheeze, although there is conflicting evidence of their benefit. We assessed the clinical efficacy of oral corticosteroids by means of a systematic review and individual participant data (IPD) meta-analysis.

**Methods:** In this systematic review with IPD meta-analysis, we systematically searched eight databases (PubMed, Ovid Embase, CINAHLplus, CENTRAL, ClinicalTrials.gov, EudraCT, EU Clinical Trials Register, WHO Clinical Trials Registry) for randomised clinical trials published from Jan 1, 1994, to June 30, 2020, comparing oral corticosteroids with placebo in children aged 12 to 71 months with acute preschool wheeze in any setting based on the Population, Intervention, Comparison, Outcomes framework. We contacted principal investigators of eligible studies to obtain deidentified individual patient data. The primary outcome was change in wheezing severity score (WSS). A key secondary outcome length of hospital stay. We also calculated a pooled estimate of six commonly reported adverse events in the follow-up period of IPD datasets. One-stage and two-stage meta-analyses employing a random-effects model were used. This study is registered with PROSPERO, CRD42020193958.

**Findings:** We identified 16 102 studies published between Jan 1, 1994, and June 30, 2020, from which there were 12 eligible trials after deduplication and screening. We obtained individual data from seven trials comprising 2172 children, with 1728 children in the eligible IPD age range; 853 (49.4%) received oral corticosteroids (544 [63.8%] male and 309 [36.2%] female) and 875 (50.6%) received placebo (583 [66.6%] male and 292 [33.4%] female). Compared with placebo, a greater change in WSS at 4 h was seen in the oral corticosteroids group (mean difference -0.31 [95% CI -0.38 to -0.24];  $p=0.011$ ) but not 12 h (-0.02 [-0.17 to 0.14];  $p=0.68$ ), with low heterogeneity between studies ( $I^2=0\%$ ;  $\tau^2<0.001$ ). Length of hospital stay was significantly reduced in the oral corticosteroids group (-3.18 h [-4.43 to -1.93];  $p=0.0021$ ;  $I^2=0\%$ ;  $\tau^2<0.001$ ). Subgroup analyses showed that this reduction was greatest in those with a history of wheezing or asthma (-4.54 h [-5.57 to -3.52];  $p_{\text{interaction}}=0.0007$ ). Adverse events were infrequently reported (four of seven datasets), but oral corticosteroids were associated with an increased risk of vomiting (odds ratio 2.27 [95% CI 0.87 to 5.88];  $\tau^2<0.001$ ). Most datasets (six of seven) had a low risk of bias.

**Interpretation:** Oral corticosteroids reduce WSS at 4 h and length of hospital stay in children with acute preschool wheeze. In those with a history of previous wheeze or asthma, oral corticosteroids provide a potentially clinically relevant effect on length of hospital stay.

**Funding:** Asthma UK Centre for Applied Research.

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## Conflict of interest statement

Declaration of interests BL received a PhD studentship from AUKCAR programme (AUK-AC-2018–01) funded by Asthma + Lung UK. SC received institutional grants for BL's PhD studentship via AUKCAR. PC reports grants from Juhani Aho Foundation for Medical Research, Allergy Research Foundation, Tampere Tuberculosis Foundation, the Research Foundation of the Pulmonary Diseases, The Finnish Medical Foundation, and The Jalmari

and Rauha Ahokas Foundation; consulting fees from ALK, Sanofi, and Thermo Fisher; payments for expert testimony from Sanofi; support for attending meetings or travel from ALK and Orion Pharma; and participation on a Data Safety Monitoring Board or Advisory Board for ALK and Sanofi. TWG reports grants from GSK, Sanofi, Regeneron, Amgen, AstraZeneca, and OM Pharma; royalties and licenses from UpToDate; consulting fees from Sanofi, Regeneron, AstraZeneca, Genentech, Polarean, and OM Pharma; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Sanofi, Regeneron, AiCME, PlatformQ Health, and Advent; support for attending meetings or travel from AiCME, PlatformQ Health, and Advent; and participation on a Data Safety Monitoring Board or Advisory Board for Best Pharmaceuticals for Children Act. JG reports grants from OM Pharma and Mariomed Biotech; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from OM Pharma, GSK, AstraZeneca, and Sanofi; payment for expert testimony from a London coroner regarding the case of a child who died of asthma; and receipt of equipment, materials, drugs, medical writing, gifts, or other services from Omron. All other authors declare no competing interests.

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. 2024 Jun;59(6):1829-1831.

doi: 10.1002/ppul.26978. Epub 2024 Mar 19.

# The current state of pediatric asthma in Australia

[Shivanthan Shanthikumar](#)<sup>1 2 3</sup>, [Nusrat Homaira](#)<sup>4 5 6</sup>, [Brett Montgomery](#)<sup>7</sup>, [Harriet Hiscock](#)<sup>3 8 9</sup>, [Katherine Chen](#)<sup>3 8 10</sup>

Affiliations expand

- PMID: 38501321
- DOI: [10.1002/ppul.26978](https://doi.org/10.1002/ppul.26978)

*No abstract available*

- [13 references](#)

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. 2024 May 30;74(743):e355-e363.

doi: 10.3399/BJGP.2023.0214. Print 2024 Jun.

# Post-hospitalisation asthma management in primary care: a retrospective cohort study

[Dhanusha Punyadasa](#)<sup>1</sup>, [Nikita Simms-Williams](#)<sup>1</sup>, [Nicola J Adderley](#)<sup>1</sup>, [Rasiah Thayakaran](#)<sup>1</sup>, [Adel H Mansur](#)<sup>2</sup>, [Krishnarajah Nirantharakumar](#)<sup>1</sup>, [Prasad Nagakumar](#)<sup>3</sup>, [Shamil Haroon](#)<sup>1</sup>

Affiliations expand

- PMID: 38438269
- PMCID: [PMC10947362](#)
- DOI: [10.3399/BJGP.2023.0214](#)

## Abstract

**Background:** Clinical guidelines recommend that patients admitted to hospital for asthma attacks are reviewed in primary care following hospital discharge.

**Aim:** To evaluate asthma management in primary care following a hospital admission for asthma and its associations with patient characteristics.

**Design and setting:** A retrospective cohort study using English primary care data from the Clinical Practice Research Datalink Aurum database and linked Hospital Episode Statistics Admitted Patient Care data.

**Method:** Patients with asthma aged  $\geq 5$  years who had at least one asthma-related hospital admission from 1 January 2017 to 31 December 2019 were included. The primary outcome was a composite of any of the following delivered in primary care within 28 days from hospital discharge: asthma review, asthma management plan, asthma medication prescriptions, demonstration of inhaler technique, or smoking cessation counselling. The association between patient characteristics and delivery of clinical care was assessed using logistic regression.

**Results:** The study included 17 457 patients. A total of 10 515 (60.2%) patients received the primary outcome within 28 days of hospital discharge. There were 2311 (13.2%) who received an asthma review, 1459 (8.4%) an asthma management plan, 9996 (57.3%) an asthma medication, 1500 (8.6%) a demonstration of inhaler technique, and 52 (1.2% of smokers) had smoking cessation counselling. Patients from Black ethnic minority groups

received less of this care (27%-54% lower odds, depending on age). However, short-acting bronchodilator prescriptions in the previous year were associated with an increased likelihood of the primary outcome.

**Conclusion:** A significant proportion of patients do not receive timely follow-up in primary care following asthma-related admissions to hospital, particularly among Black ethnic minority groups.

**Keywords:** asthma; cohort studies; ethnic and racial minorities; management; post-hospitalisation; primary health care.

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## Conflict of interest statement

Shamil Haroon reports receiving funding from NIHR and UK Research and Innovation (UKRI). Krishnarajah Nirantharakumar has been awarded research grants from NIHR, UKRI/Medical Research Council (MRC), Kennedy Trust for Rheumatology Research, Health Data Research UK, Wellcome Trust, European Regional Development Fund, Institute for Global Innovation, Boehringer Ingelheim (BI), Action Against Age-related Macular Degeneration charity, Midlands Neuroscience Teaching and Development Funds, South Asian Health Foundation, Vifor Pharma, College of Policing, and CSL Behring, with all payments made to his academic institution; Krishnarajah Nirantharakumar received consulting fees from BI, Sanofi, MSD, and holds a leadership/fiduciary role with Network for Improving Critical care Systems and Training, a charity, and Open Clinical, a social enterprise. Adel H Mansur received personal and institutional funds from AstraZeneca (AZ), GlaxoSmithKline (GSK), Novartis, Sanofi, BI, and Chiesi for talks, advisory board meetings, research, and educational grants. Nicola J Adderley reports receiving funding from NIHR outside the submitted work. Prasad Nagakumar reports receiving grants from NIHR and fees for educational talks and consultancy from Novartis, GSK, and AZ. All other authors have declared no competing interests.

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. 2024 Jun;35(6):1007-1017.

doi: 10.1007/s00198-024-07037-0. Epub 2024 Mar 2.

# Cross-sectional studies of the causal link between asthma and osteoporosis: insights from Mendelian randomization and bioinformatics analysis

[Lexin Chen](#)<sup>#1,2</sup>, [Can Li](#)<sup>#1</sup>, [Hangang Chen](#)<sup>1,2</sup>, [Yangli Xie](#)<sup>1</sup>, [Nan Su](#)<sup>1</sup>, [Fengtao Luo](#)<sup>1</sup>, [Junlan Huang](#)<sup>1</sup>, [Ruobin Zhang](#)<sup>1</sup>, [Lin Chen](#)<sup>1</sup>, [Bo Chen](#)<sup>3</sup>, [Jing Yang](#)<sup>4</sup>

Affiliations expand

- PMID: 38430243
- DOI: [10.1007/s00198-024-07037-0](https://doi.org/10.1007/s00198-024-07037-0)

## Abstract

The study, using data from Chongqing, China, and employing Mendelian randomization along with bioinformatics, establishes a causal link between asthma and osteoporosis, beyond glucocorticoid effects. Asthma may contribute to osteoporosis by accelerating bone turnover through inflammatory factors, disrupting the coupling between osteoblasts and osteoclasts, ultimately leading to osteoporosis.

**Introduction:** Asthma and osteoporosis are prevalent health conditions with substantial public health implications. However, their potential interplay and the underlying

mechanisms have not been fully elucidated. Previous research has primarily focused on the impact of glucocorticoids on osteoporosis, often overlooking the role of asthma itself.

**Methods:** We conducted a multi-stage stratified random sampling in Chongqing, China and excluded individuals with a history of glucocorticoid use. Participants underwent comprehensive health examinations, and their clinical data, including asthma status, were recorded. Logistic regression and Mendelian randomization were employed to investigate the causal link between asthma and osteoporosis. Furthermore, bioinformatics analyses and serum biomarker assessments were conducted to explore potential mechanistic pathways.

**Results:** We found a significant association between asthma and osteoporosis, suggesting a potential causal link. Mendelian Randomization analysis provided further support for this causal link. Bioinformatics analyses revealed that several molecular pathways might mediate the impact of asthma on bone health. Serum alkaline phosphatase levels were significantly elevated in the asthma group, suggesting potential involvement in bone turnover.

**Conclusion:** Our study confirms a causal link between asthma and osteoporosis and highlights the importance of considering asthma in osteoporosis prediction models. It also suggests that asthma may accelerate osteoporosis by increasing bone turnover through inflammatory factors, disrupting the coupling between osteoblasts and osteoclasts, ultimately leading to bone loss.

**Keywords:** Asthma; Bone turnover; Cross-sectional studies; Mendelian randomization; Osteoporosis.

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- [49 references](#)

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. 2024 Jun 1;36(3):304-309.

doi: 10.1097/MOP.0000000000001343. Epub 2024 Feb 23.

# Precision care in the treatment of pediatric asthma

[Lina Mahmood](#)<sup>1</sup>, [Sevdenur Keskin](#), [Akilah A Jefferson](#)

Affiliations expand

- PMID: 38411592
- PMID: PMC11042999 (available on 2025-06-01)
- DOI: [10.1097/MOP.0000000000001343](https://doi.org/10.1097/MOP.0000000000001343)

## Abstract

**Purpose of review:** Precision medicine in pediatric asthma involves identification of asthma phenotypes, genetic markers, biomarkers, and biologics that target specific pathways. This review includes a discussion of the efficacy of currently approved biologics for pediatric asthma and most recent advances in biomarker/phenotype identification and genetic associations that affect asthma care.

**Recent findings:** Biologics targeting type-2 mediated pathways have shown success in the treatment of moderate to severe asthma in pediatric and adult patients. In comparative studies, dupilumab, an interleukin-4 (IL-4) alpha receptor inhibitor, and mepolizumab, an IL-5 inhibitor, have shown more improvement in asthma exacerbation rates and lung function compared to other biologics such as tezepelumab, omalizumab and benralizumab. Other methods used to categorize asthma treatment response have been

investigated and include use of biomarkers such as fractional exhaled nitric oxide (FeNO). Genomic studies are also emerging in precision care for pediatric asthma.

**Summary:** An understanding of underlying immunologic and genetic mechanisms affecting the development of asthma in pediatric patients has resulted in the production of numerous targeted therapies that have led to improvement in lung function and reduced exacerbation burden.

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## Conflict of interest statement

Conflicts of interest. none.

- [60 references](#)

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. 2024 Jun 1;24(3):177-181.

doi: 10.1097/ACI.0000000000000975. Epub 2024 Feb 21.

# Global burden of pediatric asthma and rhinitis - what we have recently learned from epidemiology

[Sergio de Jesús Romero-Tapia<sup>1</sup>](#), [Luis García-Marcos<sup>2</sup>](#)

Affiliations expand

- PMID: 38386768
- DOI: [10.1097/ACI.0000000000000975](https://doi.org/10.1097/ACI.0000000000000975)

## Abstract

**Purpose of review:** To analyze and present recently published information on the factors that modify the burden of asthma and rhinitis in pediatric ages, such as ecological determinants; highlighting access and adherence to medications, exposure to pollutants and climate change. In addition to individual determinants such as obesity, protective & risk factors and comorbidities.

**Recent findings:** Asthma and rhinitis continue to have a significant impact worldwide on the health of affected patients, primarily children. The burden of asthma is greatest in developing countries and vulnerable populations, resulting in increased morbidity, potentially preventable asthma deaths and socioeconomic consequences.

**Summary:** A better understanding and representation of the burden of asthma and rhinitis in children can contribute to prevention strategies and improvements in the care of pediatric patients.

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- [30 references](#)

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JAAD Int



. 2024 Jan 17:15:5-11.

doi: 10.1016/j.jdin.2024.01.002. eCollection 2024 Jun.

# [A real-world study of dupilumab in patients with atopic dermatitis including patients with malignancy and other medical comorbidities](#)

[Dea Metko](#)<sup>1</sup>, [Maha Alkofide](#)<sup>2</sup>, [Mohannad Abu-Hilal](#)<sup>1,2</sup>

Affiliations [expand](#)

- PMID: 38371662
- PMCID: [PMC10869314](#)
- DOI: [10.1016/j.jdin.2024.01.002](#)

## Abstract

**Background:** Dupilumab is a monoclonal antibody approved for the treatment of moderate-to-severe atopic dermatitis (MtS-AD). Various clinical trials have established the effectiveness and safety of dupilumab for the treatment MtS-AD; however, the real-world experiences of patients treated with dupilumab with malignancy and other comorbidities are lacking.

**Objective:** To assess the real-life effectiveness and safety of dupilumab in the treatment of MtS-AD within Canadian adult patient population, including those with other significant comorbidities such as malignancy.

**Methods:** In this retrospective study, records of adult patients diagnosed with MtS-AD, with a Physician Global Assessment (PGA) score of 3 or 4, and treated with dupilumab for 52 weeks were reviewed and collected.

**Results:** A total of 155 adult patients with atopic dermatitis (AD) treated with dupilumab were included in the study. Asthma was the most common comorbidity. One hundred twenty-three (80%) patients received either phototherapy and/or at least 1 systemic agent (methotrexate and cyclosporine) before initiation of dupilumab. PGA score of 0 or 1 was achieved by 64% of patients at week 52. Adverse effects including injection site reactions, ocular surface disease, facial and neck redness, and arthropathy occurred in 6%, 10%, 8%, and 6% of patients, respectively. Three patients continued receiving dupilumab throughout pregnancy, all maintaining PGA score of 0 or 1 with no impact on pregnancy, delivery, or the newborn. Twelve patients with prior or active malignancy were included, with no reported negative impact on malignancy.

**Conclusion:** Dupilumab is an effective and safe option for patients with AD in real life, including patients with malignancy and other medical comorbidities.

**Keywords:** atopic dermatitis; comorbidities; dupilumab; malignancy; real-world experience.

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## Conflict of interest statement

Dr Alkofide has served as an adviser/consultant for, or received grants/honoraria from, or has served as a speaker for AbbVie, Eli Lilly, Galderma, Janssen, LEO Pharma, L'Oreal, Medexus, Novartis, Pfizer, Sanofi, and Sun Pharma. The other authors have no conflicts of interest to declare.

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. 2024 Jun;281(6):3017-3023.

doi: 10.1007/s00405-024-08461-y. Epub 2024 Feb 12.

# Switching of biological therapy to dupilumab in comorbid patients with severe asthma and CRSwNP

[Cecilia Rosso](#)<sup>1,2</sup>, [Eugenio De Corso](#)<sup>3</sup>, [Valerio Conti](#)<sup>4</sup>, [Letizia Nitro](#)<sup>4</sup>, [Alberto Maria Saibene](#)<sup>5</sup>, [Elena Parazzini](#)<sup>6</sup>, [Rocco Rinaldo](#)<sup>6</sup>, [Sabrina De Pascalis](#)<sup>6</sup>, [Flavio Arnone](#)<sup>4</sup>, [Stefano Centanni](#)<sup>6</sup>, [Claudio Montuori](#)<sup>7</sup>, [Leandro Maria D'Auria](#)<sup>7</sup>, [Giovanni Felisati](#)<sup>5</sup>, [Carlotta Pipolo](#)<sup>5</sup>

Affiliations expand

- PMID: 38347197
- PMCID: [PMC11065938](#)
- DOI: [10.1007/s00405-024-08461-y](#)

## Abstract

**Purpose:** Nowadays, several efficacious biologic drugs are used for severe asthma with or without chronic rhinosinusitis with nasal polyps (CRSwNP). However, it has been observed that not all comorbid patients (asthma/CRSwNP) receiving biologic treatment for asthma experience satisfactory control of both conditions equally.

**Methods:** We selected 20 patients who had both severe asthma and comorbid CRSwNP under biological treatment with benralizumab, omalizumab or mepolizumab with adequate control of asthma but inadequate control of nasal symptoms. Patients were switched to dupilumab and outcomes were evaluated at baseline (T0), at 3 months (T1), at 6 months (T2), at 12 months (T3) and finally at 18 months (T4). Data were collected at each time point including blood tests measuring eosinophil levels and total IgE, SNOT22, ACT, NPS score, rhinomanometry, olfactory testing, and nasal cytology.

**Results:** The results showed an overall improvement in all the outcomes. Peripheral eosinophilia was observed consistently with existing literature. All patients registered an improvement in sinonasal outcomes, while only one patient had a worsening of asthma. Three patients interrupted the therapy due to various causes: poor asthma control, onset of psoriasis and thrombocytopenia.

**Conclusions:** The response to a biologic treatment for CRSwNP control may be heterogenous and it seems that patients may benefit from switching improving control in equal measure in the upper and lower airway. Further studies to explore the endotype/phenotype which best fits with each biologic are mandatory to personalize the therapy.

**Keywords:** Benralizumab; Biological therapy; CRSwNP; Dupilumab; Mepolizumab; Monoclonal antibodies; Nasal polyps; Omalizumab.

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## Conflict of interest statement

The authors declare they have no financial interests, nor any interests that are directly or indirectly related to the work submitted for publication.

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- [1 figure](#)

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Meta-Analysis

Infection



. 2024 Jun;52(3):1009-1026.

doi: 10.1007/s15010-023-02156-y. Epub 2024 Jan 18.

# Risk factors for herpes zoster infections: a systematic review and meta-analysis unveiling common trends and heterogeneity patterns

[Maren Steinmann](#)<sup>1</sup>, [David Lampe](#)<sup>2</sup>, [John Grosser](#)<sup>2</sup>, [Juliana Schmidt](#)<sup>2</sup>, [Marla Louise Hohoff](#)<sup>2</sup>, [Anita Fischer](#)<sup>2</sup>, [Wolfgang Greiner](#)<sup>2</sup>

Affiliations expand

- PMID: 38236326
- DOI: [10.1007/s15010-023-02156-y](https://doi.org/10.1007/s15010-023-02156-y)

## Abstract

**Purpose:** The burden of herpes zoster (HZ) is substantial and numerous chronic underlying conditions are known as predisposing risk factors for HZ onset. Thus, a comprehensive study is needed to synthesize existing evidence. This study aims to comprehensively identify these risk factors.

**Methods:** A systematic literature search was done using MEDLINE via PubMed, EMBASE and Web of Science for studies published from January 1, 2003 to January 1, 2023. A random-effects model was used to estimate pooled Odds Ratios (OR). Heterogeneity was assessed using the  $I^2$  statistic. For sensitivity analyses basic outlier removal, leave-one-out validation and Graphic Display of Heterogeneity (GOSH) plots with different algorithms were employed to further analyze heterogeneity patterns. Finally, a multiple meta-regression was conducted.

**Results:** Of 6392 considered records, 80 were included in the meta-analysis. 21 different conditions were identified as potential risk factors for HZ: asthma, autoimmune disorders, cancer, cardiovascular disorders, chronic heart failure (CHF), chronic obstructive pulmonary disorder (COPD), depression, diabetes, digestive disorders, endocrine and metabolic disorders, hematological disorders, HIV, inflammatory bowel disease (IBD), mental health

conditions, musculoskeletal disorders, neurological disorders, psoriasis, renal disorders, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and transplantation. Transplantation was associated with the highest risk of HZ (OR = 4.51 (95% CI [1.9-10.7])). Other risk factors ranged from OR = 1.17-2.87, indicating an increased risk for all underlying conditions. Heterogeneity was substantial in all provided analyses. Sensitivity analyses showed comparable results regarding the pooled effects and heterogeneity.

**Conclusions:** This study showed an increased risk of HZ infections for all identified factors.

**Keywords:** Herpes zoster; Meta-analysis; Meta-regression; Random-effects model; Risk factors; Systematic review.

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- [132 references](#)

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. 2024 Jun;20(6):635-653.

doi: 10.1080/1744666X.2024.2306885. Epub 2024 Jan 22.

# Comparison of high- and low-molecular-weight sensitizing agents causing occupational asthma: an evidence-based insight

[Virginie Doyen](#)<sup>1</sup>, [Denyse Gautrin](#)<sup>2</sup>, [Olivier Vandenplas](#)<sup>1</sup>, [Jean-Luc Malo](#)<sup>2</sup>

Affiliations expand

- PMID: 38235552
- DOI: [10.1080/1744666X.2024.2306885](https://doi.org/10.1080/1744666X.2024.2306885)

## Abstract

**Introduction:** The many substances used at the workplace that can cause sensitizer-induced occupational asthma are conventionally categorized into high-molecular-weight (HMW) agents and low-molecular-weight (LMW) agents, implying implicitly that these two categories of agents are associated with distinct phenotypic profiles and pathophysiological mechanisms.

**Areas covered:** The authors conducted an evidence-based review of available data in order to identify the similarities and differences between HMW and LMW sensitizing agents.

**Expert opinion:** Compared with LMW agents, HMW agents are associated with a few distinct clinical features (i.e. concomitant work-related rhinitis, incidence of immediate asthmatic reactions and increase in fractional exhaled nitric oxide upon exposure) and risk factors (i.e. atopy and smoking). However, some LMW agents may exhibit 'HMW-like' phenotypic characteristics, indicating that LMW agents are a heterogeneous group of agents and that pooling them into a single group may be misleading. Regardless of the presence of detectable specific IgE antibodies, both HMW and LMW agents are associated with a mixed Th1/Th2 immune response and a predominantly eosinophilic pattern of airway inflammation. Large-scale multicenter studies are needed that use objective diagnostic criteria and assessment of airway inflammatory biomarkers to identify the pathobiological pathways involved in OA caused by the various non-protein agents.

**Keywords:** Occupational asthma; high molecular weight agents; low molecular weight agents; phenotype; sputum cells.

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. 2024 Jun;61(6):649-652.

doi: 10.1080/02770903.2023.2294913. Epub 2023 Dec 21.

# [A tailored approach to refractory severe Mepolizumab-associated headache: a case study](#)

[Carmine Salerni](#)<sup>1</sup>, [Andrea Baccelli](#)<sup>1</sup>, [Elena M Parazzini](#)<sup>1</sup>, [Rocco Rinaldo](#)<sup>2</sup>, [Stefano Centanni](#)<sup>1</sup>

Affiliations expand

- PMID: 38088891

- DOI: [10.1080/02770903.2023.2294913](https://doi.org/10.1080/02770903.2023.2294913)

## Abstract

**Introduction:** Biologic drugs have been shown to reduce asthma exacerbations, improve lung function and quality of life, reduce oral corticosteroid use in appropriately selected patients. Mepolizumab has been demonstrated to have a safety profile that is similar to placebo, however, when present side effects may lead to treatment discontinuation. Among these, headache is one of the most common.

**Case study:** We hereby describe the case of a never-smoking male patient with an eosinophilic corticosteroid-dependent severe asthma. He displayed well controlled comorbidities and good adherence to the inhaled therapy. Mepolizumab was started in 2017 with an initial remarkable clinical improvement. After three doses of biologic therapy, he reported a severe orthostatic headache associated with vomiting, unresponsive to analgesic drugs, that required hospitalization. No other cause than treatment with Mepolizumab was found to be plausibly associated with this new-onset headache. The therapeutic regimen was modified by administering Mepolizumab for two consecutive months alternated with a one-month break.

**Results:** The patient did not experience any further episodes of headache, while maintaining a good and stable control of his asthma. We were able to taper oral corticosteroids, and no flares-ups occurred in the following 5 years.

**Conclusion:** Our experience indicates that a tailored strategy for managing severe asthmatic patients, who have experienced side effects from biologic drugs, can be effective in maintaining drug efficacy while minimizing side effects. Further studies on a larger number of patients are required to demonstrate whether the positive outcomes here described are replicable on a larger scale.

**Keywords:** Mepolizumab; Severe asthma; biologic therapy; eosinophilic asthma; headache; uncontrolled asthma.

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. 2024 May 31.

doi: 10.1002/ppul.27052. Online ahead of print.

# What is the future of children and adolescents with severe asthma treated with biological therapy?

[Clara Ladoux](#)<sup>1,2</sup>, [Laurent Guilleminault](#)<sup>3,4</sup>, [Marine Michelet](#)<sup>1,2,4</sup>, [Marie Mittaine](#)<sup>1,2</sup>

Affiliations expand

- PMID: 38818871
- DOI: [10.1002/ppul.27052](https://doi.org/10.1002/ppul.27052)

*No abstract available*

**Keywords:** adolescents; biological therapy; follow-up; severe asthma; transition.

- [6 references](#)

SUPPLEMENTARY INFO

Publication types, Grants and funding expand

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Eur Respir J



# The association of blood eosinophil counts and FEV<sub>1</sub> decline: a cohort study

[Yun Soo Hong](#)<sup>1,2,3</sup>, [Hye Yun Park](#)<sup>4,3</sup>, [Seungho Ryu](#)<sup>5,6,7</sup>, [Sun Hye Shin](#)<sup>4</sup>, [Di Zhao](#)<sup>2,7</sup>, [Dave Singh](#)<sup>8</sup>, [Eliseo Guallar](#)<sup>2,7</sup>, [Juhee Cho](#)<sup>2,7</sup>, [Yoosoo Chang](#)<sup>9,6,7,10</sup>, [Seong Yong Lim](#)<sup>11,10</sup>

Affiliations expand

- PMID: 38636990
- DOI: [10.1183/13993003.01037-2023](https://doi.org/10.1183/13993003.01037-2023)

## Abstract

**Background:** Accelerated lung function decline is characteristic of COPD. However, the association between blood eosinophil counts and lung function decline, accounting for current smoking status, in young individuals without prevalent lung disease is not fully understood.

**Methods:** This is a cohort study of 629 784 Korean adults without COPD or a history of asthma at baseline who participated in health screening examinations including spirometry and differential white blood cell counts. We used a linear mixed-effects model to estimate the annual change in forced expiratory volume in 1 s (FEV<sub>1</sub>) (mL) by baseline blood eosinophil count, adjusting for covariates including smoking status. In addition, we performed a stratified analysis by baseline and time-varying smoking status.

**Results:** During a mean follow-up of 6.5 years (maximum 17.8 years), the annual change in FEV<sub>1</sub> (95% CI) in participants with eosinophil counts <100, 100-199, 200-299, 300-499 and ≥500 cells·μL<sup>-1</sup> in the fully adjusted model were -23.3 (-23.9--22.7) mL, -24.3 (-24.9--23.7) mL, -24.8 (-25.5--24.2) mL, -25.5 (-26.2--24.8) mL and -26.8 (-27.7--25.9) mL, respectively. When stratified by smoking status, participants with higher eosinophil count had a faster decline in FEV<sub>1</sub> than those with lower eosinophil count in both never- and ever-smokers, which persisted when time-varying smoking status was used.

**Conclusions:** Higher blood eosinophil counts were associated with a faster lung function decline among healthy individuals without lung disease, independent of smoking status. The findings suggest that higher blood eosinophil counts contribute to the risk of faster lung function decline, particularly among younger adults without a history of lung disease.

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## Conflict of interest statement

Conflict of interest: D. Singh reports personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Menarini, Mundipharma, Novartis, Peptinnovate, Pfizer, Pulmatrix, Theravance and Verona, outside the submitted work. The remaining authors declare no competing interests.

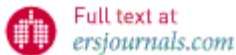
## Comment in

- [Blood eosinophils and lung function loss: from passive prediction to active prevention?](#)  
Ramakrishnan S, Montgomery B, Pavord ID. *Eur Respir J*. 2024 May 30;63(5):2400812. doi: 10.1183/13993003.00812-2024. Print 2024 May. PMID: 38816039 No abstract available.

### SUPPLEMENTARY INFO

MeSH termsexpand

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J Allergy Clin Immunol Pract

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. 2024 May 29:S2213-2198(24)00549-X.

doi: 10.1016/j.jaip.2024.05.034. Online ahead of print.

# Risk Factors for Acute Asthma Exacerbations in Adults with Mild Asthma

[Wansu Chen](#)<sup>1</sup>, [Eric J Puttock](#)<sup>2</sup>, [Michael Schatz](#)<sup>3</sup>, [William Crawford](#)<sup>4</sup>, [William M Vollmer](#)<sup>5</sup>, [Fagen Xie](#)<sup>6</sup>, [Stanley Xu](#)<sup>7</sup>, [Eva Lustigova](#)<sup>8</sup>, [Robert S Zeiger](#)<sup>9</sup>

Affiliations expand

- PMID: 38821437
- DOI: [10.1016/j.jaip.2024.05.034](https://doi.org/10.1016/j.jaip.2024.05.034)

## Abstract

**Background:** Although individuals with mild asthma account for 30-40% of acute asthma exacerbations (AAEs), relatively little attention has been paid to risk factors for AAEs in this population.

**Objective:** To identify risk factors associated with AAEs in patients with mild asthma.

**Methods (retrospective cohort study):** We used administrative data from a large managed care organization to identify 199,010 adults aged 18-85 who met study criteria for mild asthma between 2013-2018. An asthma-coded qualifying visit (index visit) was identified for each patient. We then used information at the index visit or from the year prior to the index visit to measure potential risk factors for AAEs in the subsequent year. An AAE was defined as either (1) an asthma-coded hospitalization or ED visit, or (2) an asthma-related systemic corticosteroid administration (intramuscular or intravenous) or oral corticosteroid dispensing. Poisson regression models with robust standard errors were utilized to estimate the adjusted risk ratios (aRR) for future AAEs.

**Results:** In the study cohort, mean age was 44, and 64% were female; 6.5% had AAEs within one year after the index visit. In multivariate models, age, gender, race, ethnicity, smoking status, body mass index, prior acute asthma care, and a variety of comorbidities and other clinical characteristics were significant predictors for future AAE risk.

**Conclusion:** Population-based disease management strategies for asthma should be expanded to include those with mild asthma in addition to those with moderate to severe disease.

**Keywords:** Mild asthma; acute asthma exacerbation; asthma burden; electronic health records; health care resource utilization; low utilizer; risk factor.

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Respir Res

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. 2024 May 29;25(1):227.

doi: 10.1186/s12931-024-02769-3.

# [Expression of glucocorticoid receptor and HDACs in airway smooth muscle cells is associated with response to steroids in COPD](#)

[Liang Zhou](#)<sup>1</sup>, [Michael Roth](#)<sup>1</sup>, [Eleni Papakonstantinou](#)<sup>1,2,3,4</sup>, [Michael Tamm](#)<sup>1,2</sup>, [Daiana Stolz](#)<sup>5,6,7,8</sup>

Affiliations expand

- PMID: 38812021
- PMCID: [PMC11137987](#)
- DOI: [10.1186/s12931-024-02769-3](#)

## Abstract

**Background:** Steroid insensitivity in Chronic Obstructive Pulmonary Disease (COPD) presents a problem for controlling the chronic inflammation of the airways. The glucocorticoid receptor (GR) mediates the intracellular signaling of inhaled corticosteroids (ICS) by interacting with transcription factors and histone deacetylases (HDACs). The aim of this study was to assess if COPD patients' response to ICS in vivo, may be associated with the expression of GR, the complex of GR with transcription factors, and the expression of various HDACs in vitro.

**Methods:** Primary airway smooth muscle cells (ASMC) were established from endobronchial biopsies obtained from patients with asthma (n = 10), patients with COPD (n = 10) and subjects that underwent diagnostic bronchoscopy without pathological findings and served as controls (n = 6). ASMC were also established from 18 COPD patients, 10 responders and 8 non-responders to ICS, who participated in the HISTORIC study, an investigator-initiated and driven clinical trial that proved the hypothesis that COPD patients with high ASMC in their endobronchial biopsies respond better to ICS than patients with low ASMC. Expression of GR and its isoforms GR $\alpha$  and GR $\beta$  and HDACs was investigated in primary ASMC in the absence or in the presence of dexamethasone (10<sup>-8</sup>M) by western blotting. The complex formation of GR with transcription factors was assessed by co-immunoprecipitation.

**Results:** Expression of GR and its isoform GR $\alpha$  but not GR $\beta$  was significantly reduced in ASMC from COPD patients as compared to controls. There were no significant differences in the expression of GR, GR $\alpha$  and GR $\beta$  between responders and non-responders to ICS. However, treatment with dexamethasone upregulated the expression of total GR (p = 0.004) and GR $\alpha$  (p = 0.005) after 30 min in responders but not in non-responders. The formation of the complex GR-c-Jun was increased 60 min after treatment with dexamethasone only in responders who exhibited significantly lower expression of HDAC3 (p = 0.005) and HDAC5 (p < 0.0001) as compared to non-responders.

**Conclusions:** These data suggest that ASMC from COPD patients who do not respond to treatment with ICS, are characterized by reduced GR-c-Jun complex formation and increased expression of HDAC3 and HDAC5.

**Trial registration:** ISRCTN11017699 (Registration date: 15/11/2016).

**Keywords:** Airway smooth muscle cells; Chronic obstructive pulmonary disease; Glucocorticoid receptor; Glucocorticoid sensitivity; Histone deacetylases.

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## Conflict of interest statement

The authors declare no competing interests.

- [61 references](#)

- [7 figures](#)

#### SUPPLEMENTARY INFO

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. 2024 May 29;33(172):230250.

doi: 10.1183/16000617.0250-2023. Print 2024 Apr 30.

# [The role of dendritic cells in respiratory viral infection](#)

[Elisabeth De Leeuw](#)<sup>1,2</sup>, [Hamida Hammad](#)<sup>3,2</sup>

Affiliations [expand](#)

- PMID: [38811032](#)
- PMCID: [PMC11134197](#)
- DOI: [10.1183/16000617.0250-2023](#)

# Abstract

Respiratory viral infections represent one of the major causes of death worldwide. The recent coronavirus disease 2019 pandemic alone claimed the lives of over 6 million people around the globe. It is therefore crucial to understand how the immune system responds to these threats and how respiratory infection can be controlled and constrained. Dendritic cells (DCs) are one of the key players in antiviral immunity because of their ability to detect pathogens. They can orchestrate an immune response that will, in most cases, lead to viral clearance. Different subsets of DCs are present in the lung and each subset can contribute to antiviral responses through various mechanisms. In this review, we discuss the role of the different lung DC subsets in response to common respiratory viruses, with a focus on respiratory syncytial virus, influenza A virus and severe acute respiratory syndrome coronavirus 2. We also review how lung DC-mediated responses to respiratory viruses can lead to the worsening of an existing chronic pulmonary disease such as asthma. Throughout the review, we discuss results obtained from animal studies as well as results generated from infected patients.

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## Conflict of interest statement

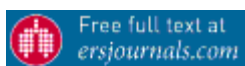
Conflict of interest: All authors have nothing to disclose.

- [75 references](#)
- [4 figures](#)

### SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Chest

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. 2024 May 28;S0012-3692(24)00659-7.

doi: 10.1016/j.chest.2024.04.023. Online ahead of print.

# CT Airway Mucus in Older People without Chronic Respiratory Illness

[Harkiran K Kooner](#)<sup>1</sup>, [Hana Serajeddini](#)<sup>2</sup>, [Rachel L Eddy](#)<sup>3</sup>, [Cory Yamashita](#)<sup>2</sup>, [Sarah Svenningsen](#)<sup>4</sup>, [Grace Parraga](#)<sup>5</sup>

Affiliations expand

- PMID: 38815621
- DOI: [10.1016/j.chest.2024.04.023](https://doi.org/10.1016/j.chest.2024.04.023)

*No abstract available*

**Keywords:** Chest CT; airway occlusions; airways disease; asthma; mucus plugs.

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BMC Public Health

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. 2024 May 28;24(1):1423.

doi: 10.1186/s12889-024-18911-1.

# Epidemiological characteristics of asthma-COPD overlap, its association with all-cause mortality, and the mediating role of depressive symptoms: evidence from NHANES 2005-2018

[Meng Zhu](#) <sup>#1,2</sup>, [An Chen](#) <sup>#3,4</sup>

Affiliations expand

- PMID: 38807148
- PMCID: [PMC11134654](#)
- DOI: [10.1186/s12889-024-18911-1](#)

## Abstract

**Background:** Asthma-COPD overlap (ACO) is a distinct and intricate respiratory condition that requires specific attention and management. The objective of this cohort study was to examine the epidemiological characteristics of ACO, explore the association between ACO and all-cause mortality, and investigate the potential mediating role of depressive symptoms in this association.

**Methods:** This retrospective cohort study used data from the National Health and Nutrition Examination Survey (NHANES) 2005-2018 and National Death Index (NDI) 2019. A total of 22,745 participants were included: 705 with ACO, 2352 with asthma-only, 853 with COPD-only, and 18,835 without asthma or COPD. The non-ACO group (N = 22,040) referred to the individuals without ACO. Statistical tests were employed to assess differences in some characteristics between the ACO group and the other groups. Cox proportional hazards models were applied to evaluate the relationship between ACO and all-cause mortality, estimating hazard ratios (HR) with 95% confidence intervals. Mediation analysis was conducted to investigate the potential mediating effects of depressive symptoms on the association of ACO with all-cause mortality.

**Results:** The prevalence of ACO was 3.10% in our study population. Compared to the non-ACO participants, the ACO participants exhibited significantly different characteristics, including higher age, a lower family income-to-poverty ratio, a higher body mass index, higher rates of comorbidities i.e., hypertension, diabetes, hyperlipidemia, cardiovascular disease, and cancer, poorer dietary habits, and a higher rate of depressive disorders. Compared to the participants without ACO, the participants with ACO exhibited a significant increase in all-cause mortality (HR = 1.908, 95%CI 1.578-1.307,  $p < 0.001$ ). The proportions mediated by depressive symptoms for ACO -associated all-cause mortality were 8.13% (CI: 4.22%-14.00%,  $p < 0.001$ ).

**Conclusions:** This study revealed a strong relationship between ACO and all-cause mortality and uncovered a potential psychological mechanism underlying this relationship. Our study indicates the possible necessity of offering comprehensive care to ACO patients, encompassing early detection, lifestyle guidance, and mental health support. Nevertheless, due to the limitations in the study design and the dataset, the results should be interpreted with caution.

**Keywords:** All-cause mortality; Asthma-COPD overlap; Depressive symptoms; Mediation analysis.

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## Conflict of interest statement

The authors declare no competing interests.

- [79 references](#)
- [1 figure](#)

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Intern Emerg Med

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. 2024 May 28.

doi: 10.1007/s11739-024-03648-x. Online ahead of print.

# Impact of electronic cigarettes (e-cigs) and heat-not-burn/heated tobacco products (HnB/HTP) on asthma and chronic obstructive pulmonary disease: a viewpoint of the Italian Society of Internal Medicine

[Paola Andreozzi](#)<sup>1</sup>, [Gualberto Gussoni](#)<sup>2</sup>, [Giorgio Sesti](#)<sup>3</sup>, [Nicola Montano](#)<sup>4</sup>, [Antonello Pietrangelo](#)<sup>5</sup>; [Italian Society of Internal Medicine \(SIMI\) Council Member Group](#)

Collaborators, Affiliations expand

- PMID: 38806787
- DOI: [10.1007/s11739-024-03648-x](https://doi.org/10.1007/s11739-024-03648-x)

## Abstract

The association of cigarette smoking with several severe and very severe diseases (oncological, cardiovascular, respiratory) which have dramatic epidemiological, medical, and financial impact, is a well-known public threat. Asthma and chronic obstructive pulmonary disease (COPD) are highly prevalent diseases in Italy, posing significant public health challenges. Tobacco smoking, a primary risk factor for COPD and a common asthma trigger, remains a critical preventable public health issue. While universally acknowledged that quitting smoking drastically reduces the risk of smoking-related health issues, a significant portion of smokers and patients find quitting challenging or undesirable, hence a need for new ways to deal with it. A worth considering alternative might be the switch to

electronic cigarettes (e-cig), and heat-not-burn/heated tobacco products (HnB/HTP). Emerging evidence suggests potential benefits in asthma and COPD management when transitioning from traditional smoking to e-cigs or HnB devices. However, the effectiveness of these products in facilitating smoking cessation is still debated, alongside concerns about their role in promoting smoking initiation among non-smokers. Internists are among the physicians who most frequently assist patients with smoking-related diseases, and in this perspective they cannot avoid paying attention to the progressive diffusion of smoking products alternative to the traditional cigarette, and to the controversies with respect to their use. In this context, the Italian Society of Internal Medicine, also recognizing a growing need for clarity for healthcare providers, has undertaken a comprehensive analysis of existing literature to offer an informed perspective on the health impact of e-cigs and HnB/HTP on asthma and COPD.

**Keywords:** Asthma; COPD; E-cigarettes; Heat-not-burn devices; Smoking cessation.

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- [84 references](#)

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[Editorial](#)

Eur Respir J

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. 2024 May 28;63(5):2400408.

doi: 10.1183/13993003.00408-2024. Print 2024 May.

# As needed ICS/formoterol: not all of Europe is equal

[Andrew Bush](#)<sup>1,2</sup>, [Winifried Randerath](#)<sup>3,4</sup>, [Nicolas Roche](#)<sup>5,6</sup>

Affiliations expand

- PMID: 38806204
- DOI: [10.1183/13993003.00408-2024](https://doi.org/10.1183/13993003.00408-2024)

*No abstract available*

## Conflict of interest statement

Conflict of interest: A. Bush is the current ERS Guidelines Director. W. Randerath is ERS Guidelines Director elect, and also reports lecture honoraria from Heinen & Löwenstein, Habel Medizintechnik, Jazz Pharmaceuticals, Inspire, Philips Respiroics, Bioprojet and Westfalen Medical, travel support from Heinen & Löwenstein, Jazz Pharmaceuticals, Philips Respiroics, Habel Medizintechnik and Bioprojet, advisory board participation with Bioprojet, Jazz Pharmaceuticals and Procter & Gamble, and leadership roles as European Respiratory Society Head of Assembly 4, and Secretary General of the German Respiratory Society. N. Roche is Chair of the ERS Scientific Committee, and also reports grants from Boehringer Ingelheim, Novartis, GSK and Pfizer, consulting fees from Boehringer Ingelheim, GSK, AstraZeneca, Sanofi, Chiesi, Pfizer, Novartis, Teva, Bayer, Austral and Biosency, lecture honoraria from Boehringer Ingelheim, GSK, AstraZeneca, Sanofi, Chiesi, Pfizer, Novartis, Teva, Zambon, MSD and Menarini, and travel support from Chiesi, AstraZeneca and GSK.

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# Biomarkers in Asthma, Potential for Therapeutic Intervention

[M Asghar Pasha](#)<sup>1</sup>, [Russell Hopp](#)<sup>2</sup>, [Nazia Habib](#)<sup>3</sup>, [Dale Tang](#)<sup>3</sup>

Affiliations expand

- PMID: 38805392
- DOI: [10.1080/02770903.2024.2361783](https://doi.org/10.1080/02770903.2024.2361783)

## Abstract

Asthma is a heterogeneous disease with multiple phenotypes that have variable risk factors and therapeutic responses. Airway hyperreactivity, inflammation and airway remodeling are hallmarks of asthma. Asthmatics exhibiting an increase in airway T2 inflammation is now classify as having T2-"high" asthma. Type 2 cytokines, IL-4, IL-5, and IL-13, along with other inflammatory mediators, lead to increased eosinophilic inflammation along with elevated FeNO in this endotype. There is no clear definition for T2-"low" asthma. Biomarkers can help identify different phenotypes and endotypes, treatment response to standard treatment or potential therapeutic targets particularly for biologics. As our knowledge of phenotypes and endotypes improved, biologics have increasingly integrated into treatment strategies for severe asthma. These treatments block specific inflammatory pathways or single mediators. Single or composite biomarkers may help to identify subsets of patients who will benefit from these treatments. However, only a few inflammatory biomarkers have validated for clinical application. As knowledge emerges, the goal would be to provide individualized care to asthmatic patients.

**Keywords:** FeNO; T2-"Low" asthma; T2-"high" asthma; biologics; biomarkers; endotype; eosinophil; periostin; phenotype; sIgE.

FULL TEXT LINKS



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J Asthma



. 2024 May 28:1-37.

doi: 10.1080/02770903.2024.2361785. Online ahead of print.

# [Associations between asthma and cognitive functioning among older adults. Does the age of asthma diagnosis matter? Results from the RAND IFLS-5 study](#)

[Nirmin F Juber](#)<sup>1,2</sup>, [Lena M Hofbauer](#)<sup>2</sup>, [Francisca S Rodriguez](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 38805388
- DOI: [10.1080/02770903.2024.2361785](https://doi.org/10.1080/02770903.2024.2361785)

## Abstract

Previous studies involving asthma and cognitive functioning have produced inconclusive results. In addition, those studies rarely accounted for the age of asthma diagnosis and asthma treatment status. To assess the associations of asthma status or age at asthma diagnosis with cognition using the Telephone Survey of Cognitive Status, we thus analyze data from a large population-based sample. Further, we investigated the possibility that

asthma treatment mediates these associations. This is a cross-sectional study from the Indonesian Family Life Survey Fifth Wave (IFLS-5) collected in 2014-2015. A weighted linear regression model was used to examine the associations between asthma and cognitive functioning scores in adults aged 50 years or older. Of the 6660 total samples included in this study, 176 participants had asthma (2.6%). We controlled for age, sex, and urbanicity with further adjustments for adult covariates or childhood covariates, as appropriate. There was no association between overall asthma status and cognitive functioning scores. However, asthma diagnosed at 0-19 years was associated with significantly higher cognitive functioning scores (Beta coefficient= 2.24, 95% CI: 0.62-0.87), compared to those without asthma. In the analysis involving current treatment status (restricted analysis), the significant association disappeared among those under current asthma treatment status, indicating that asthma treatment may mediate the association. Asthma might not be a risk factor for cognitive impairment. Observations of a significant association of pediatric asthma with higher cognitive scores need further investigation. Understanding cognitive functioning among older adults with asthma may improve the surveillance of cognitive decline in this age group.

**Keywords:** asthma; cognitive function; epidemiology; older adults; public health.

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Editorial

Respirology

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. 2024 May 28.

doi: 10.1111/resp.14758. Online ahead of print.

# Treatable traits—Where we are, where we are headed

[Vanessa Marie McDonald](#)<sup>1,2,3</sup>, [Peter Gerard Gibson](#)<sup>1,2,3</sup>

Affiliations expand

- PMID: 38804093
- DOI: [10.1111/resp.14758](https://doi.org/10.1111/resp.14758)

*No abstract available*

**Keywords:** COPD; asthma; management.

- [22 references](#)

SUPPLEMENTARY INFO

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Comparative Study

JAMA

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. 2024 May 28;331(20):1732-1740.

doi: 10.1001/jama.2024.3908.

# Racial and Ethnic Disparities in All-Cause and Cause-Specific Mortality Among US Youth

[Elizabeth R Wolf](#)<sup>1,2</sup>, [Frederick P Rivara](#)<sup>3,4,5</sup>, [Colin J Orr](#)<sup>6,7</sup>, [Anabeel Sen](#)<sup>8</sup>, [Derek A Chapman](#)<sup>8</sup>, [Steven H Woolf](#)<sup>9,10</sup>

Affiliations expand

- PMID: 38703403
- PMID: PMC11070063 (available on 2024-11-04)
- DOI: [10.1001/jama.2024.3908](https://doi.org/10.1001/jama.2024.3908)

## Abstract

**Importance:** Mortality rates in US youth have increased in recent years. An understanding of the role of racial and ethnic disparities in these increases is lacking.

**Objective:** To compare all-cause and cause-specific mortality trends and rates among youth with Hispanic ethnicity and non-Hispanic American Indian or Alaska Native, Asian or Pacific Islander, Black, and White race.

**Design, setting, and participants:** This cross-sectional study conducted temporal analysis (1999-2020) and comparison of aggregate mortality rates (2016-2020) for youth aged 1 to 19 years using US Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research database. Data were analyzed from June 30, 2023, to January 17, 2024.

**Main outcomes and measures:** Pooled, all-cause, and cause-specific mortality rates per 100 000 youth (hereinafter, per 100 000) for leading underlying causes of death were compared. Injuries were classified by mechanism and intent.

**Results:** Between 1999 and 2020, there were 491 680 deaths among US youth, including 8894 (1.8%) American Indian or Alaska Native, 14 507 (3.0%) Asian or Pacific Islander, 110 154 (22.4%) Black, 89 251 (18.2%) Hispanic, and 267 452 (54.4%) White youth. Between 2016 and 2020, pooled all-cause mortality rates were 48.79 per 100 000 (95% CI, 46.58-51.00) in American Indian or Alaska Native youth, 15.25 per 100 000 (95% CI, 14.75-15.76) in Asian or Pacific Islander youth, 42.33 per 100 000 (95% CI, 41.81-42.86) in Black youth,

21.48 per 100 000 (95% CI, 21.19-21.77) in Hispanic youth, and 24.07 per 100 000 (95% CI, 23.86-24.28) in White youth. All-cause mortality ratios compared with White youth were 2.03 (95% CI, 1.93-2.12) among American Indian or Alaska Native youth, 0.63 (95% CI, 0.61-0.66) among Asian or Pacific Islander youth, 1.76 (95% CI, 1.73-1.79) among Black youth, and 0.89 (95% CI, 0.88-0.91) among Hispanic youth. From 2016 to 2020, the homicide rate in Black youth was 12.81 (95% CI, 12.52-13.10) per 100 000, which was 10.20 (95% CI, 9.75-10.66) times that of White youth. The suicide rate for American Indian or Alaska Native youth was 11.37 (95% CI, 10.30-12.43) per 100 000, which was 2.60 (95% CI, 2.35-2.86) times that of White youth. The firearm mortality rate for Black youth was 12.88 (95% CI, 12.59-13.17) per 100 000, which was 4.14 (95% CI, 4.00-4.28) times that of White youth. American Indian or Alaska Native youth had a firearm mortality rate of 6.67 (95% CI, 5.85-7.49) per 100 000, which was 2.14 (95% CI, 1.88- 2.43) times that of White youth. Black youth had an asthma mortality rate of 1.10 (95% CI, 1.01-1.18) per 100 000, which was 7.80 (95% CI, 6.78-8.99) times that of White youth.

**Conclusions and relevance:** In this study, racial and ethnic disparities were observed for almost all leading causes of injury and disease that were associated with recent increases in youth mortality rates. Addressing the increasing disparities affecting American Indian or Alaska Native and Black youth will require efforts to prevent homicide and suicide, especially those events involving firearms.

## Conflict of interest statement

Conflict of Interest Disclosures: Dr Orr reported grants from National Institutes of Health 1K23DK132513-01A1 and an award from American Board of Pediatrics Foundation to explore the clinical supply of the pediatric subspecialty workforce outside the submitted work. No other disclosures were reported.

## Comment in

- [Injury Prevention Science and Firearm Injury in Pediatric Health.](#) Carter PM, Seewald L, Zimmerman M. *JAMA*. 2024 May 28;331(20):1712-1713. doi: 10.1001/jama.2024.4208. PMID: 38703402 No abstract available.
- [39 references](#)

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Review

Eur Respir J

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. 2024 May 28;63(5):2400150.

doi: 10.1183/13993003.00150-2024. Print 2024 May.

# Type 2 airway inflammation in COPD

[Francesca Polverino](#)<sup>1</sup>, [Don D Sin](#)<sup>2</sup>

Affiliations expand

- PMID: 38485148
- DOI: [10.1183/13993003.00150-2024](https://doi.org/10.1183/13993003.00150-2024)

## Abstract

Globally, nearly 400 million persons have COPD, and COPD is one of the leading causes of hospitalisation and mortality across the world. While it has been long-recognised that COPD is an inflammatory lung disease, dissimilar to asthma, type 2 inflammation was thought to play a minor role. However, recent studies suggest that in approximately one third of patients with COPD, type 2 inflammation may be an important driver of disease and a potential therapeutic target. Importantly, the immune cells and molecules involved in COPD-related type 2 immunity may be significantly different from those observed in severe asthma. Here, we identify the important molecules and effector immune cells involved in type 2 airway inflammation in COPD, discuss the recent therapeutic trial results of biologicals that have targeted these pathways and explore the future of therapeutic development of type 2 immune modulators in COPD.

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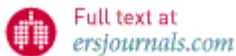
## Conflict of interest statement

Conflict of interest: F. Polverino reports support for the present manuscript from NHLBI HL149744 and Baylor College of Medicine funds outside the submitted work, grants from Victory Houston and Boehringer Ingelheim, and consulting fees from Sanofi-Regeneron, Verona Pharma and Genentech for advisory board participation; in addition, F. Polverino has received travel support to attend ATS Meeting 2023 and is a European Respiratory Journal Section Editor and RCMB programme committee chair. D.D. Sin reports support for the present manuscript as Canada Research Chair, grants from Nextone and lecture honoraria from AZ, GSK and BI; in addition, D.D. Sin is European Respiratory Journal Deputy Chief Editor and the chair of a data and safety monitoring board for an NHLBI-funded clinical trial.

### SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

### FULL TEXT LINKS



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Cell Mol Biol (Noisy-le-grand)

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. 2024 May 27;70(5):69-75.

doi: 10.14715/cmb/2024.70.5.10.

# Interplay of clinical biomarkers in allergic asthma diagnosis and severity: A case-control study

[Zainab Khaleel Mohammed](#)<sup>1</sup>, [Shukur Wasman Smail](#)<sup>2</sup>, [Christer Janson](#)<sup>3</sup>, [Kawa Amin](#)<sup>4</sup>

Affiliations expand

- PMID: 38814233
- DOI: [10.14715/cmb/2024.70.5.10](https://doi.org/10.14715/cmb/2024.70.5.10)

## Abstract

Given asthma's large phenotypic diversity, the study was aimed to use specific biomarkers to characterize Allergic asthma (AA) and its severity. Blood was collected from 42 healthy controls (HCs) and 96 patients with AA. Biomarkers related to blood cell number and function: total leukocyte count (TLCs), neutrophil, lymphocyte, monocyte, eosinophil, basophil, neutrophil-to-lymphocyte ratio (NLR), immunoglobulin E (IgE), tryptase and eosinophilic cationic protein (ECP) as well as remodelling biomarkers (Matrix metalloproteinase (MMP-9), (MMP-16), Fibroblast growth factor (FGF-18) and (FGF-23) and alpha-skeletal muscle actin-1 (ACTa-1) were measured. Significant differences were observed in hematological parameters with higher levels of total leukocytes, eosinophil, and basophil counts in the AA group compared to HCs. The disease group also had significantly higher levels of several serum biomarkers (IgE, TPs, ECP, MMP-9, MMP-16, FGF-18, FGF-23, and ACTa-1) compared to HC. Forced expiratory volume 1 (FEV1) and forced vital capacity (FVC) had a strong negative correlation with ECP, IgE, and ACTa-1. FEV1 was negatively correlated with MMP-16 and tryptase. Patients with AA have higher levels of several biomarkers, such as MMP-9, MMP-16, FGF-18, FGF-23, IgE, tryptase, and ACTa-1. In addition, IgE, tryptase, ACTa-1, and MMP-16 are related to lung function impairment in AA. This indicates that measuring multiple biomarkers may be of value in the future when diagnosing and monitoring AA.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

[Proceed to details](#)

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ERJ Open Res



. 2024 May 27;10(3):00864-2023.

doi: 10.1183/23120541.00864-2023. eCollection 2024 May.

# [The illness burden of severe asthma contrasted to people with mild-to-moderate asthma: a qualitative study](#)

[Eleanor C Majellano](#)<sup>1,2,3</sup>, [Janelle Yorke](#)<sup>4,5</sup>, [Vanessa L Clark](#)<sup>1,2,3</sup>, [Peter G Gibson](#)<sup>1,2,6</sup>, [Amber J Smith](#)<sup>1,2,3</sup>, [Leanne J Holmes](#)<sup>7</sup>, [Vanessa M McDonald](#)<sup>1,2,3,6</sup>

Affiliations expand

- PMID: 38803414
- PMCID: [PMC11129642](#)
- DOI: [10.1183/23120541.00864-2023](#)

## Abstract

**Background:** Disabling symptoms of asthma including breathlessness, cough, wheeze and chest tightness largely impact quality of life; however, how these symptoms impact people with asthma of different severity levels remains unknown. This study aimed to compare and characterise patients' symptom experience and the burden caused, their quality of life, and the medication preferences of people with severe asthma against those of people with mild-to-moderate asthma.

**Methods:** This was a multisite qualitative study involving two focus groups and semistructured interviews of adults with severe asthma undertaken in Australia and UK. Interviews were also undertaken in people with mild-to-moderate asthma. Audio recordings were transcribed and analysed thematically.

**Results:** Participants in both severe asthma and mild-to-moderate asthma groups had a mean±sd age of 57±12 years. Between the severe asthma and mild-to-moderate asthma groups, 62% of participants were female and 86% lived with family. Themes were identified: 1) what is asthma and most bothersome symptoms: both groups reported breathlessness as the most bothersome symptom; 2) impacts on life: disease-related impact differed as people with severe asthma reported significant burden in their quality of life, which encompassed emotional, physical, social and financial wellbeing; and 3) personalised and responsive care: severe asthma interviewees preferred injectable biological therapy as a mode of treatment administration.

**Conclusions:** People with asthma are burdened by breathlessness and cough and other disabling symptoms resulting in impaired quality of life. Understanding the experiences of people with asthma of different severities can improve the patient-clinician partnership.

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## Conflict of interest statement

Conflict of interest: E.C. Majellano has nothing to disclose. Conflict of interest: J. Yorke has nothing to disclose. Conflict of interest: V.L. Clark has nothing to disclose. Conflict of interest: P.G. Gibson reports grants from GlaxoSmithKline, and personal fees from AstraZeneca, Novartis and GlaxoSmithKline, outside the submitted work. Conflict of interest: A.J. Smith has nothing to disclose. Conflict of interest: L.J. Holmes reports personal fees from TEVA, GSK, AstraZeneca and Novartis, outside the submitted work. Conflict of interest: V.M. McDonald reports grants from the National Health and Medical Research Council during the conduct of the study; grants from the Hunter Medical Research Institute, the National Health and Medical Research Council, Ramaciotti Foundation and the John Hunter Hospital Charitable Trust Research, and grants and personal fees from GlaxoSmithKline and AstraZeneca, outside the submitted work.

- [39 references](#)
- [2 figures](#)

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Adv Ther



. 2024 May 27.

doi: 10.1007/s12325-024-02889-8. Online ahead of print.

# Efficacy of Tezepelumab in Patients with Severe, Uncontrolled Asthma Across Multiple Clinically Relevant Subgroups in the NAVIGATOR Study

[Tara F Carr<sup>1</sup>](#), [Wendy C Moore<sup>2</sup>](#), [Monica Kraft<sup>3</sup>](#), [Guy Brusselle<sup>4</sup>](#), [Mario Castro<sup>5</sup>](#), [Geoffrey L Chupp<sup>6</sup>](#), [Michael E Wechsler<sup>7</sup>](#), [Gillian Hunter<sup>8</sup>](#), [Andrew W Lindsley<sup>9</sup>](#), [Jean-Pierre Llanos<sup>10</sup>](#), [Luke K Burke<sup>11</sup>](#), [Shradha Chandarana<sup>12</sup>](#), [Christopher S Ambrose<sup>13</sup>](#)

Affiliations expand

- PMID: 38802635
- DOI: [10.1007/s12325-024-02889-8](https://doi.org/10.1007/s12325-024-02889-8)

## Abstract

**Introduction:** Many patients with severe asthma continue to experience symptoms and exacerbations despite treatment with standard-of-care therapy. In the phase 3 NAVIGATOR study, tezepelumab significantly reduced exacerbations over 52 weeks compared with placebo in patients with severe, uncontrolled asthma. This analysis assessed the efficacy of tezepelumab in reducing asthma exacerbations in various clinically relevant subgroups of patients in NAVIGATOR.

**Methods:** NAVIGATOR was a phase 3, multicentre, randomized, double-blind, placebo-controlled study. Participants (12-80 years old) with severe, uncontrolled asthma were randomized 1:1 to receive tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. Pre-specified and post hoc analyses were performed to evaluate the annualized asthma exacerbation rate (AAER) over 52 weeks in clinically relevant subgroups of patients defined by baseline patient characteristics, medical history, exacerbation triggers, medication eligibility and medication use before and during the study.

**Results:** Tezepelumab reduced the AAER over 52 weeks compared with placebo across a wide range of patient subgroups assessed. Reductions in exacerbations were similar across

subgroups defined by baseline patient characteristics, ranging from 48% (95% confidence interval [CI]: 21, 65) to 60% (95% CI: 44, 71) in subgroups analysed by sex, smoking history and body mass index. Among the asthma-related comorbidity subgroups investigated, patients with aspirin or NSAID sensitivity had the greatest reductions in AAER with tezepelumab compared with placebo (83%; 95% CI: 66, 91). In patients eligible to receive dupilumab, tezepelumab reduced exacerbations compared with placebo by 64% (95% CI: 54, 71). Reductions in the AAER with tezepelumab compared with placebo were also observed irrespective of exacerbation trigger category and the number of asthma controller medications patients were receiving at baseline.

**Conclusion:** These findings further support the benefits of tezepelumab in patients with severe, uncontrolled asthma and can help to inform healthcare providers' treatment decisions.

**Clinical trial registration:** NAVIGATOR ([NCT03347279](#)).

**Keywords:** Asthma; Biologics; Comorbidities; Exacerbation; Severe asthma; Tezepelumab.

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- [35 references](#)

SUPPLEMENTARY INFO

Associated dataexpand

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Nat Immunol

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. 2024 May 27.

doi: 10.1038/s41590-024-01851-8. Online ahead of print.

# CAR T cells put the brakes on asthma

[Bart N Lambrecht](#)<sup>1,2,3</sup>, [Hamida Hammad](#)<sup>4,5</sup>

Affiliations expand

- PMID: 38802513
- DOI: [10.1038/s41590-024-01851-8](https://doi.org/10.1038/s41590-024-01851-8)

*No abstract available*

- [12 references](#)

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Nat Immunol



. 2024 May 27.

doi: [10.1038/s41590-024-01834-9](https://doi.org/10.1038/s41590-024-01834-9). Online ahead of print.

## A single infusion of engineered long-lived and multifunctional T cells confers durable remission of asthma in mice

[Gang Jin](#)<sup>#1,2,3</sup>, [Yanyan Liu](#)<sup>#1,2,3</sup>, [Lixia Wang](#)<sup>1,2,3</sup>, [Zihao He](#)<sup>1,2,3</sup>, [Xiaocui Zhao](#)<sup>1,2,3</sup>, [Yuying Ma](#)<sup>1,2,3</sup>, [Yuting Jia](#)<sup>2</sup>, [Zhuoyang Li](#)<sup>1,2,3</sup>, [Na Yin](#)<sup>1,2,3</sup>, [Min Peng](#)<sup>4,5,6</sup>

Affiliations expand

- PMID: 38802511
- DOI: [10.1038/s41590-024-01834-9](https://doi.org/10.1038/s41590-024-01834-9)

## Abstract

Asthma, the most prevalent respiratory disease, affects more than 300 million people and causes more than 250,000 deaths annually. Type 2-high asthma is characterized by interleukin (IL)-5-driven eosinophilia, along with airway inflammation and remodeling caused by IL-4 and IL-13. Here we utilize IL-5 as the targeting domain and deplete BCOR and ZC3H12A to engineer long-lived chimeric antigen receptor (CAR) T cells that can eradicate eosinophils. We call these cells immortal-like and functional IL-5 CAR T cells (5T<sub>IF</sub>) cells. 5T<sub>IF</sub> cells were further modified to secrete an IL-4 mutein that blocks IL-4 and IL-13 signaling, designated as 5T<sub>IF</sub>4 cells. In asthma models, a single infusion of 5T<sub>IF</sub>4 cells in fully immunocompetent mice, without any conditioning regimen, led to sustained repression of lung inflammation and alleviation of asthmatic symptoms. These data show that asthma, a common chronic disease, can be pushed into long-term remission with a single dose of long-lived CAR T cells.

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- [49 references](#)

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Randomized Controlled Trial



. 2024 May 27;11(1):e002035.

doi: 10.1136/bmjresp-2023-002035.

# Internet-delivered cognitive-behaviour therapy for anxiety related to asthma: study protocol for a randomised controlled trial

[Marianne Bonnert](#)<sup>1,2</sup>, [Stephen Nash](#)<sup>3</sup>, [Erik M Andersson](#)<sup>4</sup>, [Sten Erik Bergström](#)<sup>5</sup>, [Christer Janson](#)<sup>6</sup>, [Catarina Almqvist](#)<sup>3,5</sup>

Affiliations expand

- PMID: 38802281
- PMCID: [PMC11131118](#)
- DOI: [10.1136/bmjresp-2023-002035](#)

## Abstract

**Introduction:** There is an established association between asthma and anxiety. The overlap between asthma symptoms and symptoms of anxiety may cause individuals to overestimate their asthma severity and restrict their daily activities leading to a low quality of life. There is currently weak evidence for treatments targeting anxiety related to asthma, but cognitive-behavioural therapy (CBT) has shown some promising but mixed results. The current randomised controlled trial will investigate if exposure-based internet-delivered CBT (Internet-CBT) is more effective than treatment as usual+medical education (TAU+ME) to relieve symptoms of anxiety and asthma control.

**Methods and analysis:** 90 participants will be randomised 1:1 to 8 weeks of Internet-CBT or TAU+ME. The primary outcome, the patient-reported Catastrophising Asthma Scale, will be analysed from baseline to the primary endpoint at 16 weeks using hierarchical linear

mixed model of the slope over time. Secondary outcomes, such as asthma control, quality of life and forced expiratory volume in 1 s, will be analysed correspondingly.

**Ethics and dissemination:** All participants will be informed about the study and leave their consent before study entry. All results will be analysed at group level and reported through publication in a peer-reviewed scientific journal within the field. The study received ethical approval by the Swedish Ethical Review Authority in January 2020 (ID: 2019-05985; 2022-01117-02).

**Trial registration number:** Registered at ClinicalTrials.gov (ID: [NCT04230369](#)).

**Keywords:** Asthma; Complementary Medicine; Psychology.

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## Conflict of interest statement

Competing interests: None declared.

- [54 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated dataexpand

FULL TEXT LINKS



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

1

Review

Expert Rev Clin Immunol

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. 2024 Jun 1.

doi: 10.1080/1744666X.2024.2363803. Online ahead of print.

# The role of histone deacetylases in inflammatory respiratory diseases: an update

[Sicen Pan](#)<sup>1,2</sup>, [Xiangdong Wang](#)<sup>1,2</sup>, [Jian Jiao](#)<sup>1,2</sup>, [Luo Zhang](#)<sup>1,2</sup>

Affiliations [expand](#)

- PMID: 38823008
- DOI: [10.1080/1744666X.2024.2363803](https://doi.org/10.1080/1744666X.2024.2363803)

## Abstract

**Introduction:** Histone deacetylases (HDACs) catalyze the removal of acetyl groups from lysine residues of histones and other proteins, generally leading to a closed chromosomal configuration and transcriptional repression. Different HDACs have distinct substrate specificities and functions in different biological processes. Accumulating evidence indicates that HDACs play a key role in the pathogenesis of multiple respiratory diseases.

**Areas covered:** After an extensive search of the PubMed database, Web of Science and ClinicalTrials.gov, covering the period from 1992 to 2024, this review summarizes recent advances in understanding the role of HDACs in inflammatory respiratory diseases, including allergic rhinitis (AR), chronic rhinosinusitis (CRS), asthma and chronic obstructive pulmonary disease (COPD). We also examine recent progress on the efficacy and potential use of histone deacetylase inhibitors (HDACi) for the treatment of these diseases.

**Expert opinion:** Available data indicate that HDACs play an important role in the development of common inflammatory respiratory diseases, and HDACi have shown promise as treatments for these diseases. However, the exact roles and underlying mechanisms of specific HDACs in disease pathogenesis require further study. Additional work is necessary to develop novel potent HDACi with high isoform selectivity.

**Keywords:** Allergic rhinitis; asthma; chronic obstructive pulmonary disease; chronic rhinosinusitis; histone deacetylase inhibitors; histone deacetylases.

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Publication types [expand](#)

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Review

Otolaryngol Head Neck Surg

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. 2024 Jun 1.

doi: 10.1002/ohn.836. Online ahead of print.

# Predicting Adherence to Topical Medications in Chronic Rhinologic Disease: A Systematic Review

[Stylianos Monos](#)<sup>1</sup>, [Flora Yan](#)<sup>1</sup>, [Caitlin C McLean](#)<sup>1</sup>

Affiliations expand

- PMID: 38822756
- DOI: [10.1002/ohn.836](https://doi.org/10.1002/ohn.836)

## Abstract

**Objective:** To determine risk factors of medical adherence and describe strategies to increase adherence in patients with chronic rhinologic disease.

**Data sources:** PubMed, SCOPUS, CINAHL, and Cochrane.

**Review methods:** Systematic review of 4 databases (PubMed, SCOPUS, CINAHL, Cochrane) from inception of databases to September 1, 2022 to identify studies that evaluated factors related to and affected by medical adherence in patients with chronic rhinologic disease.

**Results:** Of 1491 studies screened, 25 studies met inclusion criteria. Of these, 7 studies described how sensory attributes of intranasal sprays affect adherence, including odor, taste, aftertaste, and side effects. Five studies described record keeping diaries/notification systems to improve adherence, with demonstration of web-based platforms to send reminders as well as keep record of medication usage to improve adherence. Eight studies described patient-specific risk factors to nonadherence, with demonstration of increased age and conscientious personalities correlating with medical adherence. Five studies looked at pediatric patients specifically, with adherence rates in children paralleling that of adults. Additionally, nonadherence in children may have greater implications for school performance.

**Conclusion:** Overall, adherence to topical medical therapy in patients with chronic rhinologic disease is affected by patient-related and medication-specific factors which should be considered when counseling patients. Web-based diary or notification systems may help increase adherence. Additionally, children are equally adherent to topical medical therapy as adults and nonadherence may have negative implications for school performance.

**Keywords:** allergic rhinitis; chronic rhinosinusitis; medication adherence; notification system; sensory attributes; web-based diary.

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- [48 references](#)

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Pediatr Allergy Immunol

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. 2024 Jun;35(6):e14166.

doi: 10.1111/pai.14166.

# The role of adenoid immune phenotype in polysensitized children with allergic rhinitis and adenoid hypertrophy

[Lanye Hu](#)<sup>1</sup>, [Wenjun He](#)<sup>1</sup>, [Junyang Li](#)<sup>1</sup>, [Yan Miao](#)<sup>2</sup>, [Huanhuan Liang](#)<sup>2</sup>, [Youjin Li](#)<sup>1</sup>

Affiliations expand

- PMID: 38822736
- DOI: [10.1111/pai.14166](https://doi.org/10.1111/pai.14166)

## Abstract

**Background:** There is increasing interest in elucidating the relationship between adenoid hypertrophy (AH) and allergic rhinitis (AR). However, the impact of aeroallergen sensitization patterns on children with AH and AR remains unclear.

**Methods:** Patients aged 2–8 years (recruited from January 2019 to December 2022) with nasal symptoms were assessed for allergies, adenoid size, and respiratory viral infection history. The serum total immunoglobulin E (IgE) and specific IgE levels were measured, and flexible nasal endoscopy was performed. The relationship between AH, aeroallergen sensitization patterns, and lymphocyte subpopulations in adenoid samples was analyzed using flow cytometry.

**Results:** In total, 5281 children were enrolled (56.5% with AR; and 48.6% with AH). AH was more prevalent in children with AR. Compared to nonsensitized individuals, those polysensitized to molds had a higher prevalence of AH (adjusted OR 1.61, 95% CI 1.32–1.96) and a greater occurrence of two or more respiratory viral infections, particularly in adenoidectomy patients. The percentages and corrected absolute counts of regulatory T (Treg) cells, activated Tregs, class-switched memory B cells (CSMBs), natural killer (NK) T cells, and NK cell subpopulations were reduced in the adenoid tissues of children with both AH and AR (AH-AR) compared to AH-nAR children. Polysensitization in AH-AR children correlated with lower CSMB percentages.

**Conclusion:** Polysensitivity to molds is associated with an increased risk of AH in children with AR. Fewer B cells, NK cells, and Treg cells with an effector/memory phenotype were detected in the adenoids of AR children, and these lower percentages of immune cells, particularly CSMBs, were closely linked to aeroallergen sensitization models and respiratory viral infection.

**Keywords:** adenoid hypertrophy; allergic rhinitis; allergy; children; flow cytometry; immune monitoring; phenotype.

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- [23 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and funding [expand](#)

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4

Int J Tuberc Lung Dis

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. 2024 Jun 1;28(6):287-294.

doi: 10.5588/ijtld.23.0383.

# [Phenotyping chronic respiratory diseases with airways obstruction](#)

[T C Nguyen](#)<sup>1</sup>, [H V T Tran](#)<sup>1</sup>, [M H T Tran](#)<sup>1</sup>, [I Godin](#)<sup>2</sup>, [O Michel](#)<sup>3</sup>

Affiliations [expand](#)

- PMID: 38822484
- DOI: [10.5588/ijtld.23.0383](https://doi.org/10.5588/ijtld.23.0383)

## Abstract

<sec id="st1"><title>BACKGROUND</title>Given the high prevalence of asthma-chronic obstructive pulmonary disease overlap (ACO) in Vietnam, there is an urgent need to

establish a simplified strategy for categorising patients as either having asthma or chronic obstructive pulmonary disease (COPD). This classification would streamline the application of treatment recommendations outlined by the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD).

**METHODS** Patients with obstructive lung function were classified as having COPD, asthma, or ACO based on GINA/GOLD guidelines. We hypothesised that ACO-like asthma (ACO-A) would present with positive skin prick tests (SPTs) or early onset of symptoms without a history of tuberculosis (TB), while those with ACO-like COPD (ACO-B) would exhibit negative SPTs and late onset of symptoms and/or a history of TB.

**RESULTS** Among 235 patients, the prevalence of asthma, ACO-A, ACO-B, and COPD was respectively 21%, 22%, 17%, and 40%. Allergic history, rhinitis, and childhood asthma were associated with ACO-A, while high cumulative smoking was correlated with ACO-B. Socio-economic and demographic parameters, medical history, clinical features, smoking habits, lung function, and para-clinical investigations significantly differed between "all asthma" (i.e., individuals with asthma combined with ACO-A) and "all COPD" (i.e., individuals with COPD combined with ACO-B).

**CONCLUSION** Based on SPTs, history of TB, and onset age, ACO patients may be defined as people with asthma or COPD.

#### SUPPLEMENTARY INFO

MeSH termsexpand

[Proceed to details](#)

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Clin Transl Allergy

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. 2024 Jun;14(6):e12358.

doi: 10.1002/ct2.12358.

## [Relevance of individual bronchial symptoms for asthma diagnosis and](#)

# control in patients with rhinitis: A MASK-air study

[Bernardo Sousa-Pinto](#)<sup>1,2</sup>, [Gilles Louis](#)<sup>3,4</sup>, [Rafael J Vieira](#)<sup>1,2</sup>, [Wienczyslawa Czarlewski](#)<sup>5,6</sup>, [Josep M Anto](#)<sup>7,8,9</sup>, [Rita Amaral](#)<sup>1,2</sup>, [Ana Sá-Sousa](#)<sup>1,2</sup>, [Luisa Brussino](#)<sup>10,11</sup>, [G Walter Canonica](#)<sup>12,13</sup>, [Claudia Chaves Loureiro](#)<sup>14,15</sup>, [Alvaro A Cruz](#)<sup>16</sup>, [Bilun Gemicioglu](#)<sup>17,18</sup>, [Tari Haahtela](#)<sup>19</sup>, [Maciej Kupczyk](#)<sup>20</sup>, [Violeta Kvedariene](#)<sup>21,22</sup>, [Desirée E Larenas-Linnemann](#)<sup>23</sup>, [Nhân Pham-Thi](#)<sup>24,25,26</sup>, [Francesca Puggioni](#)<sup>27</sup>, [Frederico S Regateiro](#)<sup>28,29,30,31</sup>, [Jan Romantowski](#)<sup>32</sup>, [Joaquin Sastre](#)<sup>33</sup>, [Nicola Scichilone](#)<sup>34</sup>, [Luis Taborda-Barata](#)<sup>31,35</sup>, [Maria Teresa Ventura](#)<sup>36,37</sup>, [Ioana Agache](#)<sup>38</sup>, [Anna Bedbrook](#)<sup>6,39</sup>, [Alida Benfante](#)<sup>34</sup>, [Karl C Bergmann](#)<sup>40,41</sup>, [Sinthia Bosnic-Anticevich](#)<sup>42,43</sup>, [Matteo Bonini](#)<sup>44,45</sup>, [Louis-Philippe Boulet](#)<sup>46</sup>, [Guy Brusselle](#)<sup>47</sup>, [Roland Buhl](#)<sup>48</sup>, [Lorenzo Cecchi](#)<sup>49</sup>, [Denis Charpin](#)<sup>50</sup>, [Elisio M Costa](#)<sup>51</sup>, [Stefano Del Giacco](#)<sup>52</sup>, [Marek Jutel](#)<sup>53,54</sup>, [Ludger Klimek](#)<sup>55,56</sup>, [Piotr Kuna](#)<sup>20</sup>, [Daniel Laune](#)<sup>57</sup>, [Mika Makela](#)<sup>19</sup>, [Mario Morais-Almeida](#)<sup>58</sup>, [Rachel Nadif](#)<sup>59,60</sup>, [Marek Niedozytko](#)<sup>31,32</sup>, [Nikolaos G Papadopoulos](#)<sup>61</sup>, [Alberto Papi](#)<sup>62</sup>, [Oliver Pfaar](#)<sup>63</sup>, [Daniela Rivero-Yeverino](#)<sup>64</sup>, [Nicolas Roche](#)<sup>60,65,66</sup>, [Boleslaw Samolinski](#)<sup>67</sup>, [Mohamed H Shamji](#)<sup>45,68</sup>, [Aziz Sheikh](#)<sup>69</sup>, [Charlotte Suppli Ulrik](#)<sup>70,71</sup>, [Omar S Usmani](#)<sup>45,71,72</sup>, [Arunas Valiulis](#)<sup>73,74</sup>, [Arzu Yorgancioglu](#)<sup>75</sup>, [Torsten Zuberbier](#)<sup>40,41</sup>, [Joao A Fonseca](#)<sup>1,2</sup>, [Benoit Pétré](#)<sup>3</sup>, [Renaud Louis](#)<sup>4,76</sup>, [Jean Bousquet](#)<sup>6,39,40,41,60</sup>, [MASK-air think tank](#)<sup>77</sup>

Affiliations expand

- PMID: 38804596
- DOI: [10.1002/ct2.12358](https://doi.org/10.1002/ct2.12358)

Free article

## Abstract

**Rationale:** It is unclear how each individual asthma symptom is associated with asthma diagnosis or control.

**Objectives:** To assess the performance of individual asthma symptoms in the identification of patients with asthma and their association with asthma control.

**Methods:** In this cross-sectional study, we assessed real-world data using the MASK-air® app. We compared the frequency of occurrence of five asthma symptoms (dyspnea, wheezing, chest tightness, fatigue and night symptoms, as assessed by the Control of Allergic Rhinitis and Asthma Test [CARAT] questionnaire) in patients with probable, possible or no current asthma. We calculated the sensitivity, specificity and predictive values of each symptom, and assessed the association between each symptom and asthma control (measured using the e-DASTHMA score). Results were validated in a sample of patients with a physician-established diagnosis of asthma.

**Measurement and main results:** We included 951 patients (2153 CARAT assessments), with 468 having probable asthma, 166 possible asthma and 317 no evidence of asthma. Wheezing displayed the highest specificity (90.5%) and positive predictive value (90.8%). In patients with probable asthma, dyspnea and chest tightness were more strongly associated with asthma control than other symptoms. Dyspnea was the symptom with the highest sensitivity (76.1%) and the one consistently associated with the control of asthma as assessed by e-DASTHMA. Consistent results were observed when assessing patients with a physician-made diagnosis of asthma.

**Conclusions:** Wheezing and chest tightness were the asthma symptoms with the highest specificity for asthma diagnosis, while dyspnea displayed the highest sensitivity and strongest association with asthma control.

**Keywords:** asthma; diagnosis; dyspnea; mHealth; wheezing.

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. 2024 Apr 26:41:100915.

doi: 10.1016/j.lanepe.2024.100915. eCollection 2024 Jun.

# Impact of liquid sublingual immunotherapy on asthma onset and progression in patients with allergic rhinitis: a nationwide population-based study (EfficAPSI study)

[Pascal Demoly](#)<sup>1</sup>, [Mathieu Molimard](#)<sup>2</sup>, [Jean-François Bergmann](#)<sup>3</sup>, [Bertrand Delaisi](#)<sup>4</sup>, [Amandine Gouverneur](#)<sup>5</sup>, [Jade Vadel](#)<sup>5</sup>, [Cédric Collin](#)<sup>5</sup>, [Laurence Girard](#)<sup>6</sup>, [Silvia Scurati](#)<sup>6</sup>, [Philippe Devillier](#)<sup>7</sup>

Affiliations expand

- PMID: 38707866
- PMCID: [PMC11066575](#)
- DOI: [10.1016/j.lanepe.2024.100915](#)

## Abstract

**Background:** The only disease-modifying treatment currently available for allergic rhinitis (AR) is allergen immunotherapy (AIT). The main objective of the EfficAPSI real-world study (RWS) was to evaluate the impact of liquid sublingual immunotherapy (SLIT-liquid) on asthma onset and evolution in AR patients.

**Methods:** An analysis with propensity score weighting was performed using the EfficAPSI cohort, comparing patients dispensed SLIT-liquid with patients dispensed AR symptomatic medication with no history of AIT (controls). Index date corresponded to the first dispensation of either treatment. The sensitive definition of asthma event considered the first asthma drug dispensation, hospitalisation or long-term disease (LTD) for asthma, the specific one omitted drug dispensation and the combined one considered omalizumab or three ICS ± LABA dispensation, hospitalisation or LTD. In patients with pre-existing asthma, the GINA treatment step-up evolution was analysed.

**Findings:** In this cohort including 112,492 SLIT-liquid and 333,082 controls, SLIT-liquid exposure was associated with a significant lower risk of asthma onset vs. control, according to all definitions (combined: HR [95% CI] = 0.62 [0.60-0.63], sensitive: 0.77 [0.76-0.78], and specific: 0.67 [0.61-0.72]). Exposure to SLIT was associated with a one-third reduction in GINA step-up regardless baseline steps.

**Interpretation:** In this national RWS with the largest number of person-years of follow-up to date in the field of AIT, SLIT-liquid was associated with a significant reduction in the risk of asthma onset or worsening. The use of three definitions (sensitive or specific) and GINA step-up reinforced the rigorous methodology, substantiating SLIT-liquid evidence as a causal treatment option for patients with respiratory allergies.

**Funding:** Stallergenes Greer.

**Keywords:** Allergic; Asthma; Precision medicine; Rhinitis; Sublingual immunotherapy.

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## Conflict of interest statement

Pascal Demoly: fees directed to research and teaching purposes: ALK-Abelló, AstraZeneca, Ménarini, GlaxoSmithKline, Stallergenes Greer, ThermoFisherScientific, Viatris, Zambon; fees for consulting: Chiesi, Puressentiel. Mathieu Molimard: fees for consulting: ALK-Abelló, Novartis, Stallergenes Greer; Jean-François Bergmann: fees for advisory boards and counselling: Amgen, AstraZeneca, Bayer, BMS, Gilead, GlaxoSmithKline, IQVIA, Lilly, Novartis, Pfizer, Roche, Sanofi, Takeda; Silvia Scurati and Laurence Girard: Employees of Stallergenes Greer; Philippe Devillier: fees for advisory boards, lectures, consulting, or support for attending meetings: ALK-Abelló, Astra Zeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, IQVIA, LEN Médical, Menarini, Novartis, Stallergenes-Greer, Viatris.

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[Review](#)

Acta Paediatr

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. 2024 Jun;113(6):1209-1220.

doi: 10.1111/apa.17221. Epub 2024 Mar 26.

# SQ sublingual immunotherapy tablets for children with allergic rhinitis: A review of phase three trials

Péter Csonka<sup>1,2</sup>, Eckard Hamelmann<sup>3</sup>, Mirjana Turkalj<sup>4,5,6</sup>, Graham Roberts<sup>7,8,9</sup>, Douglas P Mack<sup>10</sup>

Affiliations expand

- PMID: 38529710
- DOI: [10.1111/apa.17221](https://doi.org/10.1111/apa.17221)

## Abstract

**Aim:** To provide paediatricians with a summary of efficacy and safety of SQ sublingual immunotherapy (SLIT) tablets from phase three, randomised, double-blind, placebo-controlled trials in children and adolescents with allergic rhinitis or rhinoconjunctivitis, with and without asthma.

**Methods:** PubMed searches were conducted and unpublished data were included if necessary.

**Results:** Of the 93 publications, 12 were identified reporting 10 trials. One trial was excluded as paediatric-specific efficacy data were unavailable. The nine eligible trials evaluated grass, house dust mite, ragweed and tree SLIT tablets. Consistent reductions in allergic rhinitis or rhinoconjunctivitis symptoms and medication use were observed with SQ SLIT tablets versus placebo. In a five-year trial, sustained reduction of allergic rhinoconjunctivitis symptoms, asthma symptoms and medication use were observed with SQ grass SLIT tablet versus placebo. The number-needed-to-treat to prevent asthma symptoms and medication use in one additional child during follow-up was lowest in younger children. SQ SLIT tablets were generally well tolerated across trials.

**Conclusion:** Evidence supports use of SQ SLIT tablets in children and adolescents with allergic rhinitis or rhinoconjunctivitis, with and without asthma. Long-term data demonstrate disease-modifying effects of SQ grass SLIT tablet and suggest the clinical relevance of initiating allergy immunotherapy earlier in the disease course.

**Keywords:** allergic rhinitis; asthma; paediatric; randomised controlled trials; sublingual allergy immunotherapy tablets.

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- [56 references](#)

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Review

Cytokine

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. 2024 Jun;178:156557.

doi: 10.1016/j.cyto.2024.156557. Epub 2024 Mar 7.

# [CD4+ Foxp3+ Regulatory T-cells in Modulating Inflammatory Microenvironment in Chronic Rhinosinusitis with Nasal Polyps: Progress and Future Prospect](#)

[Nur Najwa Farahin M Yusoff](#)<sup>1</sup>, [Suhana Ahmad](#)<sup>2</sup>, [Wan Faiziah Wan Abdul Rahman](#)<sup>3</sup>, [Rohimah Mohamad](#)<sup>2</sup>, [Jennifer C Boer](#)<sup>4</sup>, [Magdalena Plebanski](#)<sup>4</sup>, [Baharudin Abdullah](#)<sup>5</sup>, [Xin Chen](#)<sup>6</sup>, [Tengku Ahmad Damitri Al-Astani Tengku Din](#)<sup>7</sup>

Affiliations expand

- PMID: 38452440
- DOI: [10.1016/j.cyto.2024.156557](https://doi.org/10.1016/j.cyto.2024.156557)

## Abstract

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subtype of chronic rhinosinusitis (CRS) characterized by the presence of nasal polyps (NP) in the paranasal mucosa. Despite the complex etiology, NP is believed to result from chronic inflammation. The long-term aftermath of the type 2 response is responsible for symptoms seen in NP patients, i.e. rhinorrhea, hyposmia, and nasal obstruction. Immune cellular tolerogenic mechanisms, particularly CD4 + Foxp3 + regulatory T cells (Tregs), are crucial to curtail inflammatory responses. Current evidence suggests impaired Treg activity is the main reason underlying the compromise of self-tolerance, contributing to the onset of CRSwNP. There is compelling evidence that tumor necrosis factor 2 (TNFR2) is preferentially expressed by Tregs, and TNFR2 is able to identify the most potent suppressive subset of Tregs. Tumor necrosis factor (TNF)-TNFR2 interaction plays a decisive role in the activation and expansion of Tregs. This review summarizes current understanding of Tregs biology, focusing on the discussion of the recent advances in the study of TNF-TNFR2 axis in the upregulation of Treg function as a negative feedback mechanism in the control of chronic inflammation. The role of dysregulation of Tregs in the immunopathogenesis of CRSwNP will be analyzed. The future perspective on the harnessing Tregs-mediated self-tolerant mechanism in the management of CRSwNP will be introduced.

**Keywords:** CRSwNP; Immune tolerance; T regulatory cell; TNFR2.

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## 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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Environ Res



. 2024 Jun 1:250:118523.

doi: 10.1016/j.envres.2024.118523. Epub 2024 Feb 19.

# [A machine-learning exploration of the exposome from preconception in early childhood atopic eczema, rhinitis and wheeze development](#)

[Yizhi Dong](#)<sup>1</sup>, [Hui Xing Lau](#)<sup>2</sup>, [Noor Hidayatul Aini Suaini](#)<sup>3</sup>, [Michelle Zhi Ling Kee](#)<sup>4</sup>, [Delicia Shu Qin Ooi](#)<sup>5</sup>, [Lynette Pei-Chi Shek](#)<sup>6</sup>, [Bee Wah Lee](#)<sup>7</sup>, [Keith M Godfrey](#)<sup>8</sup>, [Elizabeth Huiwen Tham](#)<sup>9</sup>, [Marcus Eng Hock Ong](#)<sup>10</sup>, [Nan Liu](#)<sup>11</sup>, [Limsoon Wong](#)<sup>12</sup>, [Kok Hian Tan](#)<sup>13</sup>, [Jerry Kok Yen Chan](#)<sup>14</sup>, [Fabian Kok Peng Yap](#)<sup>15</sup>, [Yap Seng Chong](#)<sup>16</sup>, [Johan Gunnar Eriksson](#)<sup>17</sup>, [Mengling Feng](#)<sup>18</sup>, [Evelyn Xiu Ling Loo](#)<sup>19</sup>

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- PMID: 38382664
- DOI: [10.1016/j.envres.2024.118523](https://doi.org/10.1016/j.envres.2024.118523)

**Free article**

## Abstract

**Background:** Most previous research on the environmental epidemiology of childhood atopic eczema, rhinitis and wheeze is limited in the scope of risk factors studied. Our study adopted a machine learning approach to explore the role of the exposome starting already in the preconception phase.

**Methods:** We performed a combined analysis of two multi-ethnic Asian birth cohorts, the Growing Up in Singapore Towards healthy Outcomes (GUSTO) and the Singapore PREconception Study of long Term maternal and child Outcomes (S-PRESTO) cohorts. Interviewer-administered questionnaires were used to collect information on demography, lifestyle and childhood atopic eczema, rhinitis and wheeze development. Data training was performed using XGBoost, genetic algorithm and logistic regression models, and the top variables with the highest importance were identified. Additive explanation values were identified and inputted into a final multiple logistic regression model. Generalised structural equation modelling with maternal and child blood micronutrients, metabolites and cytokines was performed to explain possible mechanisms.

**Results:** The final study population included 1151 mother-child pairs. Our findings suggest that these childhood diseases are likely programmed in utero by the preconception and pregnancy exposomes through inflammatory pathways. We identified preconception alcohol consumption and maternal depressive symptoms during pregnancy as key modifiable maternal environmental exposures that increased eczema and rhinitis risk. Our mechanistic model suggested that higher maternal blood neopterin and child blood dimethylglycine protected against early childhood wheeze. After birth, early infection was a key driver of atopic eczema and rhinitis development.

**Conclusion:** Preconception and antenatal exposomes can programme atopic eczema, rhinitis and wheeze development in utero. Reducing maternal alcohol consumption during preconception and supporting maternal mental health during pregnancy may prevent atopic eczema and rhinitis by promoting an optimal antenatal environment. Our findings suggest a need to include preconception environmental exposures in future research to counter the earliest precursors of disease development in children.

**Keywords:** Atopic eczema; Exposome; Machine learning; Rhinitis; Wheeze.

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## 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: Yap Seng Chong reports a relationship with Abbott Nutrition that includes: funding grants and speaking and lecture fees. Keith M Godfrey reports a relationship with Abbott Nutrition that includes: funding grants and speaking and lecture fees. Yap Seng Chong reports a relationship with Nestle that includes: funding grants and speaking and lecture fees. Keith M Godfrey reports a relationship with Nestle that includes: funding grants and

speaking and lecture fees. Yap Seng Chong reports a relationship with Danone that includes: funding grants and speaking and lecture fees. Keith M Godfrey reports a relationship with Danone that includes: funding grants and speaking and lecture fees. 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. 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.

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Editorial

Eur Arch Otorhinolaryngol

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. 2024 Jun;281(6):3295-3296.

doi: 10.1007/s00405-024-08510-6. Epub 2024 Feb 15.

## [Gastroesophageal reflux disease, laryngopharyngeal reflux, and nasopharyngeal reflux in chronic rhinosinusitis patients](#)

[Antonino Maniaci](#)<sup>1,2</sup>, [Luigi A Vaira](#)<sup>1,3,4,3</sup>, [Giovanni Cammaroto](#)<sup>1,5</sup>, [Valentin Favier](#)<sup>1,6</sup>, [Jerome R Lechien](#)<sup>7,8,9</sup>

Affiliations expand

- PMID: 38358508
- DOI: [10.1007/s00405-024-08510-6](https://doi.org/10.1007/s00405-024-08510-6)

*No abstract available*

**Keywords:** Chronic; Gastroesophageal reflux disease; Laryngopharyngeal reflux; Nasopharyngeal; Otolaryngology; Rhinosinusitis; Sinusitis.

## Comment on

- [Causal analysis between gastroesophageal reflux disease and chronic rhinosinusitis.](#)  
Chen G, Guo W, Liu S, Wang Y, Zhang X. *Eur Arch Otorhinolaryngol.* 2024 Apr;281(4):1819-1825. doi: 10.1007/s00405-023-08350-w. Epub 2024 Jan 8. PMID: 38189968
- [10 references](#)

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Review

Otolaryngol Head Neck Surg

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. 2024 Jun;170(6):1659-1667.

doi: 10.1002/ohn.663. Epub 2024 Feb 5.

# Gender Differences in Adults With Chronic Rhinosinusitis: A Scoping Review

[John Behnke](#)<sup>1</sup>, [Caroline Dundervill](#)<sup>2</sup>, [Zayd Al-Asadi](#)<sup>2</sup>, [Michel Shahid](#)<sup>3</sup>, [Hassan H Ramadan](#)<sup>1</sup>, [Chadi A Makary](#)<sup>1</sup>

Affiliations expand

- PMID: 38317564
- DOI: [10.1002/ohn.663](https://doi.org/10.1002/ohn.663)

## Abstract

**Objective:** Gender differences in chronic rhinosinusitis (CRS) have been demonstrated in many studies over the last 15 years. The purpose of this scoping review is to investigate the current knowledge on gender differences in CRS and to analyze the gaps in the literature.

**Data sources:** A systematic search of PubMed, Cochrane Library, and Embase databases was performed.

**Review methods:** This scoping review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. Studies that evaluated gender differences in CRS were included in the review.

**Results:** Of the 523 abstracts reviewed, a total of 23 studies met the criteria for inclusion. Articles consisted of retrospective and prospective cohort studies. They were divided into 3 categories based on whether they evaluated gender differences in (1) presentation and baseline quality of life, (2) pathophysiology, and/or (3) outcomes of treatment. Eleven studies addressed differences in presentation, 5 addressed differences in pathophysiology, and 10 dealt with differences in outcomes after surgical or medical management. Most of the studies showed worse baseline QoL secondary to CRS in women, with outcome of treatment being similar in both genders.

**Conclusion:** The experience of CRS appears to vary between genders, with women experiencing a greater subjective burden of disease than men, though with similar outcomes after treatment. Further research is indicated, particularly involving the pathophysiology of CRS, to fully understand the underlying causes of these discrepancies.

**Keywords:** chronic rhinosinusitis; gender differences; health care disparity; scoping review.

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- [30 references](#)

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Randomized Controlled Trial

J Laryngol Otol

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. 2024 Jun;138(6):638-641.

doi: 10.1017/S0022215123002311. Epub 2024 Jan 17.

# [The effect of injection of 1:100 000 adrenaline solution in the pterygopalatine fossa on intra-operative bleeding during endoscopic](#)

# [sinonasal surgical procedures in chronic sinusitis: a blinded clinical trial](#)

[Sevil Nasirmohtaram](#)<sup>1</sup>, [Mir Mohammad Jalali](#)<sup>1</sup>, [Ali Faghih Habibi](#)<sup>1</sup>, [Maliheh Akbarpour](#)<sup>1</sup>

Affiliations expand

- PMID: 38230421
- DOI: [10.1017/S0022215123002311](https://doi.org/10.1017/S0022215123002311)

## Abstract

**Objective:** Rhinosinusitis is one of the most common reasons for a visit to otolaryngology clinics. Some patients are candidates for sinus surgery. Infiltration of 1:100 000 adrenaline in the pterygopalatine fossa was studied, with the aim of evaluating the effect on bleeding in the surgical field.

**Methods:** This double-blind clinical trial was conducted in 2021-2022 on 40 candidates for endoscopic sinus surgery. For each patient, one side of the pterygopalatine fossa was randomly selected to be infiltrated with a vasoconstrictor. Surgical field bleeding on each side was evaluated.

**Results:** Blood loss was  $35.8 \pm 20.9$  ml in the study group and  $38.4 \pm 23.7$  ml for the control group, with no statistically significant difference between groups ( $p = 0.49$ ). In addition, there was no difference between the two groups in terms of the surgical field based on Boezaart scores.

**Conclusion:** Although there are some recommendations on the usage of vasoconstrictors via the pterygopalatine foramen, debate remains.

**Keywords:** Paranasal sinuses; bleeding; endoscope; pterygopalatine fossa.

SUPPLEMENTARY INFO

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Comparative Study

Laryngoscope

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. 2024 Jun;134(6):2626-2633.

doi: 10.1002/lary.31238. Epub 2023 Dec 21.

# Radiological Versus Clinical 1-Year Outcomes of Dupilumab in Refractory CRSwNP: A Real-Life Study

[Francesco Giombi](#)<sup>1,2</sup>, [Gian Marco Pace](#)<sup>1,2</sup>, [Emanuele Nappi](#)<sup>1,2</sup>, [Gianmarco Giunta](#)<sup>1</sup>, [Giovanna Muci](#)<sup>1</sup>, [Francesca Pirola](#)<sup>3,4</sup>, [Fabio Ferrelli](#)<sup>1,3</sup>, [Enrico Heffler](#)<sup>1,2</sup>, [Giovanni Paoletti](#)<sup>1,2</sup>, [Caterina Giannitto](#)<sup>1,5</sup>, [Giuseppe Mercante](#)<sup>1,3</sup>, [Marco Francone](#)<sup>1,5</sup>, [Giuseppe Spriano](#)<sup>1,3</sup>, [Giorgio Walter Canonica](#)<sup>1,2</sup>, [Luca Malvezzi](#)<sup>1,3,4</sup>

Affiliations expand

- PMID: 38126613
- DOI: [10.1002/lary.31238](https://doi.org/10.1002/lary.31238)

## Abstract

**Objective:** To provide real-life evidence on long-term radiological changes in patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP) treated with dupilumab, and to assess possible differences between radiological and clinical results in terms of endoscopic findings and Patient-Reported-Outcomes (PROs).

**Methods:** Consecutive patients treated with dupilumab for recalcitrant CRSwNP were required to undergo CT scan at baseline (T0) and after 12 (T1) since first administration. A

group of patients also performed CT scan at 52 weeks (T2) to assess long-term outcomes. At each timepoint, patients underwent nasal endoscopy, assessment of Nasal-Polyp-Score (NPS), Lund-Kennedy-Score (LKS), and had to fill in the 22-item Sinonasal-Outcome-Test (SNOT-22) and Visual-Analogue-Scales (VAS) for sinonasal symptoms.

**Results:** In fifty-three included patients, from T0 to T1 we detected a significant reduction in mean Lund-Mackay score (LM), PROs (SNOT-22, VAS) and endoscopic (NPS, LKS) scores ( $p < 0.05$ ). In the subset of patients that reached T2 ( $n = 30$ ), compared to T1, we observed a further significant decrease in mean LM, SNOT-22, VAS, and NPS scores, but not in LKS ( $p = 0.420$ ). At T1, the highest improvement was observed in PROs (SNOT-22: 56.26%), and polyp size (NPS: 49.83%). Conversely, between T1 and T2, sinus opacification was shown to be the most improved outcome (LM: 36.86%).

**Conclusions:** Our experience showed that poorly controlled CRSwNP patients treated with dupilumab experienced significant improvement in radiologic, endoscopic and clinical disease severity. While in the initial 3 months, PROs garnered attention for showing earlier effectiveness, radiological outcomes revealed sustained and gradual efficacy in a longer term.

**Level of evidence:** Level 4. According to the Oxford Center for Evidence-Based Medicine 2011 level of evidence guidelines, this non-randomized retrospective cohort study is classified as level 4 evidence *Laryngoscope*, 134:2626-2633, 2024.

**Keywords:** CT scan; Lund Mackay; chronic rhinosinusitis; dupilumab; patients reported outcomes.

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. 2024 Jun;134(6):2513-2524.

doi: 10.1002/lary.31223. Epub 2023 Dec 19.

# Association Between Smoking and Chronic Rhinosinusitis: A Systematic Review and Meta-Analysis

[Claire Jing-Wen Tan](#)<sup>1</sup>, [Bryan Hao Wei Leow](#)<sup>1</sup>, [Benjamin Kye Jyn Tan](#)<sup>1</sup>, [Sean Fong-Jun Tan](#)<sup>2</sup>, [Neville Wei Yang Teo](#)<sup>3,4</sup>, [Tze Choong Charn](#)<sup>3,5</sup>

Affiliations expand

- PMID: 38112394
- DOI: [10.1002/lary.31223](https://doi.org/10.1002/lary.31223)

## Abstract

**Objective:** Chronic rhinosinusitis (CRS) is a prevalent inflammatory disease of the upper airway. The impact of smoking on CRS has not been clearly established. We aim to clarify the association between first-hand cigarette smoking and the prevalence and prognoses of CRS.

**Review methods:** PubMed, Embase, SCOPUS, and Cochrane Library were searched from inception until May 15, 2022. Three blinded reviewers selected relevant studies, extracted data, and evaluated study bias following a PROSPERO-registered protocol (CRD42022345585). We used random-effects meta-analyses to pool the prevalence of smoking in CRS, association between smoking status and CRS, and association of smoking with quality of life (QOL) before and after functional endoscopic sinus surgery (FESS). We also performed descriptive analyses of olfactory function, CT scores, and endoscopy scores before and after FESS.

**Results:** We included 23 cross-sectional studies, 19 cohort studies, two case-control studies, and one prospective clinical trial. The pooled prevalence of ever-smokers was 40% (95% CI = 0.30-0.51) and 33% (95% CI = 0.25-0.43) in patients with and without CRS. Compared to never-smokers, active smokers and past smokers had 1.35 (95% CI = 1.18-1.55) and 1.23 (95% CI = 1.17-1.29) higher odds of having CRS. Among patients with CRS, non-smokers reported higher initial QOL than smokers (standardized mean difference [SMD] = 0.23, 95% CI = 0.11-0.35), although post-FESS QOL was similar (SMD = 0.10, 95% CI = -0.30-0.51). Descriptive analysis found no significant correlations between smoking and post-FESS olfactory function and endoscopy scores.

**Conclusions:** Cigarette smoking is associated with higher prevalence and odds of CRS. Clinicians should be aware that smoking predisposes to CRS, but does not negatively impact the rhinologic outcomes of FESS. *Laryngoscope*, 134:2513-2524, 2024.

**Keywords:** chronic rhinosinusitis; functional endoscopic sinus surgery; olfactory dysfunction; quality of life; smoking.

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Otolaryngol Clin North Am

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. 2024 Jun;57(3):491-500.

# Treatment of the Nose for Patients with Sleep Apnea

[Jacquelyn K Callander](#)<sup>1</sup>, [Jolie L Chang](#)<sup>2</sup>

Affiliations expand

- PMID: 38072728
- DOI: [10.1016/j.otc.2023.11.002](https://doi.org/10.1016/j.otc.2023.11.002)

## Abstract

Nasal obstruction is common in patients with obstructive sleep apnea (OSA) and may variably impact symptoms and severity of OSA. It is associated with decreased continuous positive airway pressure (CPAP) compliance, and both medical and surgical management of nasal obstruction have resulted in increased CPAP adherence. Treatment of OSA with comorbid rhinitis via topical nasal steroids demonstrates a beneficial impact on daytime sleepiness. Isolated nasal surgery has been shown to result in decreased daytime sleepiness and snoring, with minimal effect on OSA severity.

**Keywords:** CPAP compliance; Nasal obstruction; Nasal surgery; Obstructive sleep apnea; Sleep-disordered breathing.

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## Conflict of interest statement

Disclosure The authors have no relevant disclosures.

SUPPLEMENTARY INFO

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Review

Laryngoscope

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. 2024 Jun;134(6):2502-2512.

doi: 10.1002/lary.31163. Epub 2023 Nov 22.

# Effectiveness of the Posterior Nasal Nerve Cryoablation in Allergic and Non-Allergic Rhinitis

[Do Hyun Kim](#)<sup>1</sup>, [Yun Jin Kang](#)<sup>2</sup>, [Soo Whan Kim](#)<sup>1</sup>, [Sung Won Kim](#)<sup>1</sup>, [Mohammed Abdullah Basurrah](#)<sup>3</sup>, [Se Hwan Hwang](#)<sup>4</sup>

Affiliations expand

- PMID: 37991147
- DOI: [10.1002/lary.31163](https://doi.org/10.1002/lary.31163)

## Abstract

**Objectives:** This study assessed the impact of cryoablation of the posterior nasal nerve on symptoms of rhinitis in individuals with allergic rhinitis (AR) and non-allergic rhinitis (NAR).

**Data sources:** PubMed, SCOPUS, Embase, Web of Science, and Cochrane databases for studies published up to June 2023.

**Review methods:** Studies that evaluated the quality of life and rhinitis-related symptom scores before and after cryotherapy treatment, as well as sham-controlled studies, were included.

**Results:** In total, 368 patients from seven studies were analyzed. Patients who underwent cryoablation showed a significant improvement in rhinitis-related symptoms in both NAR and AR. In particular, the most significant improvement was observed in symptoms of rhinorrhea and congestion. Furthermore, cryoablation improved the disease-specific quality of life evaluated using the Rhinoconjunctivitis Quality of Life Questionnaire. The rate of clinical improvement in the total nasal symptom score (total nasal symptom score [TNSS]; >30% reduction from baseline) after cryotherapy was 74%. The change in TNSS score significantly increased over time in NAR patients ( $p = 0.0041$ ). Therefore, changes in the TNSS score after 12 months of cryotherapy treatment were greater in the NAR group than in the AR group ( $p = 0.0020$ ), indicating that cryoablation is effective for both types of rhinitis and has better long-term efficacy in NAR than in AR.

**Conclusions:** Subjective symptom scores related to rhinitis, particularly for rhinorrhea and congestion, decrease after cryoablation of the posterior nasal nerve. Furthermore, the symptom improvement was greater in NAR than AR. *Laryngoscope*, 134:2502-2512, 2024.

**Keywords:** cryotherapy; meta-analysis; nose; quality of life; rhinitis.

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- [Cited by 1 article](#)
- [26 references](#)

SUPPLEMENTARY INFO

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Cell Prolif

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. 2024 May 27:e13662.

doi: 10.1111/cpr.13662. Online ahead of print.

# Tissue specific stem cell therapy for airway regeneration

[Dan Bi Park](#)<sup>1</sup>, [Jae Yoon Lee](#)<sup>2</sup>, [Sung Won Kim](#)<sup>2</sup>, [Do Hyun Kim](#)<sup>2</sup>

Affiliations expand

- PMID: 38803033
- DOI: [10.1111/cpr.13662](https://doi.org/10.1111/cpr.13662)

## Abstract

Secondary atrophic rhinitis (AR), a consequence of mucosal damage during nasal surgeries, significantly impairs patient quality of life. The lack of effective, lasting treatments underscores the need for alternative therapeutic strategies. A major impediment in advancing research is the scarcity of studies focused on secondary AR. Our study addresses this gap by developing an animal model that closely mirrors the histopathological changes observed in patients with secondary AR. These changes include squamous metaplasia, goblet cell hyperplasia, submucosal fibrosis, and glandular atrophy. Upon administering human nasal turbinate stem cells embedded in collagen type I hydrogel in these models, we observed ciliary regeneration. This finding suggests the potential therapeutic benefit of this approach. Our animal models not only emulate the clinical manifestations of secondary AR but also serve as valuable tools for evaluating the efficacy of cell-based biotechnological interventions.

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- [39 references](#)

SUPPLEMENTARY INFO

Grants and funding expand

FULL TEXT LINKS



# chronic cough

1

Lung

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. 2024 Jun;202(3):275-280.

doi: 10.1007/s00408-024-00698-y. Epub 2024 May 11.

## Cough Response to High-Dose Inhaled Corticosteroids in Patients with Chronic Cough and Fractional Exhaled Nitric Oxide Levels $\geq$ 25 ppb: A Prospective Study

[Ji-Ho Lee](#)<sup>#1</sup>, [Sung-Yoon Kang](#)<sup>#2</sup>, [Iseul Yu](#)<sup>1</sup>, [Kyung Eun Park](#)<sup>3</sup>, [Ji-Yoon Oh](#)<sup>4</sup>, [Ji-Hyang Lee](#)<sup>4</sup>, [So-Young Park](#)<sup>5</sup>, [Min-Hye Kim](#)<sup>6</sup>, [Eun-Jung Jo](#)<sup>7</sup>, [Ji-Yong Moon](#)<sup>8</sup>, [Sae-Hoon Kim](#)<sup>9</sup>, [Sang-Hoon Kim](#)<sup>10</sup>, [Byung-Jae Lee](#)<sup>11</sup>, [Woo-Jung Song](#)<sup>12,13</sup>; [Korean Academy of Asthma Allergy, Clinical Immunology Working Group on Chronic Cough](#)

Affiliations expand

- PMID: 38733542
- DOI: [10.1007/s00408-024-00698-y](https://doi.org/10.1007/s00408-024-00698-y)

### Abstract

This study aimed to investigate the effects of high-dose inhaled corticosteroids (ICS) on chronic cough patients with elevated fractional exhaled nitric oxide (FeNO) levels. In a prospective study, adults with chronic cough and FeNO  $\geq$  25 ppb, without any other apparent etiology, received fluticasone furoate (200 mcg) for three weeks. Outcomes were evaluated using FeNO levels, cough severity, and Leicester Cough Questionnaire (LCQ) before and after treatment. Of the fifty participants (average age: 58.4 years; 58% female), the treatment responder rate ( $\geq$  1.3-point increase in LCQ) was 68%, with a significant improvement in cough and LCQ scores and FeNO levels post-treatment. However, improvements in cough did not significantly correlate with changes in FeNO levels. These findings support the guideline recommendations for a short-term ICS trial in adults with

chronic cough and elevated FeNO levels, but the lack of correlations between FeNO levels and cough raises questions about their direct mechanistic link.

**Keywords:** Asthma; Corticosteroids; Cough; Eosinophilic bronchitis; Fractional exhaled nitric oxide.

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- [19 references](#)

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Review

Sleep Med Clin

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. 2024 Jun;19(2):239-251.

doi: 10.1016/j.jsmc.2024.02.004. Epub 2024 Mar 12.

# [Chronic Cough and Obstructive Sleep Apnea](#)

[Krishna M Sundar](#)<sup>1</sup>, [Amanda Carole Stark](#)<sup>2</sup>, [Peter Dicpinigaitis](#)<sup>3</sup>

Affiliations [expand](#)

- PMID: 38692749
- DOI: [10.1016/j.jsmc.2024.02.004](https://doi.org/10.1016/j.jsmc.2024.02.004)

## Abstract

Chronic cough, defined as a cough lasting more than 8 weeks, is a common medical condition occurring in 5% to 10% of the population. Its overlap with another highly prevalent disorder, obstructive sleep apnea (OSA), is therefore not surprising. The relationship between chronic cough and OSA extends beyond this overlap with higher prevalence of OSA in patients with chronic cough than in the general population. The use of continuous positive airway pressure can result in improvement in chronic cough although further studies are needed to understand which patients will experience benefit in their cough from the treatment of comorbid OSA.

**Keywords:** Cough; Cough hypersensitivity syndrome; Gastroesophageal reflux; Obstructive; Sleep apnea.

Published by Elsevier Inc.

## Conflict of interest statement

Disclosures K.M. Sundar has served as consultant in the past for Merck Inc. He is a cofounder of Hypnoscore LLC (software for population management of sleep apnea) in conjunction with the University of Utah Technology Commercialization Office. A.C. Stark has no conflicts to disclose. P. Dicipinigaitis serves as a consultant to Bellus, Chiesi, GSK, Merck, Trevi.

SUPPLEMENTARY INFO

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# Development of an Italian version of the Leicester cough questionnaire and its relationship with other symptom-specific measures for patients with chronic cough

[Alessandra Sorano](#)<sup>1</sup>, [Carlo Fumagalli](#)<sup>2</sup>, [Elenia Cinelli](#)<sup>1</sup>, [Surinder S Biring](#)<sup>3</sup>, [Giovanni A Fontana](#)<sup>1</sup>, [Federico Lavorini](#)<sup>4</sup>

Affiliations expand

- PMID: 38670318
- DOI: [10.1016/j.rmed.2024.107642](https://doi.org/10.1016/j.rmed.2024.107642)

**Free article**

## Abstract

**Objective:** To implement subjective methods for measuring the impact of chronic cough on patients' daily life, including an Italian version of the symptom-specific, health status measure for patients with chronic cough, i.e. the Leicester Cough Questionnaire (LCQ).

**Methods:** Sixty-five chronic cough patients attended a tertiary cough clinic on two separate occasions 8 weeks apart. The visual analogue scale for cough severity (VAS), the LCQ and the cough disturbance score (CDS) were administered on both occasions. The LCQ was adapted for Italian conditions following a forward-backward translation procedure. Concurrent validation, internal consistency, repeatability and responsiveness were determined.

**Results:** The CDS, VAS and LCQ were correlated (r coefficients ranging from 0.69 to 0.94,  $p < 0.01$ ). The internal consistency for each LCQ domain was high (alpha coefficient range

0.87-0.93), as was the 8-week repeatability of the LCQ in the patients (n = 36, 60 %) who displayed no change in CDS and VAS (intra-class correlation coefficient = 0.86, p < 001) over the same period. Patients who reported an improvement in CDS and VAS after 8 weeks (n = 29) also demonstrated significant improvements in each LCQ domain. The mean difference in LCQ total score before and after improvements was 2.26 (95 % CI: 1.58-4.47).

**Conclusions:** The Italian version of the LCQ appears to be just as valid as the other language versions of the questionnaire. In addition, the CDS appears to be a clinically useful, symptom-specific measure of the overall disturbance provoked by cough.

**Keywords:** Chronic cough; Cough disturbance score; Leicester cough questionnaire; VAS; Validation.

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## Conflict of interest statement

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

SUPPLEMENTARY INFO

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Pediatr Pulmonol

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. 2024 Jun;59(6):1525-1527.

# Misconceptions on behavioral cough suppression therapy for pediatric nonspecific cough: A response to Weinberger and Buettner's commentary on Fujiki et al

[Laurie Slovarp](#)<sup>1</sup>, [Marie Jette](#)<sup>2</sup>, [Jane Reynolds](#)<sup>1</sup>, [Amanda I Gillespie](#)<sup>3</sup>, [Julie Barkmeier-Kraemer](#)<sup>4</sup>, [Mary Sandage](#)<sup>5</sup>, [Jaclyn Smith](#)<sup>6</sup>, [Jemma Haines](#)<sup>7</sup>, [Anne Vertigan](#)<sup>8</sup>, [Stuart Mazzone](#)<sup>9</sup>

Affiliations expand

- PMID: 38483040
- DOI: [10.1002/ppul.26966](https://doi.org/10.1002/ppul.26966)

*No abstract available*

**Keywords:** habit cough; pediatric chronic cough; speech-language pathology; suggestion therapy.

- [13 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grants and funding expand

FULL TEXT LINKS



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Clin Gastroenterol Hepatol

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. 2024 Jun;22(6):1200-1209.e1.

doi: 10.1016/j.cgh.2024.01.021. Epub 2024 Feb 2.

# Validated Clinical Score to Predict Gastroesophageal Reflux in Patients With Chronic Laryngeal Symptoms: COuGH RefluX

[Amanda J Krause](#)<sup>1</sup>, [Alexander M Kaizer](#)<sup>2</sup>, [Dustin A Carlson](#)<sup>3</sup>, [Walter W Chan](#)<sup>4</sup>, [Chien-Lin Chen](#)<sup>5</sup>, [C Prakash Gyawali](#)<sup>6</sup>, [Andrew Jenkins](#)<sup>4</sup>, [John E Pandolfino](#)<sup>3</sup>, [Vinathi Polamraju](#)<sup>6</sup>, [Ming-Wun Wong](#)<sup>5</sup>, [Madeline Greytak](#)<sup>1</sup>, [Rena Yadlapati](#)<sup>7</sup>

Affiliations expand

- PMID: 38309491
- PMCID: [PMC11128352](#)
- DOI: [10.1016/j.cgh.2024.01.021](#)

## Abstract

**Background & aims:** Discerning whether laryngeal symptoms result from gastroesophageal reflux is clinically challenging and a reliable tool to stratify patients is needed. We aimed to develop and validate a model to predict the likelihood of gastroesophageal reflux disease (GERD) among patients with chronic laryngeal symptoms.

**Methods:** This multicenter international study collected data from adults with chronic laryngeal symptoms who underwent objective testing (upper gastrointestinal endoscopy and/or ambulatory reflux monitoring) between March 2018 and May 2023. The training phase identified a model with optimal receiver operating characteristic curves, and  $\beta$

coefficients informed a weighted model. The validation phase assessed performance characteristics of the weighted model.

**Results:** A total of 856 adults, 304 in the training cohort and 552 in the validation cohort, were included. In the training phase, the optimal predictive model (area under the curve, 0.68; 95% CI, 0.62-0.74), was the Cough, Overweight/obesity, Globus, Hiatal Hernia, Regurgitation, and male sex (COuGH RefluX) score, with a lower threshold of 2.5 and an upper threshold of 5.0 to predict proven GERD. In the validation phase, the COuGH RefluX score had an area under the curve of 0.67 (95% CI, 0.62-0.71), with 79% sensitivity and 81% specificity for proven GERD.

**Conclusions:** The externally validated COuGH RefluX score is a clinically practical model to predict the likelihood of proven GERD. The score classifies most patients with chronic laryngeal symptoms as low/high likelihood of proven GERD, with only 38% remaining as indeterminate. Thus, the COuGH RefluX score can guide diagnostic strategies and reduce inappropriate proton pump inhibitor use or testing for patients referred for evaluation of chronic laryngeal symptoms.

**Keywords:** Diagnosis; Esophageal pH Monitoring; Esophagus; Laryngopharyngeal Reflux.

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- [25 references](#)
- [2 figures](#)

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[Randomized Controlled Trial](#)



. 2024 May 28;14(5):e083085.

doi: 10.1136/bmjopen-2023-083085.

# Pulmonary rehabilitation in Iranian outpatients with mustard gas lung disease: a randomised controlled trial

[Mostafa Ghanei](#)<sup>1</sup>, [Keir E J Philip](#)<sup>2</sup>, [Mohamed R S Moghadam](#)<sup>3</sup>, [Hamed Hosseini](#)<sup>4</sup>, [Aliakbar Babaie](#)<sup>5</sup>, [Mohammad Roustanezhad](#)<sup>5</sup>, [Nicholas S Hopkinson](#)<sup>6</sup>

Affiliations expand

- PMID: 38806414
- PMCID: [PMC11138312](#)
- DOI: [10.1136/bmjopen-2023-083085](#)

## Abstract

**Objective:** People with mustard gas lung disease experience cough, sputum, breathlessness and exercise limitation. We hypothesised that pulmonary rehabilitation (PR) would be beneficial in this condition.

**Design:** An assessor-blind, two-armed, parallel-design randomised controlled clinical trial.

**Setting:** Secondary care clinics in Iran.

**Participants:** 60 men with breathlessness due to respiratory disease caused by documented mustard gas exposure, mean (SD) age 52.7 (4.36) years, MRC dyspnoea score 3.5 (0.7), St. George's Respiratory Questionnaire (SGRQ) 72.3 (15.2).

**Interventions:** Participants were allocated either to a 6-week course of thrice-weekly PR (n=31) or to usual care (n=29), with 6-week data for 28 and 26, respectively.

**Outcome measures:** Primary endpoint was change in cycle endurance time at 70% baseline exercise capacity at 6 weeks. Secondary endpoints included 6 min walk distance,

quadriceps strength and bulk, body composition and health status. For logistical reasons, blood tests that had been originally planned were not performed and 12-month follow-up was available for only a small proportion.

**Results:** At 6 weeks, cycle endurance time increased from 377 (140) s to 787 (343) s with PR vs 495 (171) s to 479 (159) s for usual care, effect size +383 (231) s ( $p < 0.001$ ). PR also improved 6 min walk distance +103.2 m (63.6-142.9) ( $p < 0.001$ ), MRC dyspnoea score -0.36 (-0.65 to -0.07) ( $p = 0.016$ ) and quality of life; SGRQ -8.43 (-13.38 to -3.48)  $p < 0.001$ , as well as quadriceps strength +9.28 Nm (1.89 to 16.66)  $p = 0.015$ .

**Conclusion:** These data suggest that PR can improve exercise capacity and quality of life in people with breathlessness due to mustard gas lung disease and support the wider provision of this form of care.

**Trial registration number:** IRCT2016051127848N1.

**Keywords:** chronic airways disease; pulmonary disease; rehabilitation medicine.

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## Conflict of interest statement

Competing interests: None declared.

- [51 references](#)
- [2 figures](#)

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Pulmonology

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. 2024 May 27:S2531-0437(24)00057-6.

doi: 10.1016/j.pulmoe.2024.04.010. Online ahead of print.

# Chronic cough in patients with obstructive sleep apnoea: A prospective cohort study

[Laurent Guilleminault](#)<sup>1</sup>, [J r mie Riou](#)<sup>2</sup>, [Sandrine Pontier](#)<sup>3</sup>, [Kamila Sedkaoui](#)<sup>3</sup>, [Fr d ric Gagnadoux](#)<sup>4</sup>, [Wojciech Trzepizur](#)<sup>4</sup>

Affiliations expand

- PMID: 38806367
- DOI: [10.1016/j.pulmoe.2024.04.010](https://doi.org/10.1016/j.pulmoe.2024.04.010)

## Free article

*No abstract available*

## Conflict of interest statement

Conflicts of interest WT received support from ASTEN for attending scientific meetings and payment from AstraZeneca for giving lectures. SP declares receipt of personal fees from ASTEN, ISIS Medical and Vitalair. FG declares receipt of personal fees from AIR LIQUIDE SANTE, INSPIRE, BIOPROJET, RESMED and SEFAM outside of the research contained in this submitted work, payment from PHILIPS RESPIRONICS, JAZZ PHARMACEUTICAL, BIOPROJET, CIDELEC and RESMED for giving presentations and non-financial support from ASTEN SANTE beyond the scope of this submitted work. The other authors have no interests to disclose.

SUPPLEMENTARY INFO

Publication types expand

FULL TEXT LINKS



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

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Review

Clin Chest Med

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. 2024 Jun;45(2):433-444.

doi: 10.1016/j.ccm.2024.02.013. Epub 2024 Apr 2.

## Interstitial Lung Abnormalities: Current Understanding

[Noriaki Wada](#)<sup>1</sup>, [Gary M Hunninghake](#)<sup>2</sup>, [Hiroto Hatabu](#)<sup>3</sup>

Affiliations expand

- PMID: 38816098
- DOI: [10.1016/j.ccm.2024.02.013](https://doi.org/10.1016/j.ccm.2024.02.013)

### Abstract

Interstitial lung abnormalities (ILAs) are incidental findings on computed tomography scans, characterized by nondependent abnormalities affecting more than 5% of any lung zone. They are associated with factors such as age, smoking, genetic variants, worsened clinical outcomes, and increased mortality. Risk stratification based on clinical and radiological features of ILAs is crucial in clinical practice, particularly for identifying cases at high risk of progression to pulmonary fibrosis. Traction bronchiectasis/bronchiolectasis index has emerged as a promising imaging biomarker for prognostic risk stratification in ILAs. These findings suggest a spectrum of fibrosing interstitial lung diseases, encompassing from ILAs to pulmonary fibrosis.

**Keywords:** Clinical management; Interstitial lung abnormalities; Interstitial lung disease; Pulmonary fibrosis; Risk stratification; Traction bronchiectasis/bronchiolectasis index.

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Review

Respir Med



. 2024 Jun;227:107661.

doi: 10.1016/j.rmed.2024.107661. Epub 2024 May 8.

# Inhaled antibiotics: A promising drug delivery strategies for efficient treatment of lower respiratory tract infections (LRTIs) associated with antibiotic resistant biofilm-dwelling and intracellular bacterial pathogens

[Nazrul Islam](#)<sup>1</sup>, [David Reid](#)<sup>2</sup>

Affiliations expand

- PMID: 38729529

- DOI: [10.1016/j.rmed.2024.107661](https://doi.org/10.1016/j.rmed.2024.107661)

**Free article**

## Abstract

Antibiotic-resistant bacteria associated with LRTIs are frequently associated with inefficient treatment outcomes. Antibiotic-resistant *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, infections are strongly associated with pulmonary exacerbations and require frequent hospital admissions, usually following failed management in the community. These bacteria are difficult to treat as they demonstrate multiple adaptational mechanisms including biofilm formation to resist antibiotic threats. Currently, many patients with the genetic disease cystic fibrosis (CF), non-CF bronchiectasis (NCFB) and chronic obstructive pulmonary disease (COPD) experience exacerbations of their lung disease and require high doses of systemically administered antibiotics to achieve meaningful clinical effects, but even with high systemic doses penetration of antibiotic into the site of infection within the lung is suboptimal. Pulmonary drug delivery technology that reliably deliver antibacterials directly into the infected cells of the lungs and penetrate bacterial biofilms to provide therapeutic doses with a greatly reduced risk of systemic adverse effects. Inhaled liposomal-packaged antibiotic with biofilm-dissolving drugs offer the opportunity for targeted, and highly effective antibacterial therapeutics in the lungs. Although the challenges with development of some inhaled antibiotics and their clinical trials have been studied; however, only few inhaled products are available on market. This review addresses the current treatment challenges of antibiotic-resistant bacteria in the lung with some clinical outcomes and provides future directions with innovative ideas on new inhaled formulations and delivery technology that promise enhanced killing of antibiotic-resistant biofilm-dwelling bacteria.

**Keywords:** Antibiotic; Bacteria; Biofilm; Lower respiratory tract infections (LRTIs); Nanoparticles; Pulmonary drug delivery; Resistant bacteria.

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## 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.

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Publication types, MeSH terms, Substances expand

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Review

Auris Nasus Larynx

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. 2024 Jun;51(3):553-568.

doi: 10.1016/j.anl.2024.02.001. Epub 2024 Mar 27.

# [Practical guide for the diagnosis and management of primary ciliary dyskinesia](#)

[Kazuhiko Takeuchi](#)<sup>1</sup>, [Miki Abo](#)<sup>2</sup>, [Hiroshi Date](#)<sup>3</sup>, [Shimpei Gotoh](#)<sup>4</sup>, [Atsushi Kamijo](#)<sup>5</sup>, [Takeshi Kaneko](#)<sup>6</sup>, [Naoto Keicho](#)<sup>7</sup>, [Satoru Kodama](#)<sup>8</sup>, [Goro Koinuma](#)<sup>9</sup>, [Mitsuko Kondo](#)<sup>10</sup>, [Sawako Masuda](#)<sup>11</sup>, [Eri Mori](#)<sup>12</sup>, [Kozo Morimoto](#)<sup>13</sup>, [Mizuho Nagao](#)<sup>14</sup>, [Atsuko Nakano](#)<sup>15</sup>, [Kaname Nakatani](#)<sup>16</sup>, [Naoya Nishida](#)<sup>17</sup>, [Tomoki Nishikido](#)<sup>18</sup>, [Hirotatsu Ohara](#)<sup>19</sup>, [Yosuke Okinaka](#)<sup>20</sup>, [Hiroshi Sakaida](#)<sup>21</sup>, [Koji Shiraishi](#)<sup>22</sup>, [Isao Suzaki](#)<sup>23</sup>, [Ichiro Tojima](#)<sup>24</sup>, [Yasuhiro Tsunemi](#)<sup>25</sup>, [Keigo Kainuma](#)<sup>26</sup>, [Nobuo Ota](#)<sup>27</sup>, [Sachio Takeno](#)<sup>28</sup>, [Shigeharu Fujieda](#)<sup>29</sup>

Affiliations expand

- PMID: 38537559
- DOI: [10.1016/j.anl.2024.02.001](https://doi.org/10.1016/j.anl.2024.02.001)

**Free article**

# Abstract

**Objective:** Primary ciliary dyskinesia (PCD) is a relatively rare genetic disorder that affects approximately 1 in 20,000 people. Approximately 50 genes are currently known to cause PCD. In light of differences in causative genes and the medical system in Japan compared with other countries, a practical guide was needed for the diagnosis and management of Japanese PCD patients.

**Methods:** An ad hoc academic committee was organized under the Japanese Rhinologic Society to produce a practical guide, with participation by committee members from several academic societies in Japan. The practical guide including diagnostic criteria for PCD was approved by the Japanese Rhinologic Society, Japanese Society of Otolaryngology-Head and Neck Surgery, Japanese Respiratory Society, and Japanese Society of Pediatric Pulmonology.

**Results:** The diagnostic criteria for PCD consist of six clinical features, six laboratory findings, differential diagnosis, and genetic testing. The diagnosis of PCD is categorized as definite, probable, or possible PCD based on a combination of the four items above. Diagnosis of definite PCD requires exclusion of cystic fibrosis and primary immunodeficiency, at least one of the six clinical features, and a positive result for at least one of the following: (1) Class 1 defect on electron microscopy of cilia, (2) pathogenic or likely pathogenic variants in a PCD-related gene, or (3) impairment of ciliary motility that can be repaired by correcting the causative gene variants in iPS cells established from the patient's peripheral blood cells.

**Conclusion:** This practical guide provides clinicians with useful information for the diagnosis and management of PCD in Japan.

**Keywords:** Bronchiectasis; Chronic rhinosinusitis; Gene variant; Nasal nitric oxide; Otitis media with effusion; iPS cells.

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SUPPLEMENTARY INFO

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Respir Med



. 2024 May 29:107683.

doi: 10.1016/j.rmed.2024.107683. Online ahead of print.

# Patients with bronchiectasis have a lower combined risk of cardiovascular risk factors and cardiovascular comorbidity compared to patients with COPD

[Martina Lo Casto](#)<sup>1</sup>, [Stefania Marino](#)<sup>1</sup>, [Marta M Zammuto](#)<sup>1</sup>, [Alessandra Tomasello](#)<sup>1</sup>, [Alida Benfante](#)<sup>1</sup>, [Nicola Scichilone](#)<sup>1</sup>, [Salvatore Battaglia](#)<sup>2</sup>

Affiliations expand

- PMID: 38821218
- DOI: [10.1016/j.rmed.2024.107683](https://doi.org/10.1016/j.rmed.2024.107683)

## Abstract

**Introduction and objectives:** Chronic respiratory diseases are associated with an increased risk of cardiovascular diseases (CVD); however, it is unknown whether some respiratory diseases are at higher risk than others. In this perspective, head-to-head studies comparing bronchiectasis and chronic obstructive pulmonary disease (COPD) are encouraged. We explored whether the prevalence of cardiovascular risk factors (diabetes mellitus and hyperlipidemia) and cardiovascular comorbidity (systemic hypertension, ischemic heart diseases, cardiac arrhythmia, stroke) are different in these two diseases.

**Methods:** The present retrospective case-control study aimed to compare patients with bronchiectasis with age and sex-matched individuals with COPD. A total of 63 patients with bronchiectasis and 63 with COPD were retained for analysis.

**Results:** Patients with bronchiectasis had a lower risk of systemic hypertension (OR 0.42 (C.I. 0.20 to 0.87)) and diabetes mellitus (OR 0.28 (C.I. 0.09 to 0.81)). In contrast, ischemic heart diseases, cardiac arrhythmia, stroke, and hyperlipidemia did not differ between the two groups. Logistic regression analysis showed that age, male sex, and COPD remain independent risk factors for having at least one condition of a composite index including the above-mentioned CVD and CV risk factors. In detail, a patient with COPD has a risk of 4.648 times (C.I. 1.48 to 15.78) for having at least one CVD compared with a patient with bronchiectasis.

**Conclusions:** The current findings suggest that subjects with bronchiectasis may experience lower cardiovascular risk than those with COPD. Larger studies are needed to confirm this preliminary observation and its clinical implications.

**Keywords:** Bronchiectasis; COPD; cardiovascular diseases; comorbidity.

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## 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.

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Eur Respir J

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. 2024 May 29:2301966.

doi: 10.1183/13993003.01966-2023. Online ahead of print.

## [Airway IL-1 \$\beta\$ is related to disease severity and mucociliary function in bronchiectasis](#)

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- PMID: 38811046
- DOI: [10.1183/13993003.01966-2023](https://doi.org/10.1183/13993003.01966-2023)

## Abstract

**Rationale:** The inflammasome is a key regulatory complex of the inflammatory response leading to IL-1 $\beta$  release and activation. IL-1 $\beta$  amplifies inflammatory responses and induces mucus secretion and hyperconcentration in other diseases. The role of IL-1 $\beta$  in bronchiectasis has not been investigated.

**Objectives:** To characterize the role of airway IL-1 $\beta$  in bronchiectasis including the association with mucus properties, ciliary function, airway inflammation, microbiome and disease severity.

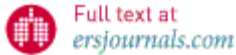
**Methods:** Stable bronchiectasis patients were enrolled in an international cohort study (n=269). IL-1 $\beta$  was measured in sputum supernatant. A validation cohort also had sputum rheology and hydration measured (n=53). For analysis, patients were stratified according to the median value of IL-1 $\beta$  in the population (High *versus* Low) to compare disease severity, airway infection, microbiome (16S rRNA sequencing), inflammation and caspase-1 activity. Primary human nasal epithelial cells grown in air-liquid interface culture were used to study IL-1 $\beta$  effect on cilia function.

**Measurements and main results:** Patients with high sputum IL-1 $\beta$  had more severe disease, increased caspase-1 activity and increased Th1, Th2 and neutrophil inflammatory response compared with patients with low IL-1 $\beta$ . The active-dominant form of IL-1 $\beta$  was associated with increased disease severity. High IL-1 $\beta$  was related to higher relative abundance of Proteobacteria in the microbiome and increased mucus solid content and viscoelastic properties. Chronic IL-1 $\beta$  treatment reduced the functionality of cilia and tight junctions of epithelial cells in-vitro.

**Conclusions:** A subset of stable bronchiectasis patients show increased airway IL-1 $\beta$ , suggesting pulmonary inflammasome activation is linked with more severe disease, airway infection, mucus dehydration and epithelial dysfunction.

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. 2024 May 28;69(6):697-712.

doi: 10.4187/respcare.12089.

# [The Rationale, Evidence, and Adaptations to Pulmonary Rehabilitation for Chronic Respiratory Diseases Other Than COPD](#)

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- PMID: 38806225
- DOI: [10.4187/respcare.12089](https://doi.org/10.4187/respcare.12089)

## Abstract

Over the last 3 decades, pulmonary rehabilitation (PR) has become an integral part of the management of COPD. Many other chronic respiratory diseases have similar systemic

manifestations including skeletal muscle impairment, commonly through deconditioning, and may benefit from PR. However, whereas many programs may accept patients with other respiratory diseases, the program may need several adaptations to optimally manage patients. This article uses the examples of interstitial lung disease including idiopathic pulmonary fibrosis, bronchiectasis, pulmonary hypertension, post lung transplantation, and post-COVID condition to highlight exemplar clinical problems. In addition, the rationale and latest evidence for PR are described alongside the adaptations to the program, including education needs of the delivery team and close integrated care with the wider clinical team. Finally, future directions for clinical care and research are discussed.

**Keywords:** Long COVID; bronchiectasis; interstitial lung disease; pulmonary hypertension; pulmonary rehabilitation; transplantation.

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## Conflict of interest statement

Dr Evans discloses relationships with Genentech/Roche and Moderna.

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Publication types, MeSH termsexpand

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