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

1

Review

COPD

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. 2024 Dec;21(1):2316594.

doi: 10.1080/15412555.2024.2316594. Epub 2024 Feb 29.

Understanding the Gaps in the Reporting of COPD Exacerbations by Patients: A Review

[Paul Jones](#)¹, [Ashraf Alzaabi](#)^{2,3}, [Alejandro Casas Herrera](#)⁴, [Mehmet Polatli](#)⁵, [Marcelo Fouad Rabahi](#)⁶, [Arturo Cortes Telles](#)⁷, [Bhumika Aggarwal](#)⁸, [Sudeep Acharya](#)⁸, [Abdelkader El Hasnaoui](#)⁹, [Chris Compton](#)¹⁰

Affiliations expand

• PMID: 38421013

• DOI: [10.1080/15412555.2024.2316594](https://doi.org/10.1080/15412555.2024.2316594)

Abstract

Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with loss of lung function, poor quality of life, loss of exercise capacity, risk of serious cardiovascular events, hospitalization, and death. However, patients underreport exacerbations, and evidence suggests that unreported exacerbations have similar negative health implications for patients as those that are reported. Whilst there is guidance for physicians to identify patients who are at risk of exacerbations, they do not help patients recognise and report them. Newly developed tools, such as the COPD Exacerbation Recognition Tool (CERT) have been designed to achieve this objective. This review focuses on the underreporting of COPD exacerbations by patients, the factors associated with this, the consequences of underreporting, and potential solutions.

Keywords: COPD; exacerbations; underreporting.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Soc Psychiatry Psychiatr Epidemiol

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. 2024 Mar 1.

doi: 10.1007/s00127-024-02645-x. Online ahead of print.

[The impact of comorbid psychiatric disorders on chronic obstructive pulmonary disease \(COPD\)](#)

hospitalizations: a nationwide retrospective study

[Gonçalo Santos](#)¹, [Ana Rita Ferreira](#)², [Manuel Gonçalves-Pinho](#)^{2,3}, [Alberto Freitas](#)⁴, [Lia Fernandes](#)^{2,5}

Affiliations expand

- PMID: 38429541
- DOI: [10.1007/s00127-024-02645-x](https://doi.org/10.1007/s00127-024-02645-x)

Abstract

Aims: To characterize the register of a secondary diagnosis of mental illnesses in all chronic obstructive pulmonary disease (COPD) hospitalizations registered in Portugal from 2008 to 2015 and explore their impact on hospitalization outcomes.

Methods: A retrospective observational study was conducted. Hospitalizations of patients with at least 40 years old, discharged between 2008 and 2015 with a primary diagnosis of COPD (ICD-9-CM codes 491.x, 492.x and 496) were retrieved from a national administrative database. Comorbid psychiatric diagnoses were identified and defined by the HCUP Clinical Classification Software (CCS) category codes 650-670 (excluding 662). Length of hospital stay (LoS), admission type, in-hospital mortality, and estimated hospital charges were analyzed according to psychiatric diagnostic categories using sex and age-adjusted models.

Results: Of 66,661 COPD hospitalizations, 25,869 (38.8%) were episodes with a registered psychiatric comorbidity. These were more likely to correspond to younger inpatients (OR = 2.16, 95%CI 2.09-2.23; $p < 0.001$), to stay longer at the hospital (aOR = 1.08, 95%CI 1.05-1.12; $p < 0.001$), to incur in higher estimated hospital charges (aOR = 1.37, 95%CI 1.33-1.42; $p < 0.001$) and to be urgently admitted (aOR = 1.33, 95%CI 1.23-1.44; $p < 0.001$). After adjustment for age, in-hospital mortality was lower for episodes with psychiatric diagnoses (aOR = 0.90; 95%CI 0.84-0.96; $p < 0.001$), except for organic and neurodegenerative diseases category and developmental disorders, intellectual disabilities and disorders usually diagnosed in infancy, childhood, or adolescence category.

Discussion: These findings corroborate the additional burden placed by psychiatric disorders on COPD hospitalizations, highlighting the importance of individualizing care to address these comorbidities and minimize their impact on treatment outcomes.

Keywords: COPD; Chronic obstructive pulmonary disease; Exacerbations; Hospitalizations; In-hospital mortality; Psychiatric comorbidity.

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- [49 references](#)

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Editorial

Ann Am Thorac Soc

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. 2024 Mar;21(3):382-383.

doi: 10.1513/AnnalsATS.202311-934ED.

[Predicting Chronic Obstructive Pulmonary Disease Exacerbations: When the Past Does Not Inform the Future](#)

[Surya P Bhatt](#)¹

Affiliations expand

- PMID: 38426829
- DOI: [10.1513/AnnalsATS.202311-934ED](https://doi.org/10.1513/AnnalsATS.202311-934ED)

No abstract available

Comment on

- [Risk Factors for Chronic Obstructive Pulmonary Disease Exacerbations among Individuals without a History of Recent Exacerbations: A COPD Gene Analysis.](#) Ferrera MC, Lopez CL, Murray S, Jain RG, Labaki WW, Make BJ, Han MK. *Ann Am Thorac Soc.* 2024 Mar;21(3):421-427. doi: 10.1513/AnnalsATS.202209-7510C.PMID: 37796613

SUPPLEMENTARY INFO

Publication types, Grants and funding expand

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BMC Pulm Med



. 2024 Mar 1;24(1):103.

doi: 10.1186/s12890-024-02902-4.

[Effects of triple therapy on disease burden in patients of GOLD groups C and D: results from the observational COPD cohort COSYCONET](#)

[Jennifer A Zader](#)¹, [Rudolf A Jörres](#)², [Imke Mayer](#)^{3,4}, [Peter Alter](#)⁵, [Robert Bals](#)^{6,7}, [Henrik Watz](#)⁸, [Pontus Mertsch](#)⁹, [Klaus F Rabe](#)^{8,10}, [Felix Herth](#)^{11,12}, [Franziska C Trudzinski](#)^{11,12}, [Tobias Welte](#)¹³, [Hans-Ulrich Kauczor](#)^{14,15}, [Jürgen Behr](#)⁹, [Julia Walter](#)⁹, [Claus F Vogelmeier](#)⁵, [Kathrin Kahnert](#)¹⁶

Affiliations expand

- PMID: 38424530
- PMCID: [PMC10905841](#)
- DOI: [10.1186/s12890-024-02902-4](#)

Abstract

Background: Randomized controlled trials described beneficial effects of inhaled triple therapy (LABA/LAMA/ICS) in patients with chronic obstructive pulmonary disease (COPD) and high risk of exacerbations. We studied whether such effects were also detectable under continuous treatment in a retrospective observational setting.

Methods: Data from baseline and 18-month follow-up of the COPD cohort COSYCONET were used, including patients categorized as GOLD groups C/D at both visits (n = 258). Therapy groups were defined as triple therapy at both visits (triple always, TA) versus its complement (triple not always, TNA). Comparisons were performed via multiple regression analysis, propensity score matching and inverse probability weighting to adjust for differences between groups. For this purpose, variables were divided into predictors of therapy and outcomes.

Results: In total, 258 patients were eligible (TA: n = 162, TNA: n = 96). Without adjustments, TA patients showed significant ($p < 0.05$) impairments regarding lung function, quality of life and symptom burden. After adjustments, most differences in outcomes were no more significant. Total direct health care costs were reduced but still elevated, with inpatient costs much reduced, while costs of total and respiratory medication only slightly changed.

Conclusion: Without statistical adjustment, patients with triple therapy showed multiple impairments as well as elevated treatment costs. After adjusting for differences between treatment groups, differences were reduced. These findings are compatible with beneficial effects of triple therapy under continuous, long-term treatment, but also demonstrate the limitations encountered in the comparison of controlled intervention studies with observational studies in patients with severe COPD using different types of devices and compounds.

Keywords: COPD; Health care costs; Lung function; Symptoms; Triple therapy.

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Conflict of interest statement

The authors declare no competing interests.

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

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Skin Res Technol

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. 2024 Mar;30(3):e13629.

doi: 10.1111/srt.13629.

[The causal relationship between psoriasis and chronic obstructive pulmonary disease: A bidirectional mendelian randomization study](#)

[Meng Liu¹](#), [Xiaolin Zhou¹](#), [Guanfei Zhang¹](#), [Luyu Liu²](#), [Chengyu Fang¹](#), [Ziyan Li¹](#), [Yan Zheng¹](#)

Affiliations expand

- PMID: 38407525
- PMCID: [PMC10895548](#)
- DOI: [10.1111/srt.13629](#)

Abstract

Purpose: Although many studies have investigated the association between psoriasis and chronic obstructive pulmonary disease (COPD), the causal relationship between psoriasis and COPD is still unknown.

Methods: We employed bidirectional Mendelian randomization to investigate the causal relationship between psoriasis and COPD. Genetic instruments for exposure were selected from two distinct genome-wide association study databases. Single nucleotide polymorphisms associated with exposures at the genome-wide significance level ($p < 5 \times 10^{-8}$) and exhibiting low linkage disequilibrium ($r^2 < 0.001$) were chosen as instrumental variables. Causality was assessed using multiple MR methods, including Inverse-Variance Weighted (IVW), MR-Egger, Weighted Median, Simple Mode, and Weighted Mode. A significance level of $p < 0.05$ was considered statistically significant. Heterogeneity was examined using Cochran's Q test, and MR-Egger regression was employed to detect pleiotropy. The robustness and reliability of the results were further evaluated through leave-one-out analysis.

Results: We found a positive causal association between psoriasis and COPD [IVW: odds ratio (OR): 1.0006; $p = 0.0056$]. Heterogeneity and pleiotropy have not been discovered, so the results of the study are reliable. In the reverse analysis, no causal association between COPD and psoriasis was found.

Conclusion: Our findings revealed that psoriasis was associated with an elevated risk of COPD. However, no causal association between COPD and psoriasis was identified in our study.

Keywords: COPD; causality; mendelian randomization; psoriasis.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

- [29 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

MeSH termsexpand

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Respir Med



. 2024 Mar;223:107559.

doi: 10.1016/j.rmed.2024.107559. Epub 2024 Feb 11.

[Analysis of body composition with bioelectrical impedance analysis in patients with severe COPD and pulmonary emphysema](#)

[Christina Rott](#)¹, [Eldridge Limen](#)², [Katharina Kriegsmann](#)³, [Felix Herth](#)⁴, [Judith Maria Brock](#)⁵

Affiliations expand

- PMID: 38350511
- DOI: [10.1016/j.rmed.2024.107559](https://doi.org/10.1016/j.rmed.2024.107559)

Free article

Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) often suffer from cachexia and malnutrition. Less is known about body composition and nutritional behaviour in patients with advanced COPD and pulmonary emphysema.

Methods: We performed a single-center prospective analysis of patients with COPD GOLD III/IV. Metabolic parameters, dietary and exercise behavior, lung function, exercise capacity

and body composition by bioelectrical impedance analysis (BIA) were analyzed. Patients with severe emphysema (emphysema index [EI] >20%) were compared to patients with mild emphysema (EI ≤ 20%).

Results: A total of 121 patients (45.5% female, mean age 64.8 ± 8.1 years, mean FEV₁ 31.0 ± 8.6%, mean RV 234.7 ± 50.6%) were analyzed, of whom 14.1% were underweight. Only 5% of the patients substituted protein and only about 1/3 performed regular exercise training. BIA showed an unfavourable body composition: body fat ↑, ECM/BCM-index ↑, phase angle ↓ (5.0 ± 0.9°), cell percentage ↓, FFMI (fat-free mass index) ↓. The 94 patients with severe emphysema (mean EI 36.6 ± 8.5%) had lower body-mass-index (22.8 ± 4.3 vs. 31.1 ± 5.8 kg/m², p < 0.001), FFMI, body weight and body fat, but did not differ significantly in the quality of body composition (e.g. phase angle). Their lipid and glucose metabolism were even better than in mild emphysema patients.

Conclusion: The finding of significantly lower BMI but similar body composition and better metabolic status in severe emphysema patients needs further investigation. However, it should not distract from the necessity to implement dietary and exercise recommendations for advanced COPD patients.

Keywords: Bioelectrical impedance analysis; Body composition; COPD; Cachexia; Endoscopic lung volume reduction; Malnutrition; Pulmonary emphysema.

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Conflict of interest statement

Declaration of competing interest Christina Rott reports consultation fees outside the submitted work from Flee Flow Medical. Eldridge Limen and Katharina Kriegsmann report no conflicts of interest. Felix Herth reports no conflicts of interest regarding this work. Judith Brock has received honoraria and consultation fees from Boehringer Ingelheim, Astra Zeneca, streamed up!, Intuitive Surgical Inc, Berlin Chemie, Olympus. These activities are outside the submitted work. All authors confirm no conflicts of interest regarding this manuscript.

SUPPLEMENTARY INFO

MeSH termsexpand

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Respir Med



. 2024 Mar;223:107563.

doi: 10.1016/j.rmed.2024.107563. Epub 2024 Feb 9.

Enhanced prothrombotic and proinflammatory activity of circulating extracellular vesicles in acute exacerbations of chronic obstructive pulmonary disease

[Dario Neri](#)¹, [Camilla Morani](#)¹, [Miriam De Francesco](#)¹, [Roberta Gaeta](#)¹, [Mariapia Niceforo](#)¹, [Mariella De Santis](#)², [Ilaria Giusti](#)³, [Vincenza Dolo](#)³, [Marta Daniele](#)⁴, [Alberto Papi](#)⁴, [Alessandro Celi](#)⁵, [Tommaso Neri](#)⁶

Affiliations expand

- PMID: 38342357
- DOI: [10.1016/j.rmed.2024.107563](https://doi.org/10.1016/j.rmed.2024.107563)

Free article

Abstract

Background: Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) are associated with a high rate of cardiovascular events. Thromboinflammation (the interplay between coagulation and inflammation) is probably involved in these events. Extracellular vesicles (EV) increase during AE-COPD, but their role in thromboinflammation in COPD is still unknown. We investigated EV-associated prothrombotic and proinflammatory activity in COPD.

Methods: Patients with AE-COPD, stable COPD (sCOPD) and age- and sex-matched subjects (controls) were enrolled. AE-COPD patients were evaluated at hospital admission and 8 weeks after discharge (recovery; longitudinal arm). In a cross-sectional arm, AE-COPD were compared with sCOPD and controls. EV-mediated prothrombotic activity was tested by measuring the concentration of EV-associated phosphatidylserine, as assessed by a prothrombinase assay, and tissue factor, as assessed by a modified one-stage clotting assay (EV-PS and EV-TF, respectively). Synthesis of interleukin-8 (IL-8) and C-C motif chemokine ligand-2 (CCL-2) by cells of the human bronchial epithelial cell line 16HBE incubated with patients' EV was used to measure EV-mediated proinflammatory activity.

Results: Twenty-five AE-COPD (median age [interquartile range] 74.0 [14.0] years), 31 sCOPD (75.0 [9.5] years) and 12 control (67.0 [3.5] years) subjects were enrolled. In the longitudinal arm, EV-PS, EV-TF, IL-8 and CCL-2 levels were all significantly higher at hospital admission than at recovery. Similarly, in the cross-sectional arm, EV-PS, EV-TF and cytokines synthesis were significantly higher in AE-COPD than in sCOPD and controls.

Conclusions: EV exert prothrombotic and proinflammatory activities during AE-COPD and may therefore be effectors of thromboinflammation, thus contributing to the higher cardiovascular risk in AE-COPD.

Keywords: Cardiovascular risk; Chronic obstructive pulmonary disease; Extracellular vesicles; Inflammation; Thrombosis.

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Conflict of interest statement

Declaration of competing interest None of the authors has relevant competing interests to declare.

SUPPLEMENTARY INFO

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Outcomes of Patients with COPD Treated with ICS/LABA Before and After Initiation of Single-Inhaler Triple Therapy with Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI)

[Meredith McCormack](#)¹, [Rosirene Paczkowski](#)², [Noelle N Gronroos](#)³, [Stephen G Noorduyn](#)^{4,5}, [Lydia Lee](#)^{6,7}, [Phani Veeranki](#)³, [Mary G Johnson](#)³, [Emmeline Igboekwe](#)⁸, [Kristin Kahle-Wroblewski](#)⁶, [Reynold Panettieri](#)⁹

Affiliations expand

- PMID: 38310193
- PMCID: [PMC10879256](#)
- DOI: [10.1007/s12325-023-02776-8](#)

Free PMC article

Abstract

Introduction: Triple therapy (fluticasone furoate/umeclidinium/vilanterol; FF/UMEC/VI) has been shown to improve symptoms and reduce exacerbations in patients with chronic obstructive pulmonary disease (COPD) and a history of exacerbations. This real-world study compared exacerbation rates and healthcare resource utilization (HCRU) before and after initiation of FF/UMEC/VI in patients with COPD previously treated with inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA).

Methods: This retrospective cohort study included commercial and Medicare Advantage with Part D administrative claims data from September 01, 2016, to March 31, 2020, of patients diagnosed with COPD. The index date was the date of the first FF/UMEC/VI claim (September 2017-March 2019). The 12 months prior to index (baseline) were used to assess patient characteristics and outcomes; the 12 months following index (follow-up) were used to assess study outcomes. All patients had ≥ 30 consecutive days' supply of any ICS/LABA dual therapy during the 12 months prior to FF/UMEC/VI initiation. Subgroup analyses included patients with ≥ 30 consecutive days' supply of budesonide/formoterol (BUD/FORM) during baseline. Analyses of patients with ≥ 1 COPD exacerbation during baseline were reported as well.

Results: The overall population included 1449 patients (mean age 70.75 years; 54.18% female), of whom 540 were patients in the BUD/FORM subgroup. Significantly fewer patients experienced any exacerbation during follow-up versus baseline (overall population 53.49% vs 62.59%; $p < 0.001$; BUD/FORM subgroup 55.00% vs 62.41%; $p = 0.004$). Effects on exacerbation reduction were more pronounced among patients with ≥ 1 exacerbation during baseline. Lower COPD-related HCRU was observed during the follow-up compared with baseline for both the overall population and the BUD/FORM subgroup.

Conclusion: Patients with COPD treated with ICS/LABA during baseline, including patients specifically treated with BUD/FORM and those with a history of ≥ 1 exacerbation, had fewer COPD exacerbations and lower COPD-related HCRU after initiating FF/UMEC/VI.

Keywords: COPD; Dual therapy; Exacerbations; FF/UMEC/VI; HCRU; ICS/LABA; Single-inhaler triple therapy.

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Conflict of interest statement

Meredith McCormack has received consulting fees from Aridis Pharmaceuticals, GSK, Boehringer Ingelheim, and MCG Diagnostics and has received royalties for authorship from UpToDate. Meredith McCormack has also served on the medical advisory board for ndd Technology. Rosirene Paczkowski, Stephen G. Noorduynd, Emmeline Igboekwe, and Kristin Kahle-Wroblewski are employees of, and/or hold stocks/shares, in GSK. Lydia Lee is a university worker hired by GSK. Noelle N. Gronroos, Phani Veeranki, and Mary G. Johnson are employees of, and hold stocks/shares in, Optum, which received funding from GSK to conduct this study. Reynold Panettieri has received research grants from AZ, RIFM, TEVA, MedImmune, and AgoMab and has featured on advertisement boards for AZ, RIFM Genentech, and Praesidia. Reynold Panettieri has also worked as a speaker for AZ, Sanofi, and Merck.

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

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Review

Respir Med

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. 2024 Mar;223:107554.

doi: 10.1016/j.rmed.2024.107554. Epub 2024 Feb 1.

[Exercise training initiated early during hospitalisation in individuals with chronic obstructive pulmonary disease is safe and improves exercise capacity and physical function at hospital discharge: A systematic review and meta-analysis](#)

[Yuin Lai](#)¹, [Vinicius Cavalheri](#)², [Abbey Sawyer](#)³, [Kylie Hill](#)⁴

Affiliations expand

- PMID: 38307320

- DOI: [10.1016/j.rmed.2024.107554](https://doi.org/10.1016/j.rmed.2024.107554)

Free article

Abstract

Background and objective: Earlier reviews of exercise in people during exacerbation of chronic obstructive pulmonary disease (COPD) included studies where exercise training was initiated late during hospital admission or shortly following hospital discharge. Our question was: in adults hospitalised with an exacerbation of COPD, does initiating exercise training early during an admission versus not initiating exercise training during admission, change outcomes measured at discharge?

Methods: Systematic review and meta-analysis. Database searches of PubMed, the Cochrane Library, PEDro and EMBASE conducted in December 2021 and updated in January 2024. Studies were included if they had at least one group that was prescribed exercise training within 48 h of hospital admission (experimental) and at least one group that received usual care which did not include prescribed exercise training (control). Outcomes included exercise capacity, physical function, adverse events and uptake of outpatient pulmonary rehabilitation programs.

Results: Ten studies (423 participants; mean FEV₁ ranging from 26 % to 50 % predicted) were included. At discharge, compared to the control group, the experimental group demonstrated better exercise capacity (standardised mean difference (SMD) 0.58, 95 % confidence interval (CI) 0.32 to 0.83; five studies, moderate effect, low certainty evidence) and physical function (SMD -0.54, 95 % CI -0.86 to -0.22; four studies, moderate effect, low certainty evidence). No observed serious adverse events were reported. None of the studies reported uptake of pulmonary rehabilitation following discharge.

Conclusion: In adults with an exacerbation of COPD, exercise training prescribed within 48 h of hospitalisation was safe and improved exercise capacity and physical function.

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Conflict of interest statement

Declaration of competing interest None of the authors have any conflict of interest to declare with the contents of this manuscript.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respir Med

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. 2024 Mar;223:107555.

doi: 10.1016/j.rmed.2024.107555. Epub 2024 Feb 1.

[Severity of bronchiectasis predicts use of and adherence to high frequency chest wall oscillation therapy - Analysis from the United States Bronchiectasis and NTM research registry](#)

[Ashwin Basavaraj](#)¹, [Radmila Choate](#)², [Brian C Becker](#)³, [Timothy R Aksamit](#)⁴, [Mark L Metersky](#)⁵; [Bronchiectasis and NTM Research Registry Investigators](#)

Affiliations expand

- PMID: 38307319
- DOI: [10.1016/j.rmed.2024.107555](https://doi.org/10.1016/j.rmed.2024.107555)

Abstract

Background: High frequency chest wall oscillation (HFCWO) is a form of airway clearance therapy that has been available since the mid-1990s and is routinely used by patients suffering from retained pulmonary secretions. Patients with cystic fibrosis (CF),

neuromuscular disease (NMD), and other disorders, including bronchiectasis (BE) and COPD (without BE), are commonly prescribed this therapy. Limited evidence exists describing HFCWO use in the BE population, its impact on long-term management of disease, and the specific patient populations most likely to benefit from this therapy. This study sought to characterize the clinical characteristics of patients with BE who have documented use of HFCWO at baseline and 1-year follow-up.

Methods: An analysis from a large national database registry of patients with BE was performed. Demographic and clinical characteristics of all patients receiving HFCWO therapy at baseline are reported. Patients were stratified into two groups based on continued or discontinued use of HFCWO therapy at 1-year follow-up.

Results: Over half (54.8 %) of patients who reported using HFCWO therapy had a Modified Bronchiectasis Severity Index (m-BSI) classified as severe, and the majority (81.4 %) experienced an exacerbation in the prior two years. Of patients with 1-year follow-up data, 73 % reported continued use of HFCWO. Compared to patients who discontinued therapy, these patients were more severe at baseline and at follow-up suggesting that patients with more severe disease are more likely to continue HFCWO therapy.

Conclusions: Patients who have more severe disease and continue to experience exacerbations and hospitalizations are more likely to continue HFCWO therapy.

Clinical trial registration: NA.

Keywords: Airway clearance therapy; Bronchiectasis; HFCWO.

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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: Ashwin Basavaraj reports writing assistance was provided by LeeAnn Phipps. AB - Consultant and Advisory Board for Baxter, Insmmed, Physio-Assist, Dymedso, Zambon. Medical education consulting for Tactile Medical. Principal investigator on clinical trial sponsored by Baxter with funding to institution. Educational grant funding received from Insmmed to institution. RC - No disclosures to report. BB - Employee relationship with Baxter. MM - Grant funding from Insmmed and COPD foundation. Consulting fees from Insmmed, Boehringer-Ingelheim, and Tactile Medical. Payment/honoraria for presentations/lectures from Insmmed. Participation on data safety monitoring/advisory board for AN2, Renovion. TA - Support as medical director of the Bronchiectasis and NTM research registry. Has participated in clinical trials sponsored by Bayer, Aradigm, Zambon.

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Editorial

Respirology

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. 2024 Mar;29(3):193-194.

doi: 10.1111/resp.14665. Epub 2024 Feb 1.

[Breaking the spiral: How negative mood can fuel exertional breathlessness in people with chronic obstructive pulmonary disease](#)

[Amy Pascoe](#)¹, [Natasha Smallwood](#)^{1,2}

Affiliations expand

- PMID: 38302100
- DOI: [10.1111/resp.14665](https://doi.org/10.1111/resp.14665)

Free article

No abstract available

Keywords: affect; chronic obstructive pulmonary disease; clinical respiratory medicine; dyspnoea; exercise and pulmonary rehabilitation; mood modulation; relaxation techniques.

- [12 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Editorial

Am J Respir Crit Care Med

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. 2024 Mar 1;209(5):472-473.

doi: 10.1164/rccm.202401-0176ED.

[Extracorporeal Carbon Dioxide Removal in Chronic Obstructive Pulmonary Disease: It Depends on the Objective!](#)

[Lise Piquilloud](#)¹

Affiliations expand

- PMID: 38285549

- DOI: [10.1164/rccm.202401-0176ED](https://doi.org/10.1164/rccm.202401-0176ED)

No abstract available

Comment on

- [Extracorporeal Carbon Dioxide Removal to Avoid Invasive Ventilation During Exacerbations of Chronic Obstructive Pulmonary Disease: VENT-AVOID Trial - A Randomized Clinical Trial.](#)

Duggal A, Conrad SA, Barrett NA, Saad M, Cheema T, Pannu S, Romero RS, Brochard L, Nava S, Ranieri VM, May A, Brodie D, Hill NS; VENT-AVOID Investigators. *Am J Respir Crit Care Med.* 2024 Mar 1;209(5):529-542. doi: 10.1164/rccm.202311-2060OC.PMID: 38261630

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Publication types [expand](#)

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Respir Med

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. 2024 Mar;223:107536.

doi: 10.1016/j.rmed.2024.107536. Epub 2024 Jan 23.

[Prognostic impact of chronic obstructive pulmonary disease in](#)

patients with heart failure with mildly reduced ejection fraction

[Felix Lau](#)¹, [Tobias Schupp](#)², [Alexander Schmitt](#)¹, [Marielen Reinhardt](#)¹, [Noah Abel](#)¹, [Mohammad Abumayyaleh](#)¹, [Kathrin Weidner](#)¹, [Daniel Duerschmied](#)¹, [Mohamed Ayoub](#)³, [Kambis Mashayekhi](#)⁴, [Muharrem Akin](#)⁵, [Niklas Ayasse](#)⁶, [Ibrahim Akin](#)¹, [Michael Behnes](#)¹

Affiliations expand

- PMID: 38272377
- DOI: [10.1016/j.rmed.2024.107536](https://doi.org/10.1016/j.rmed.2024.107536)

Abstract

Background: The aging population has led to a significant increase in heart failure (HF) patients. Related to demographic changes, the burden with comorbidities was shown to increase in patients with HF. Whereas chronic obstructive pulmonary disease (COPD) was yet demonstrated to be associated with adverse outcomes in patients with HF, the prognostic impact of COPD in HF with mildly reduced ejection fraction (HFmrEF) has not yet been clarified.

Objective: The study investigates the prognostic impact of COPD in patients hospitalized with HFmrEF.

Methods: Consecutive patients with HFmrEF were retrospectively included at one institution from 2016 to 2022. Patients with COPD were compared to patients without with regard to the primary endpoint all-cause mortality at 30 months (median follow-up). Secondary endpoints comprised in-hospital mortality, HF-related re-hospitalization, cardiac re-hospitalization and major adverse cardiac and cerebrovascular events (MACCE) at 30 months.

Results: A total of 2184 patients with HFmrEF were included with a prevalence of COPD of 12.0 %. Patients with COPD were older (median 77 vs. 75 years; $p = 0.025$), had increased burden of cardiovascular comorbidities and more advanced HF symptoms. At 30 months, patients with COPD had an increased risk of all-cause mortality compared to patients without (45 % vs. 30 %; HR = 1.667; 95 % CI 1.366-2.034; $p = 0.001$), alongside with a higher risk of re-hospitalization for worsening HF (20 % vs. 12 %; HR = 1.658; 95 % CI 1.218-2.257; $p = 0.001$).

Conclusion: COPD is independently associated with adverse outcomes in patients hospitalized with HFmrEF.

Keywords: COPD; Chronic obstructive pulmonary disease; HFmrEF; Heart failure with mildly reduced ejection fraction.

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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

MeSH termsexpand

FULL TEXT LINKS



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Am J Respir Crit Care Med

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. 2024 Mar 1;209(5):529-542.

doi: 10.1164/rccm.202311-2060OC.

[Extracorporeal Carbon Dioxide Removal to Avoid Invasive Ventilation During Exacerbations of Chronic Obstructive Pulmonary Disease: VENT-](#)

[AVOID Trial – A Randomized Clinical Trial](#)

[Abhijit Duggal](#)¹, [Steven A Conrad](#)², [Nicholas A Barrett](#)^{3,4}, [Mohamed Saad](#)⁵, [Tariq Cheema](#)⁶, [Sonal Pannu](#)⁷, [Ramiro Saavedra Romero](#)⁸, [Laurent Brochard](#)^{9,10}, [Stefano Nava](#)^{11,12}, [V Marco Ranieri](#)^{12,13}, [Alexandra May](#)¹⁴, [Daniel Brodie](#)¹⁵, [Nicholas S Hill](#)¹⁶, [VENT-AVOID Investigators](#)

Collaborators, Affiliations expand

- PMID: 38261630
- DOI: [10.1164/rccm.202311-2060OC](https://doi.org/10.1164/rccm.202311-2060OC)

Abstract

Rationale: It is unclear whether extracorporeal CO₂ removal (ECCO₂R) can reduce the rate of intubation or the total time on invasive mechanical ventilation (IMV) in adults experiencing an exacerbation of chronic obstructive pulmonary disease (COPD). **Objectives:** To determine whether ECCO₂R increases the number of ventilator-free days within the first 5 days postrandomization (VFD-5) in exacerbation of COPD in patients who are either failing noninvasive ventilation (NIV) or who are failing to wean from IMV. **Methods:** This randomized clinical trial was conducted in 41 U.S. institutions (2018-2022) (ClinicalTrials.gov ID: [NCT03255057](https://clinicaltrials.gov/ct2/show/study/NCT03255057)). Subjects were randomized to receive either standard care with venovenous ECCO₂R (NIV stratum: $n = 26$; IMV stratum: $n = 32$) or standard care alone (NIV stratum: $n = 22$; IMV stratum: $n = 33$). **Measurements and Main Results:** The trial was stopped early because of slow enrollment and enrolled 113 subjects of the planned sample size of 180. There was no significant difference in the median VFD-5 between the arms controlled by strata ($P = 0.36$). In the NIV stratum, the median VFD-5 for both arms was 5 days (median shift = 0.0; 95% confidence interval [CI]: 0.0-0.0). In the IMV stratum, the median VFD-5 in the standard care and ECCO₂R arms were 0.25 and 2 days, respectively; median shift = 0.00 (95% confidence interval: 0.00-1.25). In the NIV stratum, all-cause in-hospital mortality was significantly higher in the ECCO₂R arm (22% vs. 0%, $P = 0.02$) with no difference in the IMV stratum (17% vs. 15%, $P = 0.73$). **Conclusions:** In subjects with exacerbation of COPD, the use of ECCO₂R compared with standard care did not improve VFD-5. Clinical trial registered with www.clinicaltrials.gov ([NCT03255057](https://clinicaltrials.gov/ct2/show/study/NCT03255057)).

Keywords: COPD; ECCO₂R; mechanical ventilation.

Comment in

- [Extracorporeal Carbon Dioxide Removal in Chronic Obstructive Pulmonary Disease: It Depends on the Objective!](#)

Piquilloud L. *Am J Respir Crit Care Med*. 2024 Mar 1;209(5):472-473. doi: 10.1164/rccm.202401-0176ED. PMID: 38285549 No abstract available.

SUPPLEMENTARY INFO

Associated data, Grants and funding [expand](#)

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Review

Curr Opin Pulm Med

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. 2024 Mar 1;30(2):129-135.

doi: 10.1097/MCP.0000000000001046. Epub 2024 Jan 16.

[The role of chest computed tomography in the evaluation and management of chronic obstructive pulmonary disease](#)

[Robert M Burkes](#)^{1,2}, [Muhammad A Zafar](#)², [Ralph J Panos](#)^{1,2}

Affiliations [expand](#)

- PMID: 38227648
- DOI: [10.1097/MCP.0000000000001046](https://doi.org/10.1097/MCP.0000000000001046)

Abstract

Purpose of review: The purpose of this review is to compile recent data on the clinical associations of computed tomography (CT) scan findings in the literature and potential avenues for implementation into clinical practice.

Recent findings: Airways dysanapsis, emphysema, chronic bronchitis, and pulmonary vascular metrics have all recently been associated with poor chronic obstructive pulmonary disease (COPD) outcomes when controlled for clinically relevant covariables, including risk of mortality in the case of emphysema and chronic bronchitis. Other authors suggest that CT scan may provide insight into both lung parenchymal damage and other clinically important comorbidities in COPD.

Summary: CT scan findings in COPD relate to clinical outcomes. There is a continued need to develop processes to best implement the results of these studies into clinical practice.

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- [33 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Pulm Ther

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. 2024 Mar;10(1):109-122.

doi: 10.1007/s41030-023-00249-5. Epub 2024 Jan 9.

Aerosol Plumes of Inhalers Used in COPD

[Herbert Wachtel](#)¹, [Rachel Emerson-Stadler](#)², [Peter Langguth](#)³, [Jens M Hohlfeld](#)^{4,5,6}, [Jill Ohar](#)⁷

Affiliations expand

- PMID: 38194194
- PMCID: [PMC10881950](#)
- DOI: [10.1007/s41030-023-00249-5](#)

Free PMC article

Abstract

Introduction: The selection of inhaler device is of critical importance in chronic obstructive pulmonary disease (COPD) as the interaction between a patient's inhalation profile and the aerosol characteristics of an inhaler can affect drug delivery and lung deposition. This study assessed the in vitro aerosol characteristics of inhaler devices approved for the treatment of COPD, including a soft mist inhaler (SMI), pressurized metered-dose inhalers (pMDIs), and dry powder inhalers (DPIs).

Methods: High-speed video recording was used to visualize and measure aerosol velocity and spray duration for nine different inhalers (one SMI, three pMDIs, and five DPIs), each containing dual or triple fixed-dose combinations of long-acting muscarinic receptor antagonists and long-acting β_2 -agonists, with or without an inhaled corticosteroid. Measurements were taken in triplicate at experimental flow rates of 30, 60, and 90 l/min. Optimal flow rates were defined based on pharmacopoeial testing requirements: 30 l/min for pMDIs and SMIs, and the rate achieving a 4-kPa pressure drop against internal inhaler resistance for DPIs. Comparison of aerosol plumes was based on the experimental flow rates closest to the optimal flow rates.

Results: The Respimat SMI had the slowest plume velocity (0.99 m/s) and longest spray duration (1447 ms) compared with pMDIs (velocity: 3.65-5.09 m/s; duration: 227-270 ms) and DPIs (velocity: 1.43-4.60 m/s; duration: 60-757 ms). With increasing flow rates, SMI aerosol duration was unaffected, but velocity increased (maximum 2.63 m/s), pMDI aerosol velocity and duration were unaffected, and DPI aerosol velocity tended to increase, with a more variable impact on duration.

Conclusions: Aerosol characteristics (velocity and duration of aerosol plume) vary by inhaler type. Plume velocity was lower and spray duration longer for the SMI compared with pMDIs and DPIs. Increasing experimental flow rate was associated with faster plume velocity for DPIs and the SMI, with no or variable impact on plume duration, whereas pMDI aerosol velocity and duration were unaffected by increasing flow rate.

Keywords: Aerosol; Chronic obstructive pulmonary disease; Dry powder inhaler; Inhalation therapy; Inhaler; Pressurized metered-dose inhaler; Respiratory medicine; Soft mist inhaler.

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Conflict of interest statement

Herbert Wachtel and Rachel Emerson-Stadler are full-time employees of Boehringer Ingelheim. Peter Langguth has nothing to disclose. Jens M. Hohlfeld has received honoraria for board services, consultancy, and lectures outside the scope of this work from Boehringer Ingelheim Pharma & Co KG, CSL Behring GmbH, HAL Allergy Group, Merck & Co., Inc., Nacion Therapeutics, Novartis AG, and Roche. Jill Ohar reports consulting fees from AstraZeneca, Boehringer Ingelheim, Mylan, Sunovion, and Verona, and has received grants from Boehringer Ingelheim, Sunovion, Teva, and the Society to Improve Diagnosis in Medicine (SIDM) under a grant from the Gordon and Betty Moore Foundation.

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

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. 2024 Mar;10(1):133-142.

doi: 10.1007/s41030-023-00246-8. Epub 2024 Jan 3.

Successful Use of Easyhaler® Dry Powder Inhaler in Patients with Chronic Obstructive Pulmonary Disease; Analysis of Peak Inspiratory Flow from Three Clinical Trials

[Annette Kainu](#)^{1,2}, [Ville A Vartiainen](#)^{3,4}, [Witold Mazur](#)⁵, [Hanna Hisinger-Mölkänen](#)⁶, [Federico Lavorini](#)⁷, [Christer Janson](#)⁸, [Martin Andersson](#)⁹

Affiliations expand

- PMID: 38170393
- PMCID: [PMC10881915](#)
- DOI: [10.1007/s41030-023-00246-8](#)

Free PMC article

Abstract

Introduction: There is increasing pressure to use environmentally friendly dry powder inhalers (DPI) instead of pressurized metered-dose inhalers (pMDI). However, correct inhalation technique is needed for effective inhaler therapy, and there is persistent concern whether patients with chronic obstructive pulmonary disease (COPD) can generate sufficient inspiratory effort to use DPIs successfully. The aims of this study were to find clinical predictors for peak inspiratory flow rate (PIF) and to assess whether patients with COPD had difficulties in generating sufficient PIF with a high resistance DPI.

Methods: Pooled data of 246 patients with COPD from previous clinical trials was analyzed to find possible predictors of PIF via the DPI Easyhaler (PIFEH) and to assess the proportion of patients able to achieve an inhalation flow rate of 30 l/min, which is needed to use the Easyhaler successfully.

Results: The mean PIF was 56.9 l/min and 99% (243/246) of the study patients achieved a PIF \geq 30 l/min. A low PIF was associated with female gender and lower forced expiratory volume in 1 s (FEV1), but the association was weak and a statistical model including both only accounted for 18% of the variation seen in PIFEH.

Conclusions: Based on our results, impaired expiratory lung function or patient characteristics do not predict patients' ability to use DPIs in COPD; 99% of the patients generated sufficient PIFEH for successful dose delivery. Considering the targets for sustainability in health care, this should be addressed as DPIs are a potential option for most patients when choosing the right inhaler for the patient.

Trial registration: Two of three included trials were registered under numbers [NCT04147572](#) and [NCT01424137](#). Third trial preceded registration platforms and therefore, was not registered.

Keywords: COPD; DPI; Dry powder inhaler; Inhalation; Inhaler; Technique.

© 2023. The Author(s).

Conflict of interest statement

Annette Kainu has received consultation and lecture fees from ALK Nordic A/S, GSK Finland, and Orion Pharma. Witold Mazur had attended advisory boards and received lecture fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Orion Pharma, and Sanofi. Ville Vartianen has received consultation and lecture fees from Orion Pharma. Hanna Hisinger Molkanen is an employee of Orion Pharma. Christer Janson has received a research grant from AstraZeneca, received speaker honoraria from AstraZeneca, Boehringer Ingelheim, Chiesi, Glaxo Smith Kline, Novartis, Orion Pharma, and Sanofi-Genzyme, and has participated in the scientific advisory boards of AstraZeneca, Boehringer Ingelheim, Chiesi, Glaxo Smith Kline, Novartis, Orion Pharma, and Sanofi-Genzyme. Martin Andersson and Federico Lavorini have nothing to declare.

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

SUPPLEMENTARY INFO

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Curr Opin Pulm Med

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. 2024 Mar 1;30(2):174-178.

doi: 10.1097/MCP.0000000000001043. Epub 2023 Dec 26.

Utility of peak inspiratory flow measurement for dry powder inhaler use in chronic obstructive pulmonary disease

[Chee Hong Loh](#)¹, [Jill A Ohar](#)²

Affiliations expand

- PMID: 38164804
- DOI: [10.1097/MCP.0000000000001043](https://doi.org/10.1097/MCP.0000000000001043)

Abstract

Purpose of review: Every type of dry powder inhaler (DPI) device has its own intrinsic resistance. A patient's inspiratory effort produces a pressure drop that determines the inspiratory flow, depending on the inhaler's specific internal resistance. Optimal peak inspiratory flow (PIF) is needed for effective release of dry powder, disaggregation of drug-carrier agglomerates, and optimal deposition of respirable drug particles, particularly generation of a high fine-particle fraction to reach the small airways of the lungs. However, standardized recommendations for PIF measurements are lacking and instructions appeared vague in many instances.

Recent findings: Suboptimal PIFs are common in outpatient chronic obstructive pulmonary disease (COPD) patients and during acute exacerbations of COPD, and are associated with increased healthcare resource utilization. There is significant variation in

the results of studies which is in part related to different definitions of optimal flow rates, and considerable variation in how PIF is measured in clinical and real-life studies.

Summary: Standardization of technique will facilitate comparisons among studies. Specific recommendations for PIF measurement have been proposed to standardize the process and better ensure accurate and reliable PIF values in clinical trials and clinical practice. Clinicians can then select and personalize the most appropriate inhaler for their patients and help them achieve the optimal PIF needed for effective drug dispersion.

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- [16 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Am J Cardiol

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. 2024 Mar 1:214:25-32.

doi: 10.1016/j.amjcard.2023.12.044. Epub 2023 Dec 30.

[Complete Revascularization Strategies in Women and Men With Acute Coronary Syndrome and Multivessel Disease](#)

[Jacob J Elscot](#)¹, [Hala Kakar](#)¹, [Wijnand K den Dekker](#)¹, [Johan Bennett](#)², [Manel Sabaté](#)³, [Giovanni Esposito](#)⁴, [Joost Daemen](#)¹, [Eric Boersma](#)¹, [Nicolas M Van Mieghem](#)¹, [Roberto Diletti](#)⁵, [BIOVASC investigators](#)

Affiliations expand

- PMID: 38163579
- DOI: [10.1016/j.amjcard.2023.12.044](https://doi.org/10.1016/j.amjcard.2023.12.044)

Free article

Abstract

This prespecified substudy of the randomized Percutaneous Complete Revascularization Strategies Using Sirolimus Eluting Biodegradable Polymer Coated Stents in Patients Presenting With Acute Coronary Syndromes and Multivessel Disease (BIOVASC) trial aimed to compare immediate complete revascularization (ICR) and staged complete revascularization (SCR) in patients with acute coronary syndrome and multivessel disease, stratified by gender. The primary end point consisted of a composite of all-cause mortality, myocardial infarction, unplanned ischemia-driven revascularization, and cerebrovascular events at 1-year follow-up. The secondary end points included the individual components of the primary composite and major bleedings. We used Cox regression models to relate randomized treatment with study end points. We evaluated the multiplicative and additive interactions between gender and randomized treatment. The BIOVASC trial enrolled 338 women and 1,187 men. Women were older than men (median age 71.6 vs 63.7 years, $p < 0.001$) and had a higher prevalence of chronic obstructive pulmonary disease (10.1% vs 5.6%, $p = 0.003$), renal insufficiency (7.7% vs 4.4%, $p = 0.015$), and hypertension (60.4% vs 51.7%, $p = 0.005$). In women, the composite primary outcome occurred in 7.3% versus 12.9% (hazard ratio 0.53, 95% confidence interval 0.26 to 1.08) in patients randomly allocated to ICR and SCR, respectively, and in men in 7.7% versus 8.4% (hazard ratio 0.89, 95% confidence interval 0.60 to 1.34), with no evidence of a differential effect (interaction $p_{\text{multiplicative}} = 0.20$, $p_{\text{additive}} = 0.87$). No evidence of heterogeneity between women and men was found when comparing ICR with SCR in terms of the secondary outcomes. In conclusion, no differential treatment effect was found when comparing ICR versus SCR in women or men presenting with acute coronary syndrome and multivessel disease.

Keywords: acute coronary syndrome; gender; multivessel PCI.

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Conflict of interest statement

Declaration of competing interest Dr. Diletti has received institutional research grants from Biotronik, Medtronic, ACIST Medical Systems, and Boston Scientific. Dr. den Dekker has received institutional research grants from Biotronik. Dr. Van Mieghem has received institutional research grants from Biotronik, Abbott, Medtronic, Edwards Lifesciences, PulseCath, Abiomed, and Daiichi Sankyo; speaker fees from Abiomed and Amgen; and a travel grant from JenaValve. Dr. Bennett has received institutional grants from Biotronik, Abbott Vascular, and Shockwave Medical. Dr. Daemen has received institutional grant/research support from Abbott Vascular, Boston Scientific, ACIST Medical, Medtronic, MicroPort, Pie Medical, and ReCor medical and consultancy and speaker fees from Abbott Vascular, Abiomed, ACIST medical, Boston Scientific, Cardialysis BV, CardiacBooster, Kaminari Medical, ReCor Medical, PulseCath, Pie Medical, Sanofi, Siemens Health Care, and Medtronic. Dr. Sabaté has received consultancy fees from Abbott Vascular and iVascular. The remaining authors have no competing interest to declare.

SUPPLEMENTARY INFO

MeSH termsexpand

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Am J Physiol Lung Cell Mol Physiol

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. 2024 Mar 1;326(3):L266-L279.

doi: 10.1152/ajplung.00419.2022. Epub 2023 Dec 27.

[Small airway fibroblasts from patients with chronic obstructive pulmonary disease exhibit cellular senescence](#)

[Catherine L Wrench](#)^{1,2}, [Jonathan R Baker](#)¹, [Sue Monkley](#)³, [Peter S Fenwick](#)¹, [Lynne Murray](#)², [Louise E Donnelly](#)¹, [Peter J Barnes](#)¹

Affiliations expand

- PMID: 38150543
- DOI: [10.1152/ajplung.00419.2022](https://doi.org/10.1152/ajplung.00419.2022)

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Abstract

Small airway disease (SAD) is a key early-stage pathology of chronic obstructive pulmonary disease (COPD). COPD is associated with cellular senescence whereby cells undergo growth arrest and express the senescence-associated secretory phenotype (SASP) leading to chronic inflammation and tissue remodeling. Parenchymal-derived fibroblasts have been shown to display senescent properties in COPD, however small airway fibroblasts (SAFs) have not been investigated. Therefore, this study investigated the role of these cells in COPD and their potential contribution to SAD. To investigate the senescent and fibrotic phenotype of SAF in COPD, SAFs were isolated from nonsmoker, smoker, and COPD lung resection tissue ($n = 9-17$ donors). Senescence and fibrotic marker expressions were determined using iCELLigence (proliferation), qPCR, Seahorse assay, and ELISAs. COPD SAFs were further enriched for senescent cells using FACS Aria Fusion based on cell size and autofluorescence (10% largest/autofluorescent vs. 10% smallest/nonautofluorescent). The phenotype of the senescence-enriched population was investigated using RNA sequencing and pathway analysis. Markers of senescence were observed in COPD SAFs, including senescence-associated β -galactosidase, SASP release, and reduced proliferation. Because the pathways driving this phenotype were unclear, we used cell sorting to enrich senescent COPD SAFs. This population displayed increased p21^{CIP1} and p16^{INK4a} expression and mitochondrial dysfunction. RNA sequencing suggested these senescent cells express genes involved in oxidative stress response, fibrosis, and mitochondrial dysfunction pathways. These data suggest COPD SAFs are senescent and may be associated with fibrotic properties and mitochondrial dysfunction. Further understanding of cellular senescence in SAFs may lead to potential therapies to limit SAD progression. **NEW & NOTEWORTHY** Fibroblasts and senescence are thought to play key roles in the pathogenesis of small airway disease and COPD; however, the characteristics of small airway-derived fibroblasts are not well explored. In this study we isolate and enrich the senescent small airway-derived fibroblast (SAF) population from COPD lungs and explore the pathways driving this phenotype using bulk RNA-seq.

Keywords: COPD; fibroblast; senescence; small airway disease.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

MeSH terms, Supplementary concepts, Grants and fundingexpand

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Int J Paleopathol

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. 2024 Mar:44:33-45.

doi: 10.1016/j.ijpp.2023.11.004. Epub 2023 Dec 21.

[Ageing and disease risk factors: A new paleoepidemiological methodology for understanding disease in the past](#)

[Jo Appleby](#)¹

Affiliations expand

- PMID: 38134630
- DOI: [10.1016/j.ijpp.2023.11.004](https://doi.org/10.1016/j.ijpp.2023.11.004)

Free article

Abstract

Objectives: To outline a methodology that enables the reconstruction of age-related disease risk in past societies.

Materials: Modern epidemiological evidence considering risk factors for age-related disease is combined with contextual information about an archaeological society of interest.

Methods: Data gathered is used to create a qualitative population-specific risk model for the disease of interest. To provide a case study, a risk model is constructed for Chronic Obstructive Pulmonary Disease (COPD) in the Eastern English Bronze Age.

Results: This enables the first rigorous approach to reconstructing age-related disease risk in the past. A risk model shows a high degree of COPD risk in the Eastern English Bronze Age, with a major contribution from indoor airborne pollution and agricultural practices.

Significance: This represents a significant new approach in human paleopathology, facilitating understanding of the occurrence of a wide variety of diseases in the past, without the need for well-preserved skeletons of identified elderly individuals.

Limitations: The risk models generated are, of necessity, qualitative rather than quantitative, since we are unable to calculate the size of risk factors in the past with certainty.

Suggestions for further research: The methodology could be applied to a wide variety of diseases and for many past societies.

Keywords: Ageing; Bronze Age England; COPD; Disease risk; Old age.

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MeSH termsexpand

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Ann Am Thorac Soc

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. 2024 Mar;21(3):523-526.

doi: 10.1513/AnnalsATS.202306-575RL.

[Risk of Chronic Obstructive Pulmonary Disease \(COPD\) Hospitalizations and Deaths among Rural and Urban Veterans after Successive COPD Hospitalizations](#)

[Spyridon Fortis](#)^{1,2}, [Yubo Gao](#)^{1,2}, [Peter J Kaboli](#)^{1,2}, [Mary Vaughan Sarrazin](#)^{1,2}

Affiliations expand

- PMID: 38134432
- DOI: [10.1513/AnnalsATS.202306-575RL](https://doi.org/10.1513/AnnalsATS.202306-575RL)

No abstract available

SUPPLEMENTARY INFO

Publication types, Grants and funding expand

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Clinical Trial



[A Randomized Phase I Study of the Anti-Interleukin-33 Antibody Tozorakimab in Healthy Adults and Patients With Chronic Obstructive Pulmonary Disease](#)

[Fred Reid](#)¹, [Dave Singh](#)², [Muna Albayaty](#)³, [Rachel Moate](#)⁴, [Eulalia Jimenez](#)⁵, [Muhammad Waqas Sadiq](#)⁶, [David Howe](#)⁷, [Monica Gavala](#)⁸, [Helen Killick](#)⁹, [Adam Williams](#)¹⁰, [Surekha Krishnan](#)¹¹, [Alex Godwood](#)⁷, [Animesh Shukla](#)¹¹, [Lisa Hewitt](#)¹¹, [Alejandra Lei](#)¹², [Chris Kell](#)⁷, [Hitesh Pandya](#)¹, [Paul Newcombe](#)⁹, [Nicholas White](#)¹⁰, [Ian C Scott](#)⁹, [E Suzanne Cohen](#)¹³

Affiliations expand

- PMID: 38115209
- DOI: [10.1002/cpt.3147](https://doi.org/10.1002/cpt.3147)

Abstract

Tozorakimab is a human monoclonal antibody that neutralizes interleukin (IL)-33. IL-33 is a broad-acting epithelial "alarmin" cytokine upregulated in lung tissue of patients with chronic obstructive pulmonary disease (COPD). This first-in-human, phase I, randomized, double-blind, placebo-controlled study ([NCT03096795](#)) evaluated the safety, tolerability, pharmacokinetics (PKs), immunogenicity, target engagement, and pharmacodynamics (PDs) of tozorakimab. This was a 3-part study. In part 1, 56 healthy participants with a history of mild atopy received single escalating doses of either intravenous or subcutaneous tozorakimab or placebo. In part 2, 24 patients with mild COPD received multiple ascending doses of subcutaneous tozorakimab or placebo. In part 3, 8 healthy Japanese participants received a single intravenous dose of tozorakimab or placebo. The safety data collected included treatment-emergent adverse events (TEAEs), vital signs, and clinical laboratory parameters. Biological samples for PKs, immunogenicity, target engagement, and PD biomarker analyses were collected. No meaningful differences in the

frequencies of TEAEs were observed between the tozorakimab and placebo arms. Three tozorakimab-treated participants with COPD experienced treatment-emergent serious adverse events. Subcutaneous or intravenous tozorakimab demonstrated linear, time-independent PKs with a mean half-life of 11.7-17.3 days. Treatment-emergent anti-drug antibody frequency was low. Engagement of tozorakimab with endogenous IL-33 in serum and nasal airways was demonstrated. Tozorakimab significantly reduced serum IL-5 and IL-13 levels in patients with COPD compared with placebo. Overall, tozorakimab was well tolerated, with a linear, time-independent serum PK profile. Additionally, biomarker studies demonstrated proof of mechanism. Overall, these data support the further clinical development of tozorakimab in COPD and other inflammatory diseases.

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Publication types, MeSH terms, Substancesexpand

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24

Pulm Ther

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. 2024 Mar;10(1):69-84.

doi: 10.1007/s41030-023-00248-6. Epub 2023 Dec 19.

[Delphi Consensus on Clinical Applications of GOLD 2023](#)

Recommendations in COPD Management: How Aligned are Recommendations with Clinical Practice?

[Antonio Anzueto¹](#), [Mark Cohen²](#), [Andres L Echazarreta³](#), [Gehan Ellassal⁴](#), [Irma Godoy⁵](#), [Rafael Paramo⁶](#), [Abdullah Sayiner⁷](#), [Carlos A Torres-Duque⁸](#), [Sudeep Acharya⁹](#), [Bhumika Aggarwal⁹](#), [Hakan Erkus¹⁰](#), [Gur Levy¹¹](#)

Affiliations expand

- PMID: 38112909
- PMCID: [PMC10881920](#)
- DOI: [10.1007/s41030-023-00248-6](#)

Free PMC article

Abstract

Introduction: The objective of this Delphi study was to understand and assess the level of consensus among respiratory experts on the clinical application of GOLD 2023 recommendations in management of patients with chronic obstructive pulmonary disease (COPD).

Methods: The study comprised two online surveys and a participant meeting with 34 respiratory experts from 16 countries. Responses of 73 questions were recorded using a Likert scale ranging from 0 (disagreement) to 9 (agreement). The consensus threshold was 75%.

Results: Survey 1 and survey 2 had 34 and 32 participants, respectively; and 25 attended the participant meeting. Consensus was reached on survey 1: 28/42; survey 2: 18/30 close-ended questions. A consensus was reached on the clinical relevance of most updates in definitions and diagnosis of COPD. Mixed results for the treatment recommendations by GOLD were noted: 74% agreed with the recommendation to initiate treatment with dual bronchodilators for group E patients; 63% agreed for including inhaled corticosteroids (ICS)/long-acting β_2 agonist(LABA)/ Long-acting muscarinic receptor antagonists (LAMA) as a treatment option for GOLD B patients. Also, consensus lacked on removing ICS + LABA

as an initial therapeutic option, in countries with challenges in access to other treatment option; 88% agreed that they use GOLD recommendations in their daily clinical practice.

Conclusions: This Delphi study demonstrated a high level of consensus regarding key concepts of GOLD 2023 report, with most participants favoring recent updates in definitions, diagnosis, management, and prevention of COPD. More evidence on the etiology based management and treatment options for group B and E are required which could further strengthen clinical application of the GOLD report.

Keywords: COPD; Clinical practice; Delphi procedure; GOLD 2023.

Plain language summary

The goal of this Delphi study was to understand and assess the level of alignment among the respiratory experts on the application of key changes and recommendations proposed by the GOLD 2023 report in their routine clinical practice for the management of patients with chronic obstructive pulmonary disease (COPD). There were two online surveys in this study, and experts from 16 countries (primarily focused on developing countries) were invited to participate. Using the Delphi method, expert representatives shared their insights with the aim of optimizing patient care. The alignment was assessed in six well-defined themes: 1) Overall view on GOLD/other recommendations; 2) Assessing patients with COPD; 3) Initial pharmacological treatment in patients with COPD; 4) Vaccination for patients with COPD; 5) Follow-up pharmacological treatment in patients with COPD; and 6) Survival evidence in patients with COPD. Participants expressed a high level of agreement regarding key concepts of the GOLD 2023 report, with most of them agreeing with recent updates in definitions, diagnosis, management, and prevention of COPD. The results also highlighted the need to publish GOLD reports in multiple languages and in a shorter, pocket-sized format to increase awareness and adaptation among healthcare providers.

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Conflict of interest statement

Antonio Anzueto received funding for this study from GSK and consulting fees in personal capacity from GSK, AstraZeneca, Verona Pharma, Sanofi, Boehringer Ingelheim, Viatrix. Mark Cohen reports travel support and payment for lectures and presentations from AstraZeneca, Boehringer Ingelheim, GSK, Luminova and Novartis; payment for participation in advisory boards of AstraZeneca, Boehringer Ingelheim; and has participated in an unpaid capacity in committees for the Asociación Latinoamericana del Tórax (ALAT), and the American Thoracic Society (ATS). Andres L Echazarreta received funding from GSK for this study, payment for lectures, and meeting attendance from AstraZeneca, Kamada/Tuteur, Grifols; payment for participation in advisory boards from GSK, AstraZeneca; and payment for expert testimony from AstraZeneca. Gehan Ellassal reports receiving honoraria from GSK, AstraZeneca, and Sanofi for lectures. Irma Godoy received

funding from Sanofi for participation in advisory board and received honoraria from MSD for lecture presentation. Rafael Paramo reports receiving financial support to attend conferences and medical events from GSK, AstraZeneca, Chiesi, Novartis and Boehringer Ingelheim; consulting fees from GSK, Chiesi; and payment for participation in advisory board of GSK; and has participated in an unpaid capacity in committees for the Sociedad Queretana de neumologia y Cirugia de Torax AC and the Sociedad Mexicana de neumologia y Cirugia de Torax AC. Abdullah Sayiner received consulting fees or honoraria (for lectures and educational events) from GSK, Abdi Ibrahim, Pfizer, and Abbott. Carlos A Torres-Duque has received payment as advisory board participant or speaker from AstraZeneca, Boehringer Ingelheim, GSK, Novartis, and Sanofi-Aventis; has participated in clinical trials from AstraZeneca, Novartis, and Sanofi-Aventis; has received unrestricted grants for investigator-initiated studies at Fundacion Neumologica Colombiana from AstraZeneca, Boehringer Ingelheim, GSK, Grifols and Novartis. Sudeep Acharya is an employee of GSK and holds shares in GSK. Bhumika Aggarwal is an employee of GSK and holds shares in GSK. Hakan Erkus is an employee of GSK and holds shares in GSK. Gur Levy is an employee of GSK and holds shares in GSK.

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- [5 figures](#)

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Int Arch Occup Environ Health

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. 2024 Mar;97(2):145-154.

doi: 10.1007/s00420-023-02031-1. Epub 2023 Dec 19.

Occupational exposure to vapors, gasses, dusts, and fumes in relation to

causes of death during 24 years in Helsinki, Finland

[Juuso Jalasto](#)¹, [Ritva Luukkonen](#)², [Ari Lindqvist](#)³, [Arnulf Langhammer](#)^{4,5}, [Hannu Kankaanranta](#)^{6,7,8}, [Helena Backman](#)⁹, [Eva Rönmark](#)⁹, [Anssi Sovijärvi](#)¹⁰, [Päivi Piirilä](#)¹⁰, [Paula Kauppi](#)³

Affiliations expand

- PMID: 38112780
- PMCID: [PMC10876715](#)
- DOI: [10.1007/s00420-023-02031-1](#)

Free PMC article

Abstract

Purpose: Environmental particulate matter (PM) exposure has been shown to cause excess all-cause and disease-specific mortality. Our aim was to compare disease-specific mortality by estimated occupational exposure to vapors, gasses, dusts, and fumes (VGDF).

Methods: The data source is the Helsinki part of the population-based FinEsS study on chronic obstructive pulmonary diseases including information on age, education level, main occupation, sex, and tobacco smoking combined with death registry information. We compared estimated VGDF exposure to mortality using adjusted competing-risks regression for disease-specific survival analysis for a 24-year follow-up.

Results: Compared to the no-exposure group, the high occupational VGDF exposure group had sub-hazard ratios (sHR) of 1.7 (95% CI 1.3-2.2) for all cardiovascular-related and sHR 2.1 (1.5-3.9) for just coronary artery-related mortality. It also had sHR 1.7 (1.0-2.8) for Alzheimer's or vascular dementia-related mortality and sHR 1.7(1.2-2.4) for all respiratory disease-related mortality.

Conclusion: Long-term occupational exposure to VGDF increased the hazard of mortality- to cardiovascular-, respiratory-, and dementia-related causes. This emphasizes the need for minimizing occupational long-term respiratory exposure to dust, gasses, and fumes.

Keywords: Cardiovascular diseases; Causes of death; Dementia diseases; Occupational exposure; Respiratory diseases.

Conflict of interest statement

Dr. Kankaanranta reports fees for consultancies and lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma and SanofiGenzyme. Dr. Kauppi reports consultancy fee from Sanofi and lecture fee from GSK. Dr. Kauppi also holds positions as a member of the board of the Finnish Respiratory Society and as a member of the Grant Committee of the Tuberculosis Foundation of Finland. Dr. Backman reports fees from Astra Zeneca, Boehringer-Ingelheim and GSK. Dr. Langhammer reports fees from Astra Zeneca, Boehringer-Ingelheim and Diagnostica. All other authors declare that they have nothing to disclose.

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

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. 2024 Mar 1;30(2):136-140.

doi: 10.1097/MCP.0000000000001042. Epub 2023 Dec 15.

Selected updates on chronic obstructive pulmonary disease

[Jordina Mah](#)¹, [Andrew I Ritchie](#)^{1,2}, [Lydia J Finney](#)^{1,3}

Affiliations expand

- PMID: 38099447
- DOI: [10.1097/MCP.0000000000001042](https://doi.org/10.1097/MCP.0000000000001042)

Abstract

Purpose of review: Chronic obstructive pulmonary disease (COPD) is preventable disease and yet it remains the third greatest cause of death worldwide. This review focuses on recent updates in COPD research which have had an impact on our understanding of the epidemiology and pathophysiology of COPD.

Recent findings: Epidemiological studies of COPD have moved towards trying to understand the global impact of COPD particularly in low- and middle-income countries where disease prevalence continues to increase. In addition, we are beginning to uncover the impact of air pollution on COPD development with recent work showing a relationship between air pollution and COPD exacerbations. Advances in understanding early origins and early development of COPD have the potential to intervene earlier in the disease course to prevent disease progression. Although biomarkers such as peripheral blood eosinophilia have led to trials of biologic agents in COPD suggesting we may be entering an exciting new biologic era in COPD.

Summary: Recent advances suggest there may be a relationship between air pollution and COPD exacerbations. This requires further research to influence environmental policy. New clinical trials of biologics targeting TH2 inflammation in COPD suggest that targeted treatments with biologics may be a possibility COPD.

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. 2024 Mar 1;30(2):150-155.

doi: 10.1097/MCP.0000000000001041. Epub 2023 Dec 13.

[Pulmonary hypertension in chronic obstructive pulmonary disease: current understanding, knowledge gaps and future directions](#)

[William T Atchley](#)¹, [Teja Krishna Kakkera](#)

Affiliations expand

- PMID: 38088383
- DOI: [10.1097/MCP.0000000000001041](https://doi.org/10.1097/MCP.0000000000001041)

Abstract

Purpose of review: Despite the advent of effective and mechanistically diverse treatments for pulmonary arterial hypertension (PAH) and their positive impacts on the functional capacities and outcomes for PAH patients, the much larger population of patients with

pulmonary hypertension (PH) in chronic lung diseases like chronic obstructive pulmonary disease (PH-COPD) remain without effective therapies.

Recent findings: In this review, we will highlight advances in the understanding of PH-COPD pathobiology, the clinical impact comorbid PH has on COPD outcomes, and detail the spectrum of disease and clinical phenotypes that encompass the heterogenous disease manifestations of PH-COPD. Finally, we will examine recent studies exploring the effects of potential treatments for PH-COPD and highlight sub-populations and treatment options that warrant further study.

Summary: As the PAH population-base ages and comorbid diseases become more frequently diagnosed in PAH patients, the need to clearly delineate subpopulations for clinical applications of PH therapies and research becomes even more urgent. Through an improved understanding of the clinical phenotypes of PH-COPD and the overlap with certain subpopulations of PAH, a framework for future research and potential for therapeutic impact is highlighted.

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. 2024 Mar 1;30(2):141-149.

Chronic obstructive pulmonary disease and cardiovascular disease: mechanistic links and implications for practice

[Tetsuro Maeda](#)¹, [Mark T Dransfield](#)

Affiliations expand

- PMID: 38085609
- DOI: [10.1097/MCP.0000000000001040](https://doi.org/10.1097/MCP.0000000000001040)

Abstract

Purpose of review: Chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD) are both significant burdens on the healthcare system and often coexist. Mechanistic links between the two conditions and their clinical impact are increasingly understood.

Recent findings: Recent studies demonstrate multiple mechanisms by which the pathobiology of COPD may have negative effects on the cardiovascular system. These include extrapulmonary consequences of the COPD inflammatory state, cardiac autonomic dysfunction, which has been recently implicated in worsening respiratory symptoms and exacerbation risk, and mechanical effects of lung hyperinflation on left ventricular diastolic function. Clinical studies have consistently shown a high prevalence of CVD in COPD patients and worsened outcomes (and vice versa). Exacerbations of COPD have also been demonstrated to dramatically increase the risk of cardiovascular events. While some safety concerns exist, medications for COPD and cardiovascular disease should be used in accordance with respective guidelines. However, real-world data show suboptimal management for patients with COPD and CVD.

Summary: COPD and cardiovascular disease have complicated interrelationships. Further mechanistic studies may lead to defining better targets for interventions. Education for medical professionals and implementation of novel screening protocols should be encouraged to fill in the gaps in clinical care for these patients.

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Respirology

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. 2024 Mar;29(3):201-208.

doi: 10.1111/resp.14642. Epub 2023 Dec 3.

[Effect of experimental modulation of mood on exertional dyspnoea in chronic obstructive pulmonary disease](#)

[Pramod Sharma](#)^{1,2}, [Karlijn Scheffer](#)^{1,3}, [Menaka Louis](#)¹, [Craig R Aitken](#)^{1,2}, [Lewis Adams](#)¹, [Norman R Morris](#)^{1,2}

Affiliations expand

- PMID: 38044806
- DOI: [10.1111/resp.14642](https://doi.org/10.1111/resp.14642)

Free article

Abstract

Background and objective: Dyspnoea is a debilitating symptom in individuals with chronic obstructive pulmonary disease (COPD) and a range of other chronic cardiopulmonary diseases and is often associated with anxiety and depression. The present study examined the effect of visually-induced mood shifts on exertional dyspnoea in individuals with COPD.

Methods: Following familiarization, 20 participants with mild to severe COPD (age 57-79 years) attended three experimental sessions on separate days, performing two 5-min treadmill exercise tests separated by a 30-min interval on each day. During each exercise test, participants viewed either a positive, negative or neutral set of images sourced from the International Affective Picture System (IAPS) and rated dyspnoea or leg fatigue (0-10). Heart rate (HR) and peripheral oxygen saturation (SpO₂) were measured at 1-min intervals during each test. Mood valence ratings were obtained using Self-Assessment Manikin (SAM) scale (1-9).

Results: Mood valence ratings were significantly higher when viewing positive (end-exercise mean \pm SEM = 7.6 ± 0.3) compared to negative IAPS images (2.4 ± 0.3 , $p < 0.001$). Dyspnoea intensity (mean \pm SEM = 5.8 ± 0.4) and dyspnoea unpleasantness (5.6 ± 0.3) when viewing negative images were significantly higher compared to positive images (4.2 ± 0.4 , $p = 0.004$ and 3.4 ± 0.5 , $p = 0.003$). Eighty-five percent of participants ($n = 17$) met the minimal clinically important difference (MCID) criteria for both dyspnoea intensity and unpleasantness. HR, SpO₂ and leg fatigue did not differ significantly between conditions.

Conclusion: These findings indicate that the negative affective state worsens dyspnoea in COPD, thereby suggesting strategies aimed at reducing the likelihood of negative mood or improving the mood may be effective in managing morbidity associated with dyspnoea in COPD.

Keywords: COPD; IAPS; chronic obstructive pulmonary disease; exertional dyspnoea; leg fatigue; mood modulation; treadmill exercise.

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J Infect Dis



. 2024 Mar 1;229(Supplement_1):S70-S77.

doi: 10.1093/infdis/jiad510.

[Respiratory Syncytial Virus-Associated Hospitalization in Adults With Comorbidities in 2 European Countries: A Modeling Study](#)

[Richard Osei-Yeboah](#)¹, [Caroline Klint Johannesen](#)², [Amanda Marie Egeskov-Cavling](#)³, [Junru Chen](#)⁴, [Toni Lehtonen](#)⁵, [Arantxa Urchueguía Fornes](#)⁶, [John Paget](#)⁷, [Thea K Fischer](#)², [Xin Wang](#)¹⁴, [Harish Nair](#)¹, [Harry Campbell](#)¹

Affiliations expand

- PMID: 37970679
- DOI: [10.1093/infdis/jiad510](https://doi.org/10.1093/infdis/jiad510)

Abstract

Background: Individuals with comorbidities are at increased risk of severe respiratory syncytial virus (RSV) infection. We estimated RSV-associated respiratory hospitalization among adults aged ≥ 45 years with comorbidities in Denmark and Scotland.

Methods: By analyzing national hospital and virologic data, we estimated annual RSV-associated hospitalizations by 7 selected comorbidities and ages between 2010 and 2018. We estimated rate ratios of RSV-associated hospitalization for adults with comorbidity than the overall population.

Results: In Denmark, annual RSV-associated hospitalization rates per 1000 adults ranged from 3.1 for asthma to 19.4 for chronic kidney disease (CKD). In Scotland, rates ranged from 2.4 for chronic liver disease to 9.0 for chronic obstructive pulmonary disease (COPD). In both countries, we found a 2- to 4-fold increased risk of RSV hospitalization for adults with COPD, ischemic heart disease, stroke, and diabetes; a 1.5- to 3-fold increased risk for asthma; and a 3- to 7-fold increased risk for CKD. RSV hospitalization rates among adults aged 45 to 64 years with COPD, asthma, ischemic heart disease, or CKD were higher than the overall population.

Conclusions: This study provides important evidence for identifying risk groups and assisting health authorities in RSV vaccination policy making.

Keywords: adults; comorbidity; hospitalization; respiratory syncytial virus.

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Conflict of interest statement

Potential conflicts of interest. H. C. reports grants, personal fees, and nonfinancial support from the World Health Organization; grants and personal fees from Sanofi Pasteur; and grants from the Bill and Melinda Gates Foundation, outside this submitted work. H. C. is a shareholder in the Journal of Global Health Ltd. H. N. reports grants from Pfizer and Icosavax and consulting fees from the World Health Organization, Pfizer, Bill and Melinda Gates Foundation, Abbvie, and Sanofi, outside the submitted work. H. N. reports participation on a data safety monitoring board or advisory board for GSK, Sanofi, Merck, the World Health Organization, Janssen, Novavax, Resvinct, Icosavax, and Pfizer. X. W. reports grants from GlaxoSmithKline and consultancy fees from Pfizer, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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. 2024 Mar 1;30(2):156-166.

doi: 10.1097/MCP.0000000000001026. Epub 2023 Oct 30.

Burden, clinical features, and outcomes of post-tuberculosis chronic obstructive lung diseases

[Inderpaul Singh Sehgal](#)¹, [Sahajal Dhooria](#)¹, [Valliappan Muthu](#)¹, [Helmut J F Salzer](#)^{2,3,4}, [Ritesh Agarwal](#)¹

Affiliations expand

- PMID: 37902135
- DOI: [10.1097/MCP.0000000000001026](https://doi.org/10.1097/MCP.0000000000001026)

Abstract

Purpose of review: Post-tuberculosis lung disease (PTLD) is an increasingly recognized and debilitating consequence of pulmonary tuberculosis (PTB). In this review, we provide a comprehensive overview of PTLD with airflow obstruction (PTLD-AFO), focusing on its burden, pathophysiology, clinical manifestations, diagnostic methods, and management strategies.

Recent findings: The relationship between PTLD and airflow obstruction is complex and multifactorial. Approximately 60% of the patients with PTLD have some spirometric abnormality. Obstruction is documented in 18-22% of PTLD patients. The host susceptibility and host response to mycobacterium drive the pathogenic mechanism of PTLD. A balance between inflammatory, anti-inflammatory, and fibrotic pathways decides whether an individual with PTB would have PTLD after microbiological cure. An obstructive

abnormality in PTLD-AFO is primarily due to destruction of bronchial walls, aberrant healing, and reduction of mucosal glands. The most common finding on computed tomography (CT) of thorax in patients with PTLD-AFO is bronchiectasis and cavitation. Therefore, the 'Cole's vicious vortex' described in bronchiectasis applies to PTLD. A multidisciplinary approach is required for diagnosis and treatment. The disability-adjusted life-years (DALYs) attributed to PTLD represent about 50% of the total estimated burden of DALYs due to tuberculosis (TB). Patients with PTLD require comprehensive care that includes psychosocial support, pulmonary rehabilitation, and vaccination against respiratory pathogens. In the absence of trials evaluating different treatments for PTLD-AFO, therapy is primarily symptomatic.

Summary: PTLD with airflow obstruction has considerable burden and causes a significant morbidity and mortality. However, many aspects of PTLD-AFO still need to be answered. Studies are required to evaluate different phenotypes, especially concerning *Aspergillus* - related complications. The treatment should be personalized based on the predominant phenotype of airflow obstruction. Extensive studies to understand the exact burden, pathogenesis, and treatment of PTLD-AFO are needed.

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. 2024 Mar 1;30(2):179-184.

doi: 10.1097/MCP.0000000000001025. Epub 2023 Oct 26.

Supplemental oxygen therapy in chronic obstructive pulmonary disease: is less is more? How much is too much?

[Ayham Daher](#)¹, [Michael Dreher](#)

Affiliations expand

- PMID: 37882582
- DOI: [10.1097/MCP.0000000000001025](https://doi.org/10.1097/MCP.0000000000001025)

Abstract

Purpose of review: Currently available evidence supporting the use of supplemental oxygen therapy (SOT) in chronic obstructive pulmonary disease (COPD) is complex, and data on the mortality reduction associated with SOT usage in patients with severe daytime resting hypoxemia have not been updated since the development of other treatments.

Recent findings: No reduction in mortality was found when SOT was used in patients with moderate resting daytime, isolated nocturnal, or exercise-induced hypoxemia. However, some of these patients obtain other significant benefits during SOT, including increased exercise endurance, and a mortality reduction is possible in these 'responders'. The adverse effects of long-term oxygen therapy also need to be considered, such as reduced mobility and social stigma. Furthermore, conservative SOT could improve outcomes in the setting of COPD exacerbations compared with higher concentration oxygen regimens. Compared with usual fixed-dose SOT, automated oxygen administration devices might reduce dyspnea during exercise and COPD exacerbations.

Summary: Current recommendations for SOT need to be revised to focus on patients who respond best and benefit most from this therapy. A conservative approach to SOT can reduce side effects compared with higher concentration oxygen regimens, and automated oxygen administration devices may help to optimize SOT.

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Ann Am Thorac Soc

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. 2024 Mar;21(3):421-427.

doi: 10.1513/AnnalsATS.202209-751OC.

[Risk Factors for Chronic Obstructive Pulmonary Disease Exacerbations among Individuals without a History of Recent Exacerbations: A COPD Gene Analysis](#)

[Michael C Ferrera](#)¹, [Camden L Lopez](#)², [Susan Murray](#)², [Renu G Jain](#)³, [Wassim W Labaki](#)⁴, [Barry J Make](#)⁵, [MeiLan K Han](#)⁴

Affiliations [expand](#)

- PMID: 37796613
- DOI: [10.1513/AnnalsATS.202209-751OC](https://doi.org/10.1513/AnnalsATS.202209-751OC)

Abstract

Rationale: Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) are detrimental events in the natural history of COPD, but the risk factors associated with future exacerbations in the absence of a history of recent exacerbations are not fully understood. **Objectives:** To identify risk factors for COPD exacerbations among participants in the Genetic Epidemiology of COPD Study (COPDGene) without a history of exacerbation in the previous year. **Methods:** We identified participants with a smoking history enrolled in COPDGene who had COPD (defined as forced expiratory volume in 1 second [FEV₁]/forced vital capacity < 0.70), no exacerbation in the year before their second study site visit, and who completed at least one longitudinal follow-up questionnaire in the following 36 months. We used univariable and multivariable zero-inflated negative binomial regression models to identify risk factors associated with increased rates of exacerbation. Each risk factor's regression coefficient (β) was rounded to the nearest 0.25 and incorporated into a graduated risk score. **Results:** Among the 1,528 participants with a smoking history and COPD enrolled in COPDGene without exacerbation in the year before their second study site visit, 508 participants (33.2%) had at least one moderate or severe exacerbation in the 36 months studied. Gastroesophageal reflux disease, chronic bronchitis, high symptom burden (as measured by Modified Medical Research Council Dyspnea Scale and COPD Assessment Test), and lower FEV₁% predicted were associated with an increased risk of exacerbation. Each 1-point increase in our graduated risk score was associated with a 25-30% increase in exacerbation rate in the 36 months studied. **Conclusions:** In patients with COPD without a recent history of exacerbations, gastroesophageal reflux disease, chronic bronchitis, high symptom burden, and lower lung function are associated with increased risk of future exacerbation using a simple risk score that can be used in clinical practice.

Keywords: COPD; COPD exacerbations; chronic bronchitis; gastroesophageal reflux disease; pulmonary emphysema.

Comment in

- [Predicting Chronic Obstructive Pulmonary Disease Exacerbations: When the Past Does Not Inform the Future.](#)
Bhatt SP. *Ann Am Thorac Soc.* 2024 Mar;21(3):382-383. doi:
10.1513/AnnalsATS.202311-934ED.PMID: 38426829 No abstract available.

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Ann Am Thorac Soc



. 2024 Mar;21(3):384-392.

doi: 10.1513/AnnalsATS.202211-975OC.

[Predictors of Patient-reported and Pharmacy Refill Measures of Maintenance Inhaler Adherence in Veterans with Chronic Obstructive Pulmonary Disease](#)

[Andrew M Pattock](#)¹, [Emily R Locke](#)², [Paul L Hebert](#)^{3,2}, [Tracy Simpson](#)^{4,5}, [Catherine Battaglia](#)^{6,7}, [Ranak B Trivedi](#)^{8,9}, [Erik R Swenson](#)^{1,2}, [Jeff Edelman](#)^{1,2}, [Vincent S Fan](#)^{1,2}

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- PMID: 37774091
- DOI: [10.1513/AnnalsATS.202211-975OC](https://doi.org/10.1513/AnnalsATS.202211-975OC)

Abstract

Rationale: Suboptimal adherence to inhaled medications in patients with chronic obstructive pulmonary disease (COPD) remains a challenge. **Objectives:** To examine the sociodemographic and clinical characteristics and medication beliefs associated with adherence measured by self-report and pharmacy data. **Methods:** A cross-sectional analysis of data from a prospective observational cohort study of patients with COPD was completed. Participants underwent spirometry and completed questionnaires regarding sociodemographic data, inhaler use, dyspnea, social support, psychological and medical

comorbidities, and medication beliefs (Beliefs about Medicines Questionnaire [BMQ]). Self-reported adherence to inhaled medications was measured with the Adherence to Refills and Medications Scale (ARMS), and pharmacy-based adherence was calculated from administrative data using the ReComp score. Multivariable linear regression was used to examine the sociodemographic, clinical, and medication-belief factors associated with both adherence measures. **Results:** Among 269 participants with ARMS and ReComp data, adherence was the same for each measure (38.3%), but only 18% of participants were adherent by both measures. In multivariable adjusted analysis, a 10-year increase in age ($\beta = 0.54$; 95% confidence interval, 0.14-0.94) and the number of maintenance inhalers used ($\beta = 0.53$; 0.04-1.02) were associated with increased adherence by self-report. Improved ReComp adherence was associated with chronic prednisone use ($\beta = 0.18$; 0.04-0.31) and the number of maintenance inhalers used ($\beta = 0.11$; 0.05-0.17). In adjusted analyses examining patient beliefs about medications, increases in the COPD-specific BMQ concerns score ($\beta = -0.10$; -0.17 to -0.02) were associated with reduced self-reported adherence. No significant associations between ReComp adherence and BMQ score were found in adjusted analyses. **Conclusions:** Adherence to inhaled COPD medications was poor as measured by self-report or pharmacy refill data. There were notable differences in factors associated with adherence based on the method of adherence measurement. Older age, chronic prednisone use, the number of prescribed maintenance inhalers used, and patient beliefs about medication safety were associated with adherence. Overall, fewer variables were associated with adherence as measured based on pharmacy refills. Pharmacy refill-based and self-reported adherence may measure distinct aspects of adherence and may be affected by different factors. These results also underscore the importance of addressing patient beliefs when developing interventions to improve medication adherence.

Keywords: COPD; chronic obstructive pulmonary disease; maintenance inhaler; medication adherence.

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Prognostic Factors of Mortality in Nonchronic Obstructive Pulmonary Disease Chronic Lung Disease: A Scoping Review

[Sheryl Hui Xian Ng¹](#), [Gin Tsen Chai^{2,3}](#), [Pradeep Paul George¹](#), [Palvinder Kaur¹](#), [Wan Fen Yip¹](#), [Zi Yan Chiam⁴](#), [Han Yee Neo⁴](#), [Woan Shin Tan¹](#), [Allyn Hum^{4,5}](#)

Affiliations expand

- PMID: 37702606
- DOI: [10.1089/jpm.2023.0263](https://doi.org/10.1089/jpm.2023.0263)

Abstract

Introduction: Patients with chronic lung disease (CLD) experience a heavy symptom burden at the end of life, but their uptake of palliative care is notably low. Having an understanding of a patient's prognosis would facilitate shared decision making on treatment options and care planning between patients, families, and their clinicians, and complement clinicians' assessments of patients' unmet palliative needs. While literature on prognostication in patients with chronic obstructive pulmonary disease (COPD) has been established and summarized, information for other CLDs remains less consolidated. Summarizing the mortality risk factors for non-COPD CLDs would be a novel contribution to literature. Hence, we aimed to identify and summarize the prognostic factors associated with non-COPD CLDs from the literature. **Methods:** We conducted a scoping review following published guidelines. We searched MEDLINE, Embase, PubMed, CINAHL, Cochrane Library, and Web of Science for studies published between 2000 and 2020 that described non-COPD CLD populations with an all-cause mortality risk period of up to three years. Only primary studies which reported associations with mortality adjusted through multivariable analysis were included. **Results:** Fifty-five studies were reviewed, with 53

based on interstitial lung disease (ILD) or connective tissue disease-associated ILD populations and two in bronchiectasis populations. Prognostic factors were classified into 10 domains, with pulmonary function and disease being the largest. Older age, lower forced vital capacity, and lower carbon monoxide diffusing capacity were most commonly investigated and associated with statistically significant increases in mortality risks. **Conclusions:** This comprehensive overview of prognostic factors for patients with non-COPD CLDs would facilitate the identification and prioritization of candidate factors to predict short-term mortality, supporting tool development for decision making and to identify high-risk patients for palliative needs assessments. Literature focused on patients with ILDs, and more studies should be conducted on other CLDs to bridge the knowledge gap.

Keywords: bronchiectasis; interstitial lung disease; palliative care; prognostic factors; scoping review.

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Chronic Illn

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. 2024 Mar;20(1):96-104.

doi: 10.1177/17423953231163450. Epub 2023 Mar 9.

[Acceptability of a peer-led self-management program for people living](#)

with chronic obstructive pulmonary disease in regional Southern Tasmania in Australia: A qualitative study

[Innocent Tawanda Mudzingwa](#)¹, [Jennifer E Ayton](#)²

Affiliations expand

- PMID: 36895141
- PMCID: [PMC10865749](#)
- DOI: [10.1177/17423953231163450](#)

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Abstract

Objectives: People living with chronic obstructive pulmonary disease (COPD) in regional communities experience a higher disease burden and have poorer access to support services. This study sought to investigate the acceptability of a peer-led self-management program (SMP) in regional Tasmania, Australia.

Methods: This descriptive qualitative study, underpinned by interpretivism used semi-structured one-to-one interviews to gather data to explore COPD patients' views of peer-led SMPs. Purposeful sampling recruited a sample of 8 women and 2 men. Data was analysed using a thematic approach.

Results: The three final themes, 'Normality and Living with the disease', a 'Platform for sharing' and 'Communication mismatch' suggest that peer-led SMPs could offer an opportunity to share experiences. The themes also suggest that COPD often manifested as a deviation from 'normal life'. Communication was often felt to be ambiguous leading to tension between the health experts and people living with the condition.

Discussion: Peer-led SMP has the potential to provide the much-needed support for people living with COPD in regional communities. This will ensure that they are empowered to live with the condition with dignity and respect. Benefits of exchanging ideas and socialisation should not be ignored and may enhance sustainability of SMPs.

Keywords: COPD; allied health; patient perspective; peer-led self-management program; qualitative study.

Conflict of interest statement

Declaration of conflicting interestsThe authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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

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Review

Chronic Illn

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. 2024 Mar;20(1):3-22.

doi: 10.1177/17423953231153337. Epub 2023 Feb 6.

Contextual factors for the successful implementation of self-management

interventions for chronic diseases: A qualitative review of reviews

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Affiliations expand

- PMID: 36744382
- DOI: [10.1177/17423953231153337](https://doi.org/10.1177/17423953231153337)

Abstract

Objectives: To identify and describe the most relevant contextual factors (CFs) from the literature that influence the successful implementation of self-management interventions (SMIs) for patients living with type 2 diabetes mellitus, obesity, COPD and/or heart failure.

Methods: We conducted a qualitative review of reviews. Four databases were searched, 929 reviews were identified, 460 screened and 61 reviews met the inclusion criteria. CFs in this paper are categorized according to the Tailored Implementation for Chronic Diseases framework.

Results: A great variety of CFs was identified on several levels, across all four chronic diseases. Most CFs were on the level of the patient, the professional and the interaction level, while less CFs were obtained on the level of the intervention, organization, setting and national level. No differences in main themes of CFs across all four diseases were found.

Discussion: For the successful implementation of SMIs, it is crucial to take CFs on several levels into account simultaneously. Person-centered care, by tailoring SMIs to patients' needs and circumstances, may increase the successful uptake, application and implementation of SMIs in real-life practice. The next step will be to identify the most important CFs according to various stakeholders through a group consensus process.

Keywords: Chronic illness; contextual factors; implementation; review; self-management interventions.

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.

- [Cited by 2 articles](#)

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Eur Respir J

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. 2024 Feb 29;63(2):2302263.

doi: 10.1183/13993003.02263-2023. Print 2024 Feb.

[Interalveolar pore morphology in \(pre-\)COPD stages and associations with small airways](#)

[Stijn E Verleden](#)^{1,2,3}, [Therese S Lapperre](#)^{3,4}, [Annemiek Snoeckx](#)^{5,6}, [Wen Wen](#)^{7,2}, [Suresh K Yogeswaran](#)², [Geert M Verleden](#)³, [Veronique Verplancke](#)³, [Reinier R L Wener](#)^{3,4}, [Senada Koljenovic](#)⁸, [Dieter J E Peeters](#)⁸, [Jeroen M H Hendriks](#)^{7,2}

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- PMID: 38423590
- DOI: [10.1183/13993003.02263-2023](https://doi.org/10.1183/13993003.02263-2023)

No abstract available

Conflict of interest statement

Conflicts of interest: The authors have no potential conflicts of interest to disclose.

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Eur Respir J

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. 2024 Feb 29;63(2):24E6302.

doi: 10.1183/13993003.E6302-2024. Print 2024 Feb.

[**ERJ Podcast February 2024: Beetroot juice and cardiovascular risk in COPD**](#)

No authors listed

- PMID: 38423589
- DOI: [10.1183/13993003.E6302-2024](https://doi.org/10.1183/13993003.E6302-2024)

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Am J Respir Crit Care Med



. 2024 Feb 29.

doi: 10.1164/rccm.202302-0231OC. Online ahead of print.

[Epigenome-Wide Association Studies of COPD and Lung Function: A Systematic Review](#)

[Sandra Casas-Recasens](#)^{1,2}, [Raisa Cassim](#)³, [Núria Mendoza](#)^{1,2}, [Alvar Agusti](#)^{1,4,5,6}, [Caroline Lodge](#)³, [Shuai Li](#)^{7,8,9,10}, [Dinh Bui](#)³, [David Martino](#)^{11,12}, [Shyamali C Dharmage](#)³, [Rosa Faner](#)^{1,4,13,14}

Affiliations expand

- PMID: 38422471
- DOI: [10.1164/rccm.202302-0231OC](https://doi.org/10.1164/rccm.202302-0231OC)

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) results from gene-environment interactions over the lifetime. These interactions are captured by epigenetic changes, such as DNA methylation. This systematic review synthesizes evidence from epigenome-wide association studies (EWAS) related to COPD and lung function.

Methods: Systematic literature search on PubMed, Embase and CINAHL databases, identified 1947 articles that investigated epigenetic changes associated with COPD/lung function; 17 of them met our eligibility criteria from which data was manually extracted.

Differentially methylated positions (DMPs) and/or annotated genes, were considered replicated if identified by ≥ 2 studies with a $p < 1 \times 10^{-4}$.

Results: Ten studies profiled DNA methylation changes in blood and 7 in respiratory samples, including surgically resected lung tissue (n=3), small airways epithelial brushings (n=2), bronchoalveolar lavage (n=1) and sputum (n=1). Main results showed: (1) high variability in study design, covariates and effect sizes, which prevented a formal meta-analysis; (2) in blood samples, 51 DMPs were replicated in relation to lung function and 12 related to COPD; (3) in respiratory samples, 42 DMPs were replicated in relation to COPD but none in relation to lung function; and, (4) in COPD vs. control studies, 123 genes (2.6% of total) were shared between ≥ 1 blood and ≥ 1 respiratory sample and associated with chronic inflammation, ion transport and coagulation.

Conclusions: There is high heterogeneity across published COPD/lung function EWAS studies. A few genes (n=123; 2.6%) were replicated in blood and respiratory samples, suggesting that blood can recapitulate some changes in respiratory tissues. These findings have implications for future research.

Keywords: COPD; chronic bronchitis; emphysema; methylation; omics.

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Acta Cardiol

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. 2024 Feb 29:1-10.

doi: 10.1080/00015385.2024.2319955. Online ahead of print.

[Heart failure worsens leg muscle strength and endurance in coexistence](#)

patients with COPD and heart failure reduced ejection fraction

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Affiliations expand

- PMID: 38420970
- DOI: [10.1080/00015385.2024.2319955](https://doi.org/10.1080/00015385.2024.2319955)

Abstract

Purpose: Exercise intolerance and dyspnoea are clinical symptoms in both heart failure (HF) reduced ejection fraction (HFrEF) and chronic obstructive pulmonary disease (COPD), which are suggested to be associated with musculoskeletal dysfunction. We tested the hypothesis that HFrEF + COPD patients would present lower muscle strength and greater fatigue compared to compared to the COPD group. **Methods:** We included 25 patients with HFrEF + COPD (100% male, age 67.8 ± 6.9) and 25 patients with COPD alone (100% male, age 66.1 ± 9.1). In both groups, COPD severity was determined as moderate-to-severe according to the GOLD classification ($FEV_1/FVC < 0.7$ and predicted post-bronchodilator FEV_1 between 30%-80%). Knee flexor-extensor muscle performance (torque, work, power and fatigue) were measured by isokinetic dynamometry in age and sex-matched patients with HFrEF + COPD and COPD alone; Functional capacity was assessed by the cardiopulmonary exercise test, the 6-min walk test (6MWT) and the four-minute step test. **Results:** The COPD group exhibited reduced lung function compared to the HFrEF + COPD group, as evidenced by lower FEV_1/FVC (58.0 ± 4.0 vs. 65.5 ± 13.9 ; $p < 0.0001$, respectively) and FEV_1 (51.3 ± 17.0 vs. 62.5 ± 17.4 ; $p = 0.026$, respectively) values. Regarding musculoskeletal function, the HFrEF + COPD group showed a knee flexor muscles impairment, however this fact was not observed in the knee extensors muscles. Power peak of the knee flexor corrected by muscle mass was significantly correlated with the 6MWT ($r = 0.40$; $p < 0.05$), number of steps ($r = 0.30$; $p < 0.05$) and work rate_{peak} ($r = 0.40$; $p < 0.05$) in the HFrEF + COPD and COPD groups. **Conclusion:** The presence of HFrEF in patients with COPD worsens muscular weakness when compared to isolated COPD.

Keywords: Lung disease; exercise; heart disease; isokinetic; skeletal muscle.

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J Appl Physiol (1985)



. 2024 Feb 29.

doi: 10.1152/jappphysiol.00694.2022. Online ahead of print.

[Airway tree caliber heterogeneity and airflow obstruction among older adults](#)

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Affiliations expand

- PMID: 38420676
- DOI: [10.1152/jappphysiol.00694.2022](https://doi.org/10.1152/jappphysiol.00694.2022)

Abstract

Introduction: Smaller mean airway tree caliber is associated with airflow obstruction and chronic obstructive pulmonary disease (COPD). We investigated whether airway tree caliber heterogeneity was associated with airflow obstruction and COPD.

Methods: Two community-based cohorts (MESA Lung, CanCOLD) and a longitudinal case-control study of COPD (SPIROMICS) performed spirometry and computed tomography measurements of airway lumen diameters at standard anatomic locations and total lung volume. Percent-predicted airway lumen diameters were calculated using sex-specific reference equations accounting for age, height and lung volume. The association of airway tree caliber heterogeneity, quantified as the standard deviation (SD) of percent-predicted

airway lumen diameters, with baseline forced expired volume in 1-second (FEV_1), FEV_1 /forced vital capacity (FEV_1/FVC) and COPD, as well as longitudinal spirometry, were assessed using regression models adjusted for age, sex, height, race-ethnicity, and mean airway tree caliber.

Results: Among 2,505 MESA Lung participants (mean \pm SD age: 69 \pm 9 years; 53% female, mean airway tree caliber: 99 \pm 10% predicted, airway tree caliber heterogeneity: 14 \pm 5%; median follow-up: 6.1 years), participants in the highest quartile of airway tree caliber heterogeneity exhibited lower FEV_1 (adjusted mean difference: -125 ml, 95%CI:-171,-79), lower FEV_1/FVC (adjusted mean difference: -0.01, 95%CI:-0.02,-0.01), and higher odds of COPD (adjusted OR 1.42, 95%CI:1.01-2.02) when compared with the lowest quartile, whereas longitudinal changes in FEV_1 and FEV_1/FVC did not differ significantly. Observations in CanCOLD and SPIROMICS were consistent.

Conclusion: Among older adults, airway tree caliber heterogeneity was associated with airflow obstruction and COPD at baseline but was not associated with longitudinal changes in spirometry.

Keywords: airflow obstruction; airway tree caliber heterogeneity; chronic obstructive pulmonary disease; computed tomography.

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. 2024 Feb 18;10(4):e26437.

doi: 10.1016/j.heliyon.2024.e26437. eCollection 2024 Feb 29.

Does PaCO₂ correction have an impact on survival of patients with chronic respiratory failure and long-term non-invasive ventilation?

[Audrey Thomas](#)¹, [Sandrine Jaffré](#)¹, [Vianney Gardiolle](#)², [Tanguy Perennec](#)³, [Frédéric Gagnadoux](#)⁴, [François Goupil](#)⁵, [Cédric Bretonnière](#)¹, [Vivien Danielo](#)¹, [Jean Morin](#)¹, [François-Xavier Blanc](#)¹

Affiliations expand

- PMID: 38420381
- PMCID: [PMC10901024](#)
- DOI: [10.1016/j.heliyon.2024.e26437](#)

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Abstract

Background and objective: Non-invasive ventilation (NIV) improves survival of patients with chronic respiratory failure (CRF). Most often, pressure settings are made to normalize arterial blood gases. However, this objective is not always achieved due to intolerance to increased pressure or poor compliance. Few studies have assessed the effect of persistent hypercapnia on ventilated patients' survival. Data from the Pays de la Loire Respiratory Health Research Institute cohort were analyzed to answer this question.

Study design and methods: NIV-treated adults enrolled between 2009 and 2019 were divided into 5 subgroups: obesity-hypoventilation syndrome (OHS), COPD, obese COPD, neuromuscular disease (NMD) and chest wall disease (CWD). PaCO₂ correction was defined as the achievement of a PaCO₂ < 6 kPa or a 20% decrease in baseline PaCO₂ in COPD patients. The endpoint was all-cause mortality. Follow-up was censored in case of NIV discontinuation.

Results: Data from 431 patients were analyzed. Median survival was 103 months and 148 patients died. Overall, PaCO₂ correction was achieved in 74% of patients. Bivariate analysis did not show any survival difference between patients who achieved PaCO₂ correction and

those who remained hypercapnic: overall population: $p = 0.74$; COPD: $p = 0.97$; obese COPD: $p = 0.28$; OHS: $p = 0.93$; NMD: $p = 0.84$; CWD: $p = 0.28$.

Conclusion: Moderate residual hypercapnia under NIV does not negatively impact survival in CRF patients. In individuals with poor tolerance of pressure increases, residual hypercapnia can therefore be tolerated under long-term NIV. Larger studies, especially with a higher number of patients with residual $\text{PaCO}_2 > 7$ kPa, are needed to confirm these results.

Keywords: Chronic obstructive pulmonary disease; Chronic respiratory failure; Hypercapnia; Non-invasive ventilation; Obesity-hypoventilation syndrome; Survival.

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Conflict of interest statement

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.

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

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Respir Res

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. 2024 Feb 28;25(1):104.

doi: 10.1186/s12931-024-02710-8.

The effect of combining an inhaled corticosteroid and a long-acting muscarinic antagonist on human airway epithelial cells in vitro

[Maria Gabriella Matera](#)¹, [Barbara Rinaldi](#)², [Cecilia Calabrese](#)³, [Carmela Belardo](#)², [Luigino Calzetta](#)⁴, [Mario Cazzola](#)⁵, [Clive Page](#)⁶

Affiliations expand

- PMID: 38419021
- PMCID: [PMC10902985](#)
- DOI: [10.1186/s12931-024-02710-8](#)

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Abstract

Background: Airway epithelial cells (AECs) are a major component of local airway immune responses. Direct effects of type 2 cytokines on AECs are implicated in type 2 asthma, which is driven by epithelial-derived cytokines and leads to airway obstruction. However, evidence suggests that restoring epithelial health may attenuate asthmatic features.

Methods: We investigated the effects of passive sensitisation on IL-5, NF- κ B, HDAC-2, ACh, and ChAT in human bronchial epithelial cells (HBEpCs) and the effects of fluticasone furoate (FF) and umeclidinium (UME) alone and in combination on these responses.

Results: IL-5 and NF- κ B levels were increased, and that of HDAC-2 reduced in sensitised HBEpCs. Pretreatment with FF reversed the effects of passive sensitisation by concentration-dependent reduction of IL-5, resulting in decreased NF- κ B levels and restored HDAC-2 activity. Addition of UME enhanced these effects. Sensitized HBEpCs also exhibited higher ACh and ChAT levels. Pretreatment with UME significantly reduced ACh levels, and addition of FF caused a further small reduction.

Conclusion: This study confirmed that passive sensitisation of AECs results in an inflammatory response with increased levels of IL-5 and NF- κ B, reduced levels of HDAC-2, and higher levels of ACh and ChAT compared to normal cells. Combining FF and UME was

found to be more effective in reducing IL-5, NF- κ B, and ACh and restoring HDAC-2 compared to the individual components. This finding supports adding a LAMA to established ICS/LABA treatment in asthma and suggests the possibility of using an ICS/LAMA combination when needed.

Keywords: Airway epithelial cells; Asthma; Inflammation; Inhaled corticosteroid; Long-acting muscarinic antagonists.

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Conflict of interest statement

MGM participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of ABC Farmaceutici, Almirall, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline and Novartis, was a consultant to Chiesi Farmaceutici and GSK, and her department was funded by GSK and Novartis. CC received honoraria for lectures from AstraZeneca, GSK, Sanofi and Novartis, and support for attending meetings and/or travel received from AstraZeneca, GSK, Sanofi and Novartis. LC has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis, received nonfinancial support from AstraZeneca, received a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; has been a consultant to ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon. MC participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of Abdi Ibrahim, Alkem, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, Eurodrug, GSK, Glenmark, Lallemand, Mankind Pharma, Menarini Group, Mundipharma, Novartis, Pfizer, Recipharm, Sanofi, Teva, Verona Pharma and Zambon, and is or was a consultant to ABC Farmaceutici, AstraZeneca, Chiesi Farmaceutici, GSK, Lallemand, Novartis, Ockham Biotech, Recipharm, Verona Pharma and Zambon. CP has acted as a consultant to Eurodrug, Recipharm, Glycosynnovation and PrEP Biopharma, and also holds equity in Verona Pharma. BR and CB declare no conflict of interest.

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- [2 figures](#)

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Respir Res



. 2024 Feb 28;25(1):106.

doi: 10.1186/s12931-024-02729-x.

Local heterogeneity of normal lung parenchyma and small airways disease are associated with COPD severity and progression

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Affiliations expand

- PMID: 38419014
- PMCID: [PMC10903150](#)
- DOI: [10.1186/s12931-024-02729-x](#)

Free PMC article

Abstract

Background: Small airways disease (SAD) is a major cause of airflow obstruction in COPD patients and has been identified as a precursor to emphysema. Although the amount of SAD in the lungs can be quantified using our Parametric Response Mapping (PRM) approach, the full breadth of this readout as a measure of emphysema and COPD

progression has yet to be explored. We evaluated topological features of PRM-derived normal parenchyma and SAD as surrogates of emphysema and predictors of spirometric decline.

Methods: PRM metrics of normal lung (PRM^{Norm}) and functional SAD (PRM^{fSAD}) were generated from CT scans collected as part of the COPDGene study ($n = 8956$). Volume density (V) and Euler-Poincaré Characteristic (χ) image maps, measures of the extent and coalescence of pocket formations (i.e., topologies), respectively, were determined for both PRM^{Norm} and PRM^{fSAD} . Association with COPD severity, emphysema, and spirometric measures were assessed via multivariable regression models. Readouts were evaluated as inputs for predicting FEV_1 decline using a machine learning model.

Results: Multivariable cross-sectional analysis of COPD subjects showed that V and χ measures for PRM^{fSAD} and PRM^{Norm} were independently associated with the amount of emphysema. Readouts χ^{fSAD} (β of 0.106, $p < 0.001$) and V^{fSAD} (β of 0.065, $p = 0.004$) were also independently associated with $\text{FEV}_1\%$ predicted. The machine learning model using PRM topologies as inputs predicted FEV_1 decline over five years with an AUC of 0.69.

Conclusions: We demonstrated that V and χ of fSAD and Norm have independent value when associated with lung function and emphysema. In addition, we demonstrated that these readouts are predictive of spirometric decline when used as inputs in a ML model. Our topological PRM approach using PRM^{fSAD} and PRM^{Norm} may show promise as an early indicator of emphysema onset and COPD progression.

Keywords: Chronic obstructive pulmonary disease; Computed tomography of the chest; Emphysema; Machine learning; Parametric response mapping; Small airways disease.

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Conflict of interest statement

Wassim W. Labaki reports personal fees from Continuing Education Alliance. Benjamin A. Hoff and Craig J. Galban are co-inventors and patent holders of tPRM, which the University of Michigan has licensed to Imbio, LLC. Craig J. Galban is co-inventor and patent holder of PRM, which the University of Michigan has licensed to Imbio, LLC. Benjamin A. Hoff and Craig J. Galban have financial interest in Imbio, LLC. Charles R. Hatt is employed by Imbio, LLC. David A. Lynch reports funds paid to the institution from NIH and personal payments from Boehringer Ingelheim. MeiLan K. Han reports personal fees from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, Novartis, Pulmonx, Teva, Verona, Merck, Mylan, Sanofi, DevPro, Aerogen, Polarian, Regeneron, Amgen, UpToDate, Altesa Biopharma, Medscape, NACE, MDBriefcase and Integrity. She has received either in kind research support or funds paid to the institution from the NIH, Novartis, Sunovion, Nuaira, Sanofi, AstraZeneca, Boehringer Ingelheim, Gala Therapeutics, Biodesix, the COPD Foundation and the American Lung Association. She has participated in Data Safety Monitoring Boards for Novartis and Medtronic with funds paid to the institution. She has

received stock options from Meissa Vaccines and Altesa Biopharma. For the remaining authors none were declared.

- [35 references](#)
- [5 figures](#)

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BMJ Open

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. 2024 Feb 28;14(2):e075257.

doi: 10.1136/bmjopen-2023-075257.

[Screening and early warning system for chronic obstructive pulmonary disease with obstructive sleep apnoea based on the medical Internet of Things in three levels of healthcare: protocol for a prospective, multicentre, observational cohort study](#)

[Zihan Pan](#)^{#1,2}, [Sha Liao](#)^{#1}, [Wanlu Sun](#)^{#3}, [Haoyi Zhou](#)⁴, [Shuo Lin](#)⁵, [Dian Chen](#)¹, [Simin Jiang](#)¹, [Huanyu Long](#)¹, [Jing Fan](#)¹, [Furong Deng](#)⁶, [Wenlou Zhang](#)⁶, [Baiqi Chen](#)⁶, [Junyi Wang](#)^{1,6}, [Yongwei Huang](#)^{1,7}, [Jianxin Li](#)⁸, [Yahong Chen](#)⁹

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- PMID: 38418236
- DOI: [10.1136/bmjopen-2023-075257](https://doi.org/10.1136/bmjopen-2023-075257)

Free article

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are prevalent respiratory diseases in China and impose significant burdens on the healthcare system. Moreover, the co-occurrence of COPD and OSA exacerbates clinical outcomes significantly. However, comprehensive epidemiological investigations in China remain scarce, and the defining characteristics of the population affected by COPD and OSA, alongside their intrinsic relationship, remain ambiguous.

Methods and analysis: We present a protocol for a prospective, multicentre, observational cohort study based on a digital health management platform across three different healthcare tiers in five sites among Chinese patients with COPD. The study aims to establish predicative models to identify OSA among patients with COPD and to predict the prognosis of overlap syndrome (OS) and acute exacerbations of COPD through the Internet of Things (IoT). Moreover, it aims to evaluate the feasibility, effectiveness and cost-effectiveness of IoT in managing chronic diseases within clinical settings. Participants will undergo baseline assessment, physical examination and nocturnal oxygen saturation measuring. Specific questionnaires screening for OSA will also be administered. Diagnostic lung function tests and polysomnography will be performed to confirm COPD and OSA, respectively. All patients will undergo scheduled follow-ups for 12 months to record the changes in symptoms, lung functions and quality of life. Primary outcomes include the prevalence and characteristics of OS, while secondary outcomes encompass OS prognosis and the feasibility of the management model in clinical contexts. A total of 682 patients with COPD will be recruited over 12-24 months.

Ethics and dissemination: The study has been approved by Peking University Third Hospital, and all study participants will provide written informed consent. Study results will be published in an appropriate journal and presented at national and international conferences, as well as relevant social media and various stakeholder engagement activities.

Trial registration number: [NCT04833725](https://www.clinicaltrials.gov/ct2/show/study/NCT04833725).

Keywords: Chronic airways disease; Clinical Trial; Primary Care; Pulmonary Disease, Chronic Obstructive; SLEEP MEDICINE; Telemedicine.

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Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH terms, Associated dataexpand

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Respiration



. 2024 Feb 28.

doi: 10.1159/000537918. Online ahead of print.

[Associations of depressive and anxiety disorders with pulmonary disorders in the community – the PneumoLaus and PsyCoLaus studies](#)

[Brice Touilloux](#), [Alessio Casutt](#), [Marie-Pierre F Strippoli](#), [Alexandra Lenoir](#), [Simone Janett](#), [Peter Vollenweider](#), [Julien Vaucher](#), [Laurent Nicod](#), [Martin Preisig](#), [Christophe Von Garnier](#)

- PMID: 38417406
- DOI: [10.1159/000537918](https://doi.org/10.1159/000537918)

Abstract

Introduction: Mental health disorders figure among the many comorbidities of obstructive respiratory diseases. The multisystemic characteristics of chronic respiratory disease and its impact on quality of life could affect depressive and/or anxiety disorders. We aimed to evaluate the association of spirometric indices, ventilatory disorders and self-reported respiratory diseases with psychiatric disorders considering potential confounders.

Methods: We analysed data from CoLaus|PsyCoLaus, a Swiss population-based cohort study, consisting of 2'774 participants (56% women; mean age: 62.3 (SD=±9.9) years) who performed spirometry and completed semi-structured psychiatric interviews. We defined ventilatory disorders using GLI-2012 references. Major depressive episode (MDE) and anxiety disorders were defined using the DSM-IV (Diagnostic and Statistical Manual).

Results: 630 subjects (22.7%) presented a recent MDE. Reversible obstructive ventilatory disorders were associated with recent MDE (OR=1.94, 95% CI 95 1.10-3.43) and recent anxiety disorders (2.21 [1.16-4.22]) only in unadjusted model. Self-reported COPD and asthma were associated with MDE with ORs of 2.49 (95%CI, 1.19-5.27) and 1.56 (95% CI, 1.04-2.35) after adjustment, respectively. Possible restrictive ventilatory impairment was positively associated with recent anxiety disorders (OR=2.46, 1.10-5.51). Z-scores of FEV1, FVC and maximum mid expiratory flow (MMEF) were not associated with psychiatric disorders. There was no association between ventilatory disorders and MDE in adjusted models.

Conclusions: In this cross-sectional population-based study, the association between respiratory disorders and depressive disorders was observed for self-reported COPD and asthma, but not with objective diagnoses based on spirometry. Lung volumes are not associated with psychiatric disorders. Further prospective studies will be necessary to understand the significance of the association.

The Author(s). Published by S. Karger AG, Basel.

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Review

Respir Care

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. 2024 Feb 28;69(3):366-375.

doi: 10.4187/respcare.11039.

[The Impact of Positive Expiratory Pressure Therapy on Hyperinflation in Patients With COPD](#)

[Juliana Ribeiro Fonseca Franco de Macedo](#)¹, [Elinaldo da Conceição dos Santos](#)¹, [Gregory Reyhler](#)¹, [William Poncin](#)²

Affiliations expand

- PMID: 38416659
- DOI: [10.4187/respcare.11039](https://doi.org/10.4187/respcare.11039)

Abstract

Background: Lung hyperinflation is a typical clinical feature of patients with COPD. Given the association between breathing at elevated lung volumes and the manifestation of severe debilitating symptoms, therapeutic interventions such as positive expiratory pressure (PEP) therapy and its variations (temporary, oscillatory) have been devised to mitigate lung hyperinflation. However, the efficacy of these interventions remains to be conclusively demonstrated.

Methods: A systematic review with meta-analysis of randomized trials was conducted following the PRISMA guidelines. Seven databases were screened with no date or language restriction. Two authors independently applied eligibility criteria and assessed the risk of bias of included studies using the Cochrane risk-of-bias tool. Outcomes were lung

hyperinflation measures detected through changes in inspiratory capacity (IC), functional residual capacity (FRC), total lung capacity (TLC), and residual volume (RV), as well as FEV₁, FVC, dyspnea, and physical capacity. Pooled standardized mean differences (SMDs) or mean differences (MDs) and 95% CI were calculated using a random-effects model.

Results: Seven trials, all with a high risk of bias, were included. Compared to control group, RV significantly decreased (4 studies, $n = 231$; SMD -0.42 [95% CI -0.77 to -0.08], $P = .02$), dyspnea improved ($n = 321$, SMD -1.17 [95% CI -1.68 to -0.66], $P < .001$), and physical capacity increased (5 studies, $n = 311$; MD 30.1 [95% CI 19.2 - 41.0] m, $P < .001$) with PEP therapy. There was no significant difference between PEP therapy and the control group in TLC, FVC, or FEV₁. Only one study reported changes in inspiratory capacity as well as FRC.

Conclusions: In patients with COPD, the effect of PEP therapy on lung hyperinflation is unclear owing to the non-consistent change in lung hyperinflation outcomes, insufficient data, and lack of high-quality trials. Dyspnea and physical capacity might improve with PEP therapy.

Keywords: COPD; hyperinflation; positive expiratory pressure; systematic review.

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Conflict of interest statement

The authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Editorial

Respir Care

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. 2024 Feb 28;69(3):379-381.

doi: 10.4187/respcare.11914.

[Go With the Flow: The Dilemma of Long-Term Oxygen Prescription After Recovery](#)

[Claudia Crimi](#)¹, [Andrea Cortegiani](#)²

Affiliations expand

- PMID: 38416658
- DOI: [10.4187/respcare.11914](https://doi.org/10.4187/respcare.11914)

No abstract available

Conflict of interest statement

Dr Cortegiani declares a patent, 102019000020532, not discussed in the present study and no conflict of interests related to this work. Dr Crimi has disclosed no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

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Home Oxygen After Hospitalization for COVID-19: Results From the Multi-Center OXFORD Study

[Michael B Freedman](#)¹, [Yoo Jin Kim](#)², [Ramandeep Kaur](#)², [Bijal V Jain](#)², [Ayodeji O Adegunsoye](#)², [Yu-Che Chung](#)², [Julie A DeLisa](#)², [Jessica M Gardner](#)², [Howard S Gordon](#)², [Jared A Greenberg](#)², [Malvika Kaul](#)², [Nader Khouzam](#)², [Stephanie L Labedz](#)², [Babak Mokhlesi](#)², [Jacob Rintz](#)², [Israel Rubinstein](#)², [Analisa Taylor](#)², [David L Vines](#)², [Lubna Ziauddin](#)², [Lynn B Gerald](#)², [Jerry A Krishnan](#)²

Affiliations expand

- PMID: 38176902
- DOI: [10.4187/respcare.11436](https://doi.org/10.4187/respcare.11436)

Abstract

Background: In the first months of the pandemic, prior to the introduction of proven-effective treatments, 15-37% of patients hospitalized with COVID-19 were discharged on home oxygen. After proven-effective treatments for acute COVID-19 were established by evidence-based guidelines, little remains known about home oxygen requirements following hospitalization for COVID-19.

Methods: This was a retrospective, multi-center cohort study of subjects hospitalized for COVID-19 between October 2020-September 2021 at 3 academic health centers. Information was abstracted from electronic health records at the index hospitalization and for 60 d after discharge. The World Health Organization COVID-19 Clinical Progression Scale score was used to identify patients with severe COVID-19.

Results: Of 517 subjects (mean age 58 y, 47% female, 42% Black, 36% Hispanic, 22% with severe COVID-19), 81% were treated with systemic corticosteroids, 61% with remdesivir, and 2.5% with tocilizumab. About one quarter of subjects were discharged on home oxygen (26% [95% CI 22-29]). Older age (adjusted odds ratio [aOR] 1.02 per 5 y [95% CI 1.02-1.02]), higher body mass index (aOR 1.02 per kg/m² [1.00-1.04]), diabetes (yes vs no,

aOR 1.73 [1.46-2.02]), severe COVID-19 (vs moderate, aOR 3.19 [2.19-4.64]), and treatment with systemic corticosteroids (yes vs no, aOR 30.63 [4.51-208.17]) were associated with an increased odds of discharge on home oxygen. Comorbid hypertension (yes vs no, aOR 0.71 [0.66-0.77]) was associated with a decreased odds of home oxygen. Within 60 d of hospital discharge, 50% had documentation of pulse oximetry; in this group, home oxygen was discontinued in 46%.

Conclusions: About one in 41 subjects were prescribed home oxygen after hospitalization for COVID-19, even after guidelines established proven-effective treatments for acute illness. Evidence-based strategies to reduce the requirement for home oxygen in patients hospitalized for COVID-19 are needed.

Keywords: Long COVID; SARS-CoV-2; durable medical equipment; hypoxemia; post-acute sequelae of SARS-CoV-2.

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Conflict of interest statement

Dr Adegunsoye discloses relationships with the National Institute of Health, Genentech, Inogen, and Boehringer Ingelheim. Dr Gerald discloses relationships with the National Institute of Health, American Lung Association, UpToDate, American Lung Association of Arizona, and the Arizona Asthma Coalition. Dr Krishnan discloses relationships with the National Institutes of Health, COPD Foundation, Regeneron, Sergey Brin Family Foundation, Patient-Centered Outcomes Research Institute, American Lung Association, GSK, AstraZeneca, CereVu Medical, Propeller Health and ResMed, BData, University of Chicago, American Academy of Asthma, Allergy, and Immunology, Global Initiative for Asthma, American Thoracic Society, Central Society of Clinical and Translational Research, and the Respiratory Health Association. Dr Vines discloses relationships with the Rice Foundation, Teleflex Medical, Elsevier, Dräger, Mayo Clinic Didier Memorial Lecture, and the National Board for Respiratory Care. The remaining authors have disclosed no conflicts of interest.

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J Allergy Clin Immunol Pract



. 2024 Feb 27:S2213-2198(24)00196-X.

doi: 10.1016/j.jaip.2024.02.022. Online ahead of print.

Respiratory Diseases Associated with Organic Dust Exposure

[Jill A Poole](#)¹, [Jose L Zamora-Sifuentes](#)², [Leticia De Las Vecillas](#)³, [Santiago Quirce](#)⁴

Affiliations expand

- PMID: 38423290
- DOI: [10.1016/j.jaip.2024.02.022](https://doi.org/10.1016/j.jaip.2024.02.022)

Abstract

Organic dusts are complex bioaerosol mixtures comprised of dust and particulate matter of organic origin. These include components from bacteria, fungi, pollen, and viruses to fragments of animals and plants commonplace to several environmental/occupational settings encompassing agriculture/farming, grain processing, waste/recycling, textile, cotton, woodworking, bird breeding, and more. Organic dust exposures are linked to development of chronic bronchitis, chronic obstructive pulmonary disease (COPD), asthma, asthma-like syndrome, byssinosis, hypersensitivity pneumonitis (HP), and idiopathic pulmonary fibrosis (IPF). Risk factors of disease development include cumulative dust exposure, smoking, atopy, timing/duration, and nutritional factors. The immunopathogenesis predominately involves Toll-like receptor signaling cascade, Th1/Th17 lymphocyte responses, neutrophil influx, and potentiation of manifestations associated with allergy. The true prevalence of airway disease directly attributed to organic dust, especially in a workplace setting, remains challenging. Diagnostic confirmation can be difficult and complicated by hesitancy from workers to seek medical care, driven by fears of potential labor-related consequence. Clinical respiratory and systemic presentations coupled with allergy testing, lung function patterns of obstructive versus restrictive disease, and radiological characteristics are typically utilized to delineate these various organic dust-associated respiratory diseases. Prevention, risk reduction, and management primarily

focus on reducing exposure to the offending dust, managing symptoms, and preventing disease progression.

Keywords: asthma; fibrosis; hypersensitivity pneumonitis; obstructive lung disease; occupational; organic dust.

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BMC Pulm Med



. 2024 Feb 27;24(1):102.

doi: 10.1186/s12890-024-02915-z.

[Prevalence, risk factors, and clinical characteristics of pulmonary embolism in patients with acute exacerbation of COPD in Plateau regions: a prospective cohort study](#)

[Chenlu Yang](#)^{#1}, [Yajun Tuo](#)^{#2}, [Xuefeng Shi](#)^{#2}, [Jie Duo](#)^{#2}, [Xin Liu](#)³, [Fang Zhang](#)², [Xiaokai Feng](#)^{4,5}

Affiliations [expand](#)

- PMID: 38413975

- PMID: [PMC10900782](#)
- DOI: [10.1186/s12890-024-02915-z](#)

Free PMC article

Abstract

Background and objective: To investigate pulmonary thromboembolism (PE) in acute exacerbation of chronic obstructive pulmonary disease (AE-COPD) patients in plateau regions, we performed a prospective cohort study to evaluate the prevalence, risk factors and clinical characteristics of PE in the cohort of hospitalized patients at high altitude.

Methods: We did a prospective study with a total of 636 AE-COPD patients in plateau regions. Demographic and clinical data, laboratory data, including ultrasound scans of the lower extremities and cardiac ultrasound, and computed tomographic pulmonary angiography (CTPA) variables were obtained, and comparisons were made between groups with and without PE. We also conducted logistic regression to explore the risk factors of PE.

Results: Of the 636 patients hospitalized with AE-COPD (age 67.0 ± 10.7 years, 445[70.0%] male), 188 patients developed PE (29.6% [95% CI: 26.0%, 33.1%]). Multivariable logistic regression showed that ethnic minorities, D-dimer > 1 mg/L, AST > 40 U/L, chest pain, cardiac insufficiency or respiratory failure, Padua score > 3 , and DVT were associated with a higher probability of PE.

Conclusions: The prevalence of PE is high and those with a higher Padua score, the occurrence of deep venous thrombosis, higher neutrophil count, chest pain, cardiac insufficiency or respiratory failure, higher levels of AST, and a higher level of D-dimer had a higher risk of PE. The analysis of AE-COPD may help to provide more accurate screening for PE and improve clinical outcomes of patients with AE-COPD in plateau regions.

Keywords: Acute exacerbations of chronic obstructive pulmonary disease; Plateau regions; Prevalence; Pulmonary thromboembolism; Risk factors.

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Conflict of interest statement

The authors declare no competing interests.

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

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Multicenter Study

PLoS One

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. 2024 Feb 27;19(2):e0298573.

doi: 10.1371/journal.pone.0298573. eCollection 2024.

[Impact of combined pulmonary fibrosis and emphysema on lung cancer risk and mortality in rheumatoid arthritis: A multicenter retrospective cohort study](#)

[Shunsuke Mori](#)¹, [Yukitaka Ueki](#)², [Mizue Hasegawa](#)³, [Kazuyoshi Nakamura](#)⁴, [Kouya Nakashima](#)⁵, [Toshihiko Hidaka](#)⁶, [Koji Ishii](#)⁷, [Hironori Kobayashi](#)⁸, [Tomoya Miyamura](#)⁹

Affiliations expand

- PMID: 38412181

- PMCID: [PMC10898759](#)

- DOI: [10.1371/journal.pone.0298573](https://doi.org/10.1371/journal.pone.0298573)

Free PMC article

Abstract

Objective: Combined pulmonary fibrosis and emphysema (CPFE) is a syndrome characterized by the coexistence of emphysema and fibrotic interstitial lung disease (ILD). The aim of this study was to examine the effect of CPFE on lung cancer risk and lung cancer-related mortality in patients with rheumatoid arthritis (RA).

Methods: We conducted a multicenter retrospective cohort study of patients newly diagnosed with lung cancer at five community hospitals between June 2006 and December 2021. Patients were followed until lung cancer-related death, other-cause death, loss to follow-up, or the end of the study. We used the cumulative incidence function with Gray's test and Fine-Gray regression analysis for survival analysis.

Results: A total of 563 patients with biopsy-proven lung cancer were included (82 RA patients and 481 non-RA patients). The prevalence of CPFE was higher in RA patients than in non-RA patients (40.2% vs. 10.0%) at lung cancer diagnosis. During follow-up, the crude incidence rate of lung cancer-related death was 0.29 and 0.10 per patient-year (PY) in RA and non-RA patients, and 0.32 and 0.07 per PY in patients with CPFE and patients without ILD or emphysema, respectively. The estimated death probability at 5 years differed between RA and non-RA patients (66% vs. 32%, $p < 0.001$) and between patients with CPFE and patients without ILD or emphysema (71% vs. 24%, $p < 0.001$). In addition to clinical cancer stage and no surgery within 1 month, RA and CPFE were identified as independent predictive factors for increased lung cancer-related mortality (RA: adjusted hazard ratio [HR], 2.49; 95% confidence interval [CI], 1.65-4.76; CPFE: adjusted HR 2.01; 95% CI 1.24-3.23).

Conclusions: RA patients with lung cancer had a higher prevalence of CPFE and increased cancer-related mortality compared with non-RA patients. Close monitoring and optimal treatment strategies tailored to RA patients with CPFE are important to improve the poor prognosis of lung cancer.

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Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: S. Mori received honoraria for lectures from AbbVie GK, Eli Lilly Japan

K.K., Pfizer Japan Inc., Chugai Pharmaceutical Co. Ltd., Janssen Pharmaceutical K.K., Boehringer Ingelheim Japan, and Taisho Pharma Co., Ltd. and received research funds from AbbVie GK, Asahikasei Pharma Corp, and Chugai Pharmaceutical Co., Ltd. Y. Ueki received honoraria for lectures from AbbVie GK, Eli Lilly Japan K.K., Pfizer Japan Inc., Asahikasei Pharma Corp., Astellas Pharma Inc., Bristol-Myers K.K., Chugai Pharmaceutical Co. Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Ono Pharmaceutical Co., and Takeda Pharmaceutical Co., Ltd. T. Hidaka received honoraria for lectures from AbbVie GK, Eli Lilly Japan K.K., Pfizer Japan Inc., Asahi Kasei Pharma Corp., Bristol-Myers K.K., Chugai Pharmaceutical Co., Ltd., and Eisai Co. K. Nakamura received honoraria for lectures from AstraZeneca K.K. The other authors had no financial relationships that could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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- [2 figures](#)

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Monaldi Arch Chest Dis

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. 2024 Feb 27.

doi: 10.4081/monaldi.2024.2849. Online ahead of print.

[Role of detailed psychological evaluation and treatment in pulmonary](#)

rehabilitation programs for patients with chronic obstructive pulmonary disease

[Anna Jacob](#)¹, [Kranti Garg](#)², [Kashish Dutta](#)³, [Varinder Saini](#)⁴, [Deepak Aggarwal](#)⁵, [Ajeet Sidana](#)⁶

Affiliations [expand](#)

- PMID: 38411459
- DOI: [10.4081/monaldi.2024.2849](https://doi.org/10.4081/monaldi.2024.2849)

Free article

Abstract

Psychological co-morbidities are common in chronic obstructive pulmonary disease (COPD) but remain overlooked. Psychosocial interventions are deemed to promote mental health and optimize management. This study aimed to determine the role of detailed psychological evaluation and treatment in the comprehensive management of COPD. COPD patients after screening with the general health questionnaire-12 (GHQ-12) for psychological co-morbidity were divided into three groups (26 patients each): i) group A [GHQ-12 score < 3, received pulmonary rehabilitation (PR) and standard medical management]; ii) and iii) group B and C (GHQ-12 score > 3, in addition, received management by a psychiatrist and counseling by a pulmonologist, respectively). At baseline and 8 weeks of follow-up, all participants were evaluated for respiratory [forced expiratory volume in the first second (FEV1), six-minute walk distance (6-MWD), St. George's respiratory questionnaire (SGRQ), modified medical research council (mMRC) dyspnea scale], and psychological [GHQ-12, patient distress thermometer (PDT), coping strategy checklist (CSCL), World Health Organization-quality of life-brief (WHOQOL-Bref-26), and depression anxiety stress scales (DASS)] parameters. Psychological distress (GHQ-12 > 3) decreased significantly at follow-up, with 11.5% and 53.8% of patients having psychological distress in groups B and C, respectively, versus baseline ($p < 0.001$). mMRC score, SGRQ score, FEV1 and 6-MWD significantly improved in all three groups. Improvement in mMRC and SGRQ was maximal in group B when compared with the other groups. PDT, CSCL, and WHO-QOL-Bref-26 scores improved significantly at follow-up in all three groups, with maximum improvement in group B, followed by group C, and then group A. The DASS score also improved maximally in group B. Patients should be screened for psychological co-morbidities using simple screening tools. PR plays an important role in improving the psychology of COPD patients. However, results are better with directed

psycho-educative sessions by non-experts and best with definitive treatment by psychiatrists.

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Review

Expert Rev Respir Med

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. 2024 Feb 27.

doi: 10.1080/17476348.2024.2324086. Online ahead of print.

[Diversity in pulmonary rehabilitation clinical trials: a systematic review of the literature](#)

[Sunaina Chopra](#)^{1,2}, [Shivani Rana](#)³, [Reenal Patel](#)³, [Tessa Hamilton](#)³, [Alyssa Dalip](#)³, [Param Malhi](#)³, [Pat G Camp](#)^{2,3}

Affiliations expand

- PMID: 38410864
- DOI: [10.1080/17476348.2024.2324086](https://doi.org/10.1080/17476348.2024.2324086)

Abstract

Background: Underrepresentation of minority groups in clinical trials may hinder the potential benefits of pulmonary rehabilitation (PR) programs for individuals with chronic obstructive pulmonary disease (COPD). The aim of this work was to determine whether participants in PR randomized control trials (RCTs) conducted in the U.S.A., Canada, the UK, and Australia are representative of ethnicity, sex, gender, and sociodemographic characteristics.

Research design: A systematic search was performed for relevant literature from inception to December 2022. Titles and abstracts were screened before undergoing a full article review. Relevant data on reporting of age, sex, gender, ethnicity, and sociodemographic characteristics of participants was extracted.

Results: Thirty-six RCTs met the inclusion criteria. Only six percent of publications reported on ethnicity, with $\geq 90\%$ of participants reported as 'White.' All 36 papers reported on age, with the mean between 60-69 years old. 35 studies reported on sex (97%), with the majority (67%) reporting more male than female participants. There was no mention of different genders in any paper. Other sociodemographic factors were reported in 7 (19%) papers.

Conclusions: Inclusivity and representation in clinical trials are essential to ensure that research findings are generalizable. Clinical trialists need to consider the demographics of today's society during recruitment.

Keywords: COPD; Clinical trials; ethnicity; inclusivity; pulmonary rehabilitation; race.

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[Review](#)

Chest



. 2024 Feb 26:S0012-3692(24)00276-9.

doi: 10.1016/j.chest.2024.02.040. Online ahead of print.

How I Do It Applying non-invasive ventilation in treatment of acute exacerbation of chronic obstructive pulmonary disease using evidence-based interprofessional clinical practice

[Mary Jo S Farmer](#)¹, [Christine Callahan](#)², [Ashley M Hughes](#)³, [Karen Riska](#)⁴, [Nicholas Hill](#)⁵

Affiliations expand

- PMID: 38417700
- DOI: [10.1016/j.chest.2024.02.040](https://doi.org/10.1016/j.chest.2024.02.040)

Abstract

When administered as first-line intervention to patients admitted with acute hypercapnic respiratory failure secondary to chronic obstructive pulmonary disease exacerbation in conjunction with guideline recommended therapies, noninvasive ventilation (NIV) has been shown to reduce mortality and endotracheal intubation. Opportunities to increase uptake of NIV continue to exist despite inclusion of this therapy in clinical guidelines. Identifying patients appropriate for NIV, and subsequently providing close monitoring to determine an improvement in clinical condition involves a team consisting of physician, nurse and respiratory therapist in institutions that successfully implement NIV. We describe to our knowledge the first known evidence-based algorithm speaking to initiation, titration, monitoring, and weaning of NIV in treatment of acute exacerbation of chronic obstructive pulmonary disease that incorporates the necessary interprofessional collaboration among physicians, nurses and respiratory therapists caring for these patients.

Keywords: Acute exacerbation of COPD (AECOPD); chronic obstructive pulmonary disease (COPD); interprofessional team; noninvasive ventilation (NIV).

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Editorial

ERJ Open Res

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. 2024 Feb 26;10(1):01012-2023.

doi: 10.1183/23120541.01012-2023. eCollection 2024 Jan.

[Optimising upper-limb exercise in patients with COPD: another step towards personalised pulmonary rehabilitation?](#)

[Rainer Gloeckl](#)^{1,2}, [Fabio Pitta](#)³, [Andre Nyberg](#)⁴

Affiliations [expand](#)

- PMID: 38410717
- PMCID: [PMC10895419](#)

- DOI: [10.1183/23120541.01012-2023](https://doi.org/10.1183/23120541.01012-2023)

Free PMC article

Abstract

Upper-limb interval training may be a promising new modality in pulmonary rehabilitation <https://bit.ly/41KSLAs>.

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Conflict of interest statement

Conflict of interest: R. Gloeckl received institutional study funding from the Bavarian Health and Food Safety Authority, and speakers' fees and advisory board fees from AstraZeneca, Böhringer Ingelheim, Chiesi, CSL Behring, GSK and Sanofi, outside the submitted work. Conflict of Interest: F. Pitta received speakers' fees from Böhringer Ingelheim. Conflict of Interest: A. Nyberg reports institutional grants from the European Research Council, The Swedish Research Council, and the Swedish Heart and Lung Foundation; and is Secretary of the Physiotherapy Assembly within the European Respiratory Society.

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

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. 2024 Feb 26;10(1):00836-2023.

ERS International Congress 2023: highlights from the Clinical Techniques, Imaging and Endoscopy Assembly

[Antonio Moretti](#)^{1,2}, [Pia Iben Pietersen](#)^{3,4}, [Maged Hassan](#)⁵, [Hanaa Shafiek](#)⁵, [Helmut Prosch](#)⁶, [Adam Domonkos Tarnoki](#)^{7,8}, [Jouke T Annema](#)¹, [Mohammed Munavvar](#)⁹, [Peter I Bonta](#)¹, [Walter de Wever](#)¹⁰, [Amanda Dandanell Juul](#)^{11,12}

Affiliations expand

- PMID: 38410712
- PMCID: [PMC10895430](#)
- DOI: [10.1183/23120541.00836-2023](#)

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Abstract

The Clinical Techniques, Imaging and Endoscopy Assembly is involved in the diagnosis and treatment of several pulmonary diseases, as demonstrated at the 2023 European Respiratory Society (ERS) International Congress in Milan, Italy. From interventional pulmonology, the congress included several exciting results for the use of bronchoscopy in lung cancer, including augmented fluoroscopy, robotic-assisted bronchoscopy and cryobiopsies. In obstructive lung disease, the latest results on bronchoscopic treatment of emphysema with hyperinflation and chronic bronchitis were presented. Research on using cryobiopsies to diagnose interstitial lung disease was further explored, with the aims of elevating diagnostic yield and minimising risk. For imaging, the latest updates in using artificial intelligence to overcome the increased workload of radiologists were of great interest. Novel imaging in sarcoidosis explored the use of magnetic resonance imaging, photon-counting computed tomography and positron emission tomography/computed tomography in the diagnostic work-up. Lung cancer screening is still a hot topic and new results were presented regarding incorporation of biomarkers, identifying knowledge gaps and improving screening programmes. The use of ultrasound in respiratory medicine is an expanding field, which was demonstrated by the large variety in studies presented at the

2023 ERS Congress. Ultrasound of the diaphragm in patients with amyotrophic lateral sclerosis and myasthenia gravis was used to assess movements and predict respiratory fatigue. Furthermore, studies using ultrasound to diagnose or monitor pulmonary disease were presented. The congress also included studies regarding the training and assessment of competencies as an important part of implementing ultrasound in clinical practice.

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Conflict of interest statement

Conflict of interest: A. Moretti was the winner of a research fellowship grant from SIP (Italian Respiratory Society), outside the submitted work; and reports support for attending meetings from Amsterdam UMC, outside the submitted work. P.I. Pietersen reports a grant from Boehringer Ingelheim for travel and accommodation for the European Society of Thoracic Imaging Winter Course 2022, outside the submitted work. H. Prosch reports research grants or contracts from Boehringer Ingelheim, AstraZeneca, Siemens Healthineers, the Christian Doppler Research Association and the EU Commission (EU4Health, Horizon Europe Health), outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, BMS, Boehringer Ingelheim, Bracco, Daiichi Sankyo, Janssen, MSD, Novartis, Roche, Sanofi, Siemens Healthineers and Takeda, outside the submitted work; support for attending meetings and/or travel from Boehringer Ingelheim, outside the submitted work; and participation on a data safety monitoring or advisory board for BMS, Boehringer Ingelheim, Janssen, MSD, Roche and Sanofi, outside the submitted work. H. Shafiek reports a grant for a research fellowship from the Ministry of Higher Education and Scientific Research of Egypt to work in Spain for 6 months (April 2021 to October 2021), outside the submitted work; support from the ERS to attend the International Congress in Milan in 2023, outside the submitted work; and was leader of the bronchoscopy unit of Alexandria Faculty of Medicine, Egypt between October 2022 and September 2023, and is leader of the bronchoscopy unit of Smouha University Hospital, Alexandria, Egypt, from April 2023 to present, outside the submitted work. A.D. Tarnoki reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Boehringer Ingelheim, outside the submitted work; and is ERS Imaging Group chair 2022–2024. J.T. Annema reports support for the present manuscript from Mauna Kea Technologies and a grant from Mauna Kea Technologies, outside the submitted work. M. Munavvar reports honorarium for teaching from Olympus Europe, Becton Dickinson and Chiesi, outside the submitted work; and sponsorship for travel from Chiesi, outside the submitted work. P.I. Bonta reports institutional research grants from AstraZeneca, Mauna Kea and Boston Scientific, outside the submitted work. A.D. Juul reports research funding from Danish Cancer Society and Danish Center for Lung Cancer Research, outside the submitted work. All other authors have nothing to disclose.

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. 2024 Feb 26;10(1):00779-2023.

doi: 10.1183/23120541.00779-2023. eCollection 2024 Jan.

[Upper-limb interval versus constant-load exercise in patients with COPD: a physiological crossover study](#)

[Mara Paneroni](#)¹, [Ioannis Vogiatzis](#)², [Alessandro Cavicchia](#)³, [Beatrice Salvi](#)¹, [Laura Bertacchini](#)¹, [Massimo Venturelli](#)³, [Michele Vitacca](#)¹

Affiliations [expand](#)

- PMID: 38410701
- PMCID: [PMC10895421](#)
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Abstract

Objective: Upper-limb exercise is recommended for patients with COPD, albeit there are limited data concerning the optimal modality to implement. We compared interval (INT-EX) to continuous (CONT-EX) upper-limb exercise in terms of exercise tolerance, ventilatory and metabolic responses when both conditions were sustained at an equivalent work rate.

Methods: 26 stable COPD patients undertook three upper-limb exercise sessions to initially establish peak work rate (PWR) *via* an incremental exercise test and subsequently two equivalent work rate tests to the limit tolerance in balanced order: 1) INT-EX consisting of 30-s work at 100% PWR interspersed with 30-s work at 40% of PWR; and 2) CONT-EX at 70% PWR.

Results: 20 patients (76.9%) had longer tolerance during INT-EX, while six out of 26 (23.1%) exhibited longer tolerance during CONT-EX. The average endurance time was 434.1 ± 184.7 and 315.7 ± 128.7 s for INT-EX and CONT-EX, respectively. During INT-EX at isotime (*i.e.* when work completed was the same between INT-EX and CONT-EX), the majority of patients manifested lower oxygen uptake, minute ventilation, pulmonary hyperinflation, heart rate, symptoms and higher CO₂ blood concentration. Patients with longer INT-EX had a lower comorbidity score (Cumulative Illness Rating Scale: 1.58 ± 0.30 *versus* 1.88 ± 0.29 , $p=0.0395$) and better-preserved lung function (forced vital capacity $84.7 \pm 15.31\%$ *versus* $67.67 \pm 20.56\%$, $p=0.0367$; forced expiratory volume in 1 s 57.15 ± 14.59 *versus* $44.67 \pm 12.99\%$ predicted, $p=0.0725$) compared to patients with longer CONT-EX.

Conclusion: INT-EX is more sustainable than CONT-EX for the majority of COPD patients with moderate obstruction, leading to lower dynamic hyperinflation and symptoms at isotime. Further studies need to define the benefits of its application during pulmonary rehabilitation.

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Conflict of interest statement

Conflicts of interest: I. Vogiatzis is an associate editor of this journal. The remaining authors have no potential conflicts of interest to disclose.

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ERJ Open Res



. 2024 Feb 26;10(1):00838-2023.

doi: 10.1183/23120541.00838-2023. eCollection 2024 Jan.

Global mortality and readmission rates following COPD exacerbation-related hospitalisation: a meta-analysis of 65 945 individual patients

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Affiliations expand

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- PMCID: [PMC10895439](#)
- DOI: [10.1183/23120541.00838-2023](#)

Abstract

Background: Exacerbations of COPD (ECOPD) have a major impact on patients and healthcare systems across the world. Precise estimates of the global burden of ECOPD on mortality and hospital readmission are needed to inform policy makers and aid preventive strategies to mitigate this burden. The aims of the present study were to explore global in-hospital mortality, post-discharge mortality and hospital readmission rates after ECOPD-related hospitalisation using an individual patient data meta-analysis (IPDMA) design.

Methods: A systematic review was performed identifying studies that reported in-hospital mortality, post-discharge mortality and hospital readmission rates following ECOPD-related hospitalisation. Data analyses were conducted using a one-stage random-effects meta-analysis model. This study was conducted and reported in accordance with the PRISMA-IPD statement.

Results: Data of 65 945 individual patients with COPD were analysed. The pooled in-hospital mortality rate was 6.2%, pooled 30-, 90- and 365-day post-discharge mortality rates were 1.8%, 5.5% and 10.9%, respectively, and pooled 30-, 90- and 365-day hospital readmission rates were 7.1%, 12.6% and 32.1%, respectively, with noticeable variability between studies and countries. Strongest predictors of mortality and hospital readmission included noninvasive mechanical ventilation and a history of two or more ECOPD-related hospitalisations <12 months prior to the index event.

Conclusions: This IPDMA stresses the poor outcomes and high heterogeneity of ECOPD-related hospitalisation across the world. Whilst global standardisation of the management and follow-up of ECOPD-related hospitalisation should be at the heart of future implementation research, policy makers should focus on reimbursing evidence-based therapies that decrease (recurrent) ECOPD.

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Conflict of interest statement

Conflict of interest: K. Waeijen-Smit, M. Cruksen, S. Keene, T.J. Ringbæk, F. Fabbian, C-t. Lun, B. Ergan, C. Esteban, J.M. Quintana Lopez, C.L. Chang, R.J. Hancox, E. Shafuddin, H. Ellis, C. Janson, G. Gudmundsson, D. Epstein, A. Lacoma, C. Osadnik, I. Alia, F. Spannella, Z. Karakurt, H. Mehravaran, C. Utens, M.D. de Kruif, F.W.S. Ko, S.P. Trethewey, K. Vermeersch, S. Zilberman-Itskovich, C. Echevarria, R.T.M. Sprooten, P. Faverio, H.J. Prins and S. Houben-Wilke have no grants or personal fees to report. Conflict of interest: M. Miravittles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Kamada, Takeda, Zambon, CSL Behring, Specialty Therapeutics, Janssen, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim,

Chiesi, GlaxoSmithKline, CSL Behring, Inhibrx, Ferrer, Menarini, Mereo Biopharma, Spin Therapeutics, ONO Pharma, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi and Grifols and research grants from Grifols. Conflict of interest: E. Crisafulli has received honoraria for lecturing, scientific advisory boards and participation in clinical studies for AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis, Qbgroup and Sanofi. Conflict of interest: A. Torres reports speaker/consulting honoraria from Pfizer, MSD, Janssen and Biomerieux. Conflict of interest: C. Mueller has received research support from the Swiss National Science Foundation, the Swiss Heart Foundation, the University of Basel, the University Hospital Basel, the KTI, Abbott, Beckman Coulter, BRAHMS, Idorsia, LSI-Medience, Ortho Diagnostics, Novartis, Roche, Siemens, SpinChip and Singulex, as well as speaker/consulting honoraria from Amgen, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Daiichi Sankyo, Idorsia, Novartis, Osler, Roche, SpinChip and Sanofi, all outside the submitted work. Conflict of interest: P. Schuetz has received grants from Nestle, Abbot, bioMerieux and Thermofisher outside the submitted work. Conflict of interest: E. Mekov has received grants and personal fees from Chiesi, and speaker or consulting fees from AstraZeneca and Chiesi. Conflict of interest: T.H. Harries is supported by a National Institute for Health and Care Research Academic Clinical Lectureship. Conflict of interest: J.L. López-Campos has received honoraria during the last 3 years for lecturing, scientific advice, participation in clinical studies or writing for publications for (alphabetical order): AstraZeneca, Bial, Boehringer, Chiesi, CSL Behring, Faes, Ferrer, Gebro, Grifols, GSK, Megalabs, Menarini and Novartis. Conflict of interest: C.S. Ulrik has received personal fees and grants from AstraZeneca, Chiesi, Boehringer Ingelheim, GSK, Novartis, Sanofi, Menarini, TEVA, ALK-Abello, Takeda, Orion Pharma, TFF Pharmaceuticals and Covis Pharma outside the submitted work. Conflict of interest: J. Dominguez has received honoraria for lectures from Oxford Immunotec (UK) and received payments for license transference from GenID (Germany), and grants from La Fundació La Marató TV3, Instituto de Salud Carlos III (CP03/00112), Catalan Pulmonology Society (SOCAP), Catalan Pulmonology Foundation (FUCAP) and Spanish Society of Pulmonology and Thoracic Surgery (SEPAR). Conflict of interest: A.M. Turner reports research grants outside the submitted work from AstraZeneca, Resmed, Phillips, Chiesi, Grifols, CSL Behring and NIHR, and honoraria from GSK and Boehringer Ingelheim. Conflict of interest: D. Bumbacea has received grants and personal fees in the last 3 years from AstraZeneca, Eli Lilly, Novartis, Sanofi and Synairgen outside of the submitted work. Conflict of interest: PBM has received grants and personal fees from Philips, ResMed, Breas, Chiesi, Fischer & Paykel and, Sanofi outside the submitted work. Conflict of interest: J. Steer has received grants and honoraria, outside the submitted work, from Chiesi, Menarini Group, AstraZeneca and Pfizer. Conflict of interest: S.C. Bourke has received research grants from GSK (BEC COPD IRAS 285200), and additional support from Radiometer for an NIHR-funded study (NIVOW IRAS 313485), Philips, ResMed, and Pfizer Open Air, took part in clinical advisory boards with Philips and AstraZeneca, and has received honoraria from Boehringer Ingelheim, Chiesi, GSK, and AstraZeneca. Conflict of interest: N. Lane reports research grants from Bright Northumbria and The ResMed Foundation; and nonfinancial support from Chiesi and BREAS outside the submitted work. Conflict of interest: J. de Batlle acknowledges receiving financial support from Instituto de Salud Carlos III (Miguel Servet 2019: CP19/00108), co-funded by the European Social Fund,

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Eur J Med Res

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[Unraveling the causality between chronic obstructive pulmonary disease and its common comorbidities using bidirectional Mendelian randomization](#)

[Zihan Wang](#)¹, [Yongchang Sun](#)²

Affiliations expand

- PMID: 38403592
- PMCID: [PMC10895842](#)
- DOI: [10.1186/s40001-024-01686-x](#)

Free PMC article

Abstract

Background: Chronic obstructive pulmonary disease (COPD) frequently coexists with various diseases, yet the causal relationship between COPD and these comorbidities remains ambiguous. As a result, the aim of our study is to elucidate the potential causality between COPD and its common comorbidities.

Methods: We employed the Mendelian randomization (MR) method to analyze single nucleotide polymorphism (SNP) data of common comorbidities with COPD from FinnGen and Integrative Epidemiology Unit (IEU) databases. Causality was primarily assessed using the inverse variance weighting (IVW) method. Multivariable Mendelian randomization (MVMR) analysis was also conducted to eliminate the interference of smoking-related phenotypes. Sensitivity analysis was conducted to ensure the reliability of our findings.

Results: Preliminary univariable MR revealed an increased risk of lung squamous cell carcinoma (LUSC) (IVW: OR = 1.757, 95% CI = 1.162-2.657, P = 0.008), chronic kidney disease (CKD) (IVW: OR = 1.193, 95% CI = 1.072-1.326, P < 0.001), chronic periodontitis (IVW: OR = 1.213, 95% CI = 1.038-1.417, P = 0.012), and heart failure (HF) (IVW: OR = 1.127, 95% CI = 1.043-1.218, P = 0.002). Additionally, the reverse MR analysis indicated that genetic susceptibility to HF (IVW: OR = 1.272, 95% CI = 1.084-1.493, P = 0.003), obesity (IVW: OR = 1.128, 95% CI = 1.056-1.205, P < 0.001), depression (IVW: OR = 1.491, 95% CI = 1.257-1.770, P < 0.001), and sleep apnea syndrome (IVW: OR = 1.209, 95% CI = 1.087-1.345, P < 0.001) could raise the risk of COPD. The MVMR analysis showed no causal effect of COPD on susceptibility to chronic periodontitis after adjusting for smoking.

Conclusions: Our study identified that COPD may elevate the risk of LUSC, HF, and CKD. Additionally, our analysis revealed that HF, sleep apnea symptoms, depression, and obesity might also increase the susceptibility to COPD. These findings revealed a potential causal relationship between COPD and several prevalent comorbidities, which may provide new insights for disease early prediction and prevention.

Keywords: COPD; Causality; Comorbidity; Mendelian randomization; Single nucleotide polymorphisms.

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Conflict of interest statement

The authors declare no competing interests.

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

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Review

Am J Cardiol

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doi: 10.1016/j.amjcard.2024.02.022. Online ahead of print.

[Traditional and Advanced Echocardiographic Evaluation in](#)

Chronic Obstructive Pulmonary Disease: The Forgotten Relationship

[Mihail Celeski](#)¹, [Andrea Segreti](#)², [Dajana Polito](#)¹, [Daniele Valente](#)¹, [Luisa Vicchio](#)¹, [Giuseppe Di Gioia](#)³, [Gian Paolo Ussia](#)¹, [Raffaele Antonelli Incalzi](#)⁴, [Francesco Grigioni](#)¹

Affiliations expand

- PMID: 38412881
- DOI: [10.1016/j.amjcard.2024.02.022](https://doi.org/10.1016/j.amjcard.2024.02.022)

Abstract

Chronic obstructive pulmonary disease (COPD) is a significant preventable and treatable clinical disorder defined by a persistent, typically progressive airflow obstruction. This disease has a significant negative impact on mortality and morbidity worldwide. However, the complex interaction between the heart and lungs is usually underestimated, necessitating more attention to improve clinical outcomes and prognosis. Indeed, COPD significantly impacts ventricular function, right and left chamber architecture, tricuspid valve functionality, and pulmonary blood vessels. Accordingly, more emphasis should be paid to their diagnosis since cardiac alterations may occur very early before COPD progresses and generate pulmonary hypertension (PH). Echocardiography enables a quick, noninvasive, portable, and accurate assessment of such changes. Indeed, recent advancements in imaging technology have improved the characterization of the heart chambers and made it possible to investigate the association between a few cardiac function indices and clinical and functional aspects of COPD. This review aims to describe the intricate relationship between COPD and heart changes and provide basic and advanced echocardiographic methods to detect early right ventricular and left ventricular morphologic alterations and early systolic and diastolic dysfunction. Additionally, it is crucial to comprehend the clinical and prognostic significance of functional tricuspid regurgitation in COPD and PH and the currently available trans-catheter therapeutic approaches for its treatment. Moreover, it is also essential to assess non-invasively PH and pulmonary resistance in COPD patients by applying new echocardiographic parameters. In conclusion, echocardiography should be employed more frequently in assessing COPD patients since it may aid in discovering previously unrecognized heart abnormalities and selecting the most appropriate treatment to improve the patient's symptoms, quality of life, and survival.

Keywords: Chronic Obstructive Pulmonary Disease; Echocardiography; Pulmonary Hypertension; Tricuspid Valve Regurgitation.

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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Respirology

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. 2024 Feb 25.

doi: 10.1111/resp.14683. Online ahead of print.

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

[Kate Petrie](#)¹, [Michael J Abramson](#)², [Johnson George](#)^{1,2}

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 ≥ 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 FEV₁ /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 FEV₁ /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 FEV₁ /FVC < 0.70 compared to those with FEV₁ /FVC ≥ 0.70 . Males aged 50-years, current smokers with SOB and FEV₁ /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 FEV₁ /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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**"Multimorbidity"[Mesh Terms] OR
Multimorbidity[Text Word]**



Development and acceptability of PETS-Now, an electronic point-of-care tool to monitor treatment burden in patients with multiple chronic conditions: a multi-method study

[David T Eton](#)¹, [Kathleen J Yost](#)², [Jennifer L Ridgeway](#)³, [Bayly Bucknell](#)², [Mike Wambua](#)⁴, [Natalie C Erbs](#)⁵, [Summer V Allen](#)⁵, [Elizabeth A Rogers](#)⁶, [Roger T Anderson](#)⁷, [Mark Linzer](#)⁸

Affiliations expand

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- DOI: [10.1186/s12875-024-02316-5](https://doi.org/10.1186/s12875-024-02316-5)

Abstract

Background: The aim of this study was to develop a web-based tool for patients with multiple chronic conditions (MCC) to communicate concerns about treatment burden to their healthcare providers.

Methods: Patients and providers from primary-care clinics participated. We conducted focus groups to identify content for a prototype clinical tool to screen for treatment burden by reviewing domains and items from a previously validated measure, the Patient Experience with Treatment and Self-management (PETS). Following review of the prototype, a quasi-experimental pilot study determined acceptability of using the tool in clinical practice. The study protocol was modified to accommodate limitations due to the Covid-19 pandemic.

Results: Fifteen patients with MCC and 18 providers participated in focus groups to review existing PETS content. The pilot tool (named PETS-Now) consisted of eight domains (Living Healthy, Health Costs, Monitoring Health, Medicine, Personal Relationships, Getting

Healthcare, Health Information, and Medical Equipment) with each domain represented by a checklist of potential concerns. Administrative burden was minimized by limiting patients to selection of one domain. To test acceptability, 17 primary-care providers first saw 92 patients under standard care (control) conditions followed by another 90 patients using the PETS-Now tool (intervention). Each treatment burden domain was selected at least once by patients in the intervention. No significant differences were observed in overall care quality between patients in the control and intervention conditions with mean care quality rated high in both groups (9.3 and 9.2, respectively, out of 10). There were no differences in provider impressions of patient encounters under the two conditions with providers reporting that patient concerns were addressed in 95% of the visits in both conditions. Most intervention group patients (94%) found that the PETS-Now was easy to use and helped focus the conversation with the provider on their biggest concern (98%). Most providers (81%) felt they had learned something new about the patient from the PETS-Now.

Conclusion: The PETS-Now holds promise for quickly screening and monitoring treatment burden in people with MCC and may provide information for care planning. While acceptable to patients and clinicians, integration of information into the electronic medical record should be prioritized.

Keywords: Multimorbidity; Patient-reported experience; Patient-reported outcomes; Primary health care; Quality of health care; Quality of life; Self-management; Telehealth.

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. 2024 Mar-Apr;73(2):126-137.

doi: 10.1097/NNR.0000000000000708. Epub 2024 Jan 6.

Social Determinants of Health and Multimorbidity Among Adults 50 Years and Older in the United States

[Jung Eun Lee](#), [Emily Haynes](#), [Susan DeSanto-Madeya](#), [Young Man Kim](#)

- PMID: 38411567
- DOI: [10.1097/NNR.0000000000000708](https://doi.org/10.1097/NNR.0000000000000708)

Abstract

Background: Living with two or more chronic conditions simultaneously-known as multimorbidity-has become increasingly prevalent as the aging population continues to grow. However, the factors that influence the development of multimorbidity are still not fully understood.

Objectives: The purpose of this study was to investigate the prevalence of multimorbidity among U.S. adults 50 years and older and identify associated factors with multimorbidity.

Methods: We used data from four cycles from the National Health and Nutrition Examination Survey (2011-2018) to examine the associations between social determinants of health and multimorbidity among American adults aged 50 years and older. A set of variables on socioeconomic status and health behaviors was chosen based on the social determinants of health conceptual framework developed by the World Health Organization. In our study, 4,552 participants were included. All analyses were accounted for a complex survey design and the use of survey weights. Multiple logistic regression analyses were performed to examine the associated factors with multimorbidity.

Results: The average age was 63.1 years, and 52.9% were female. The average number of chronic conditions was 2.27. The prevalence of multimorbidity was 63.8%, with high cholesterol and hypertension being the most prevalent conditions. In the adjusted model, age, gender, household income, citizenship status, health insurance, healthcare access, body mass index, and smoking status were found to be associated with living with multimorbidity.

Discussion: Our results indicate that continued efforts aimed at promoting smoking cessation and maintaining a healthy weight will be beneficial in preventing the onset of chronic conditions. Additional research is warranted to gain a deeper understanding of the interrelationships between gender, race/ethnicity, household income, citizenship status, health insurance, and healthcare access as social determinants of health in the context of multimorbidity. Further research will help us develop targeted interventions and policies to address disparities and improve health outcomes for individuals with multimorbidity.

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Conflict of interest statement

The authors have no conflicts of interest to disclose.

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Arch Gerontol Geriatr

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. 2024 Mar:118:105287.

doi: 10.1016/j.archger.2023.105287. Epub 2023 Nov 25.

[Gender-specific association of the accumulation of chronic conditions and](#)

disability in activities of daily living with depressive symptoms

[Mengxiao Hu](#)¹, [Haiyang Yu](#)¹, [Yike Zhang](#)¹, [Bowen Xiang](#)¹, [Qing Wang](#)²

Affiliations expand

- PMID: 38029545
- DOI: [10.1016/j.archger.2023.105287](https://doi.org/10.1016/j.archger.2023.105287)

Abstract

Background: In the era of rapid aging with a rising prevalence of multimorbidity, complex interactions between physical and psychological conditions have challenged the health care system. However, little is known about the association of the accumulation of chronic conditions and disability in activities of daily living with depressive symptoms, especially in developed countries.

Methods: This population-based cohort study used data from the Health and Retirement Study. A total of 22,335 middle-aged and older adults participated in the 2014 (T1), 2016 (T2), and 2018 (T3) waves of the cohort were included. The accumulation of chronic conditions and disability were defined as the number of chronic diseases and the five activities of daily living. Depressive symptoms were measured by the Center for Epidemiologic Studies Depression Scale. A longitudinal mediation model with a cross-lagged panel model was run. As robust check, the models were applied with a longer follow-up period (from 2012 to 2018). Additionally, results were estimated in China.

Results: Bidirectional associations have been found among the accumulation of chronic conditions, disability, and depressive symptoms, especially between disability and depression. Disability (T2) mediated 11.11 % and 16.87 % of the association between the accumulation of chronic conditions (T1) and depression (T3) for men and women in the United States. The results were consistent in robust analysis.

Conclusions: This study found that men and women routinely experienced disability and depressive symptoms because of the accumulation of chronic conditions. In terms of depressive symptoms, women were more sensitive to the accumulation of chronic conditions through disability.

Keywords: Depressive symptoms; Disability in activities of daily living; Longitudinal mediating effect; The accumulation of chronic conditions.

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Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no competing interests.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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Int J Cardiol

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. 2024 Mar 1:398:131605.

doi: 10.1016/j.ijcard.2023.131605. Epub 2023 Nov 22.

Multimorbidity in atrial fibrillation for clinical implications using the Charlson Comorbidity Index

[Moonki Jung](#)¹, [Pil-Sung Yang](#)², [Daehoon Kim](#)¹, [Jung-Hoon Sung](#)², [Eunsun Jang](#)¹, [Hee Tae Yu](#)¹, [Tae-Hoon Kim](#)¹, [Jae-Sun Uhm](#)¹, [Hui-Nam Pak](#)¹, [Moon-Hyoung Lee](#)¹, [Boyoung Joung](#)²

Affiliations expand

- PMID: 38000669

- DOI: [10.1016/j.ijcard.2023.131605](https://doi.org/10.1016/j.ijcard.2023.131605)

Abstract

Background: Predicting survival in atrial fibrillation (AF) patients with comorbidities is challenging. This study aimed to assess multimorbidity in AF patients using the Charlson Comorbidity Index (CCI) and its clinical implications.

Methods: We analyzed 451,368 participants from the Korea National Health Insurance Service-Health Screening cohort (2002-2013) without prior AF diagnoses. Patients were categorized into new-onset AF and non-AF groups, with a high CCI defined as ≥ 4 points. Antithrombotic treatment and outcomes (all-cause death, stroke, major bleeding, and heart failure [HF] hospitalization) were evaluated over 9 years.

Results: In total, 9.5% of the enrolled patients had high CCI. During follow-up, 12,241 patients developed new-onset AF. Among AF patients, antiplatelet drug use increased significantly in those with high CCI (adjusted odds ratio [OR] 1.05, 95% confidence interval [CI] 1.02-1.08, $P < .001$). However, anticoagulants were significantly less prescribed in patients with high CCI (OR 0.97, 95%CI 0.95-0.99, $P = .012$). Incidence of adverse events (all-cause death, stroke, major bleeding, HF hospitalization) progressively increased in this order: low CCI without AF, high CCI without AF, low CCI with AF, and high CCI with AF (all $P < .001$). Furthermore, high CCI with AF had a significantly higher risk compared to low CCI without AF (all-cause death, adjusted hazard ratio [aHR] 2.52, 95% CI 2.37-2.68, $P < .001$; stroke, aHR 1.43, 95% CI 1.29-1.58, $P < .001$; major bleeding, aHR 1.14, 95% CI 1.04-1.26, $P = .007$; HF hospitalization, aHR 4.75, 95% CI 4.03-5.59, $P < .001$).

Conclusions: High CCI predicted increased antiplatelet use and reduced oral anticoagulant prescription. AF was associated with higher risks of all-cause death, stroke, major bleeding, and HF hospitalization compared to high CCI.

Keywords: Anticoagulation; Atrial fibrillation; Charlson Comorbidity Index; Multimorbidity.

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Conflict of interest statement

Declaration of Competing Interest BJ has served as a speaker for Bayer, BMS/Pfizer, Medtronic, and Daiichi-Sankyo and received research funds from Medtronic and Abbott. No fees were received directly or personally. The remaining authors have no other relationships or activities that could appear to have influenced the submitted work.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS



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J Geriatr Oncol

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. 2024 Mar;15(2):101654.

doi: 10.1016/j.jgo.2023.101654. Epub 2023 Nov 3.

[A care pathway for older patients with multimorbidity including cancer – Design of the GERONTE pathway](#)

[P A L Nelleke Seghers](#)¹, [Siri Rostoft](#)², [Shane O'Hanlon](#)³, [Lien Degol](#)⁴, [Cindy Kenis](#)⁵, [Hans Wildiers](#)⁶, [Pierre Soubeyran](#)⁷, [Marije E Hamaker](#)⁸

Affiliations [expand](#)

- PMID: 37925337
- DOI: [10.1016/j.jgo.2023.101654](https://doi.org/10.1016/j.jgo.2023.101654)

Free article

No abstract available

Keywords: Care coordination; Geriatric oncology; Multimorbidity; Patient- centred care pathway; Quality of life.

Conflict of interest statement

Declaration of Competing Interest Pierre Soubeyran: Board member with TEVA, Sandoz, BMS and Eisai. All other authors: No competing interests to declare.

SUPPLEMENTARY INFO

MeSH termsexpand

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Int J Stroke

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. 2024 Mar;19(3):348-358.

doi: 10.1177/17474930231210397. Epub 2023 Nov 22.

[Association of multimorbidity with mortality after stroke stratified by age, severity, etiology, and prior disability](#)

[Matthew B Downer](#)¹, [Ramon Luengo-Fernandez](#)¹, [Lucy E Binney](#)¹, [Sergei Gutnikov](#)¹, [Louise E Silver](#)¹, [Aubretia McColl](#)¹, [Peter M Rothwell](#)¹

Affiliations expand

- PMID: 37850450
- PMCID: [PMC10903144](#)

- DOI: [10.1177/17474930231210397](https://doi.org/10.1177/17474930231210397)

Free PMC article

Abstract

Background: Multimorbidity is common in patients with stroke and is associated with increased medium- to long-term mortality, but its value for clinical decision-making and case-mix adjustment will depend on other factors, such as age, stroke severity, etiological subtype, prior disability, and vascular risk factors.

Aims: In the absence of previous studies, we related multimorbidity to long-term post-stroke mortality with stratification by these factors.

Methods: In patients ascertained in a population-based stroke incidence study (Oxford Vascular Study; 2002-2017), we related pre-stroke multimorbidity (weighted/unweighted Charlson comorbidity index (CCI)) to all-cause/vascular/non-vascular mortality (1/5/10 years) using regression models adjusted/stratified by age, sex, predicted early outcome (THRIVE score), stroke severity (NIH stroke scale (NIHSS)), etiology (Trial of Org 10172 in Acute Stroke Treatment (TOAST)), premorbid disability (modified Rankin Scale (mRS)), and non-CCI risk factors (hypertension, hyperlipidemia, atrial fibrillation, smoking, deprivation, anxiety/depression).

Results: Among 2454 stroke patients (M/SD age: 74.1/13.9 years; 48.9% male; M/SD NIHSS: 5.7/7.0), 1375/56.0% had ≥ 1 CCI comorbidity and 685/27.9% had ≥ 2 . After age/sex adjustment, multimorbidity (unweighted CCI ≥ 2 vs 0) predicted (all p s < 0.001) mortality at 1 year (aHR = 1.57, 95% CI = 1.38-1.78), 5 years (aHR = 1.73, 95% CI = 1.53-1.96), and 10 years (aHR = 1.79, 95% CI = 1.58-2.03). Although multimorbidity was independently associated with premorbid disability (mRS > 2 : aOR = 2.76, 2.13-3.60) and non-CCI risk factors (hypertension: 1.56, 1.25-1.95; hyperlipidemia: 2.58, 2.03-3.28; atrial fibrillation: 2.31; 1.78-2.98; smoking: 1.37, 1.01-1.86), it predicted death after adjustment for all measured confounders (10-year-aHR = 1.56, 1.37-1.78, $p < 0.001$), driven mainly by non-vascular death (aHR = 1.89, 1.55-2.29). Predictive value for 10-year all-cause death was greatest in patients with lower expected early mortality: lower THRIVE score ($p_{\text{int}} < 0.001$), age < 75 years (aHR = 2.27, 1.71-3.00), NIHSS < 5 (1.84, 1.53-2.21), and lacunar stroke (3.56, 2.14-5.91). Results were similar using the weighted CCI.

Conclusion: Pre-stroke multimorbidity is highly prevalent and is an independent predictor of death after stroke, supporting its inclusion in case-mix adjustment models and in informing decision-making by patients, families, and carers. Prediction in younger patients and after minor stroke, particularly for non-vascular death, suggests potential clinical utility in targeting interventions that require survival for 5-10 years to achieve a favorable risk/benefit ratio.

Data access statement: Data requests will be considered by the Oxford Vascular Study (OXVASC) Study Director (P.M.R.-peter.rothwell@ndcn.ox.ac.uk).

Keywords: Chronic disease; epidemiology; long-term outcomes; multimorbidity; post-stroke mortality; prognosis.

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.

DisclosuresP.M.R. has received honoraria for Data Monitoring Boards, Advisory Boards, and lectures from Bayer, Sanofi, Bristol Myers Squibb (BMS), and Abbott. All other authors have no disclosures.

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

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Sage Journals
Open access full text



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[Observational Study](#)

Med Klin Intensivmed Notfmed

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. 2024 Mar;119(2):123-128.

doi: 10.1007/s00063-023-01037-4. Epub 2023 Jun 28.

Sepsis and underlying comorbidities in intensive care unit patients : Analysis of the cause of death by different clinicians-a pilot study

[Daniel O Thomas-Rüddel](#)^{1,2}, [Holger Fröhlich](#)^{3,4}, [Daniel Schwarzkopf](#)^{5,6}, [Frank Bloos](#)^{5,6}, [Reimer Riessen](#)³

Affiliations expand

- PMID: 37380812
- PMCID: [PMC10901974](#)
- DOI: [10.1007/s00063-023-01037-4](#)

Free PMC article

Abstract

in [English](#), [German](#)

Background: There is an ongoing debate as to whether death with sepsis is primarily caused by sepsis or, more often, by the underlying disease. There are no data on the influence of a researcher's background on such an assessment. Therefore, the aim of this analysis was to assess the cause of death in sepsis and the influence of an investigator's professional background on such an assessment.

Materials and methods: We performed a retrospective observational cohort study of sepsis patients treated in the medical intensive care unit (ICU) of a tertiary care center. For deceased patients, comorbidities and severity of illness were documented. The cause of death (sepsis or comorbidities or both combined) was independently assessed by four assessors with different professional backgrounds (medical student, senior physician in the medical ICU, anesthesiological intensivist, and senior physician specialized in the predominant comorbidity).

Results: In all, 78 of 235 patients died in hospital. Agreement between assessors about cause of death was low (κ 0.37, 95% confidence interval 0.29-0.44). Depending on the

assessor, sepsis was the sole cause of death in 6-12% of cases, sepsis and comorbidities in 54-76%, and comorbidities alone in 18-40%.

Conclusions: In a relevant proportion of patients with sepsis treated in the medical ICU, comorbidities contribute significantly to mortality, and death from sepsis without relevant comorbidities is a rare event. Designation of the cause of death in sepsis patients is highly subjective and may be influenced by the professional background of the assessor.

Keywords: Cause of death; Comorbidity; Multimorbidity; Sepsis; Septic shock.

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Conflict of interest statement

D.O. Thomas-Rüddel, H. Fröhlich, D. Schwarzkopf, F. Bloos and R. Riessen declare that they have no competing interests.

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

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[Review](#)

Health Psychol Rev

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. 2024 Mar;18(1):165-188.

Mapping interventional components and behavior change techniques used to promote self-management in people with multimorbidity: a scoping review

[Madalina Jäger](#)^{1,2,3}, [Graziella Zangger](#)^{1,2}, [Alessio Bricca](#)^{1,2}, [Mette Dideriksen](#)^{1,2}, [Susan M Smith](#)⁴, [Julie Midtgaard](#)^{5,6}, [Rod S Taylor](#)⁷, [Søren T Skou](#)^{1,2}

Affiliations expand

- PMID: 36811829
- PMCID: [PMC7615688](#)
- DOI: [10.1080/17437199.2023.2182813](#)

Free PMC article

Abstract

Ageing populations and improved survival, have contributed to a rise in the number of people living with multimorbidity, raising issues related to polypharmacy, treatment burden, competing priorities and poor coordination of care. Self-management programs are increasingly included as an essential component of interventions to improve outcomes in this population. However, an overview of how interventions supporting self-management in patients with multimorbidity is missing. This scoping review focused on mapping the literature on patient-centered interventions for people living with multimorbidity. We searched several databases, clinical registries, and grey literature for RCTs published between 1990-2019 describing interventions that supported self-management in people with multimorbidity. We included 72 studies that were found to be very heterogeneous when it comes to the population, delivery modes and modalities, intervention elements and facilitators. The results pointed to an extensive use of cognitive behavioral therapy as a basis for interventions, as well as behavior change theories and disease management frameworks. The most coded behavior change techniques stemmed from the categories Social Support, Feedback and monitoring and Goals and Planning. To allow for implementation of effective interventions in clinical practice, improved reporting of intervention mechanisms in RCTs is warranted.

Keywords: Multimorbidity; behavior change techniques; scoping review; self-management.

Conflict of interest statement

Disclosure statement

No potential conflict of interest was reported by the author(s).

- [Cited by 1 article](#)
- [121 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

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

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9

Aging Clin Exp Res

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. 2024 Feb 29;36(1):48.

doi: 10.1007/s40520-024-02706-w.

[Comparison of three frailty measures for predicting hospitalization and mortality in the Canadian Longitudinal Study on Aging](#)

[Romain Pasquet](#) ^{#1}, [Mengting Xu](#) ^{#1,2}, [Marie-Pierre Sylvestre](#) ^{1,2}, [Mark R Keezer](#) ^{3,4,5}

Affiliations expand

- PMID: 38418612
- PMCID: [PMC10902012](#)
- DOI: [10.1007/s40520-024-02706-w](#)

Free PMC article

Abstract

Background: Few studies have compared different measures of frailty for predicting adverse outcomes. It remains unknown which frailty measurement approach best predicts healthcare utilization such as hospitalization and mortality.

Aims: This study aims to compare three approaches to measuring frailty—grip strength, frailty phenotype, and frailty index—in predicting hospitalization and mortality among middle-aged and older Canadians.

Methods: We analyzed baseline and the first 3-year follow-up data for 30,097 participants aged 45 to 85 years from the comprehensive cohort of the Canadian Longitudinal Study on Aging (CLSA). Using separate logistic regression models adjusted for multimorbidity, age and biological sex, we predicted participants' risks for overnight hospitalization in the past 12 months and mortality, at the first 3-year follow-up, using each of the three frailty measurements at baseline. Model discrimination was assessed using Harrell's c-statistic and calibration assessed using calibration plots.

Results: The predictive performance of all three measures of frailty were roughly similar when predicting overnight hospitalization and mortality risk among CLSA participants. Model discrimination measured using c-statistics ranged from 0.67 to 0.69 for hospitalization and 0.79 to 0.80 for mortality. All measures of frailty yielded strong model calibration.

Discussion and conclusion: All three measures of frailty had similar predictive performance. Discrimination was modest for predicting hospitalization and superior in predicting mortality. This likely reflects the objective nature of mortality as an outcome and the challenges in reducing the complex concept of healthcare utilization to a single variable such as any overnight hospitalization.

Keywords: CLSA; Frailty index; Frailty phenotype; Grip strength; Predictive performance.

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Conflict of interest statement

MX, RP, and MPS do not report any relevant competing interests. MRK reports unrestricted educational grants from UCB, Eisai and Jazz Pharmaceuticals, and research grants for investigator-initiated studies from UCB and Eisai.

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

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

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Arch Gerontol Geriatr

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. 2024 Feb 28:122:105391.

doi: 10.1016/j.archger.2024.105391. Online ahead of print.

Grip strength buffers the harmful association between multimorbidity and depression among middle-aged and older adults

[Clément Blanchet](#)¹, [Miguel Peralta](#)², [Marcelo de Maio Nascimento](#)³, [Élvio R Gouveia](#)⁴, [Gerson Ferrari](#)⁵, [Tiago D Ribeiro](#)⁶, [Adilson Marques](#)⁷

Affiliations expand

- PMID: 38428268
- DOI: [10.1016/j.archger.2024.105391](https://doi.org/10.1016/j.archger.2024.105391)

Abstract

Background: Grip strength (GS) is associated to both multimorbidity and depression, however its possible moderating effect is unknown. This study aimed to investigate GS moderating effect on the association between multimorbidity and depression.

Methods: Data from SHARE wave 8 was used. Participant were 41457 middle-aged and older adults (17954 men) from 18 European countries. A regression analysis was conducted for the moderating effect of sex- and age-specific GS quartiles (W) on the association between number of chronic diseases (X_1) or multimorbidity (X_2) and depression symptoms (Y).

Results: More chronic diseases were associated with greater depressive symptomatology (men: $B = 0.39$, 95 % CI: 0.35, 0.42; women: $B = 0.42$, 95 % CI: 0.39, 0.45). On the other hand, being in a higher GS quartile was associated with fewer depression symptoms, and this association was stronger the higher the quartile was. Having a higher GS represented a decrease in depression symptoms associated with multimorbidity for men (quartile 1: $B = 0.85$, 95 % CI = 0.74, 0.95 vs. quartile 4: $B = 0.49$, 95 % CI = 0.38, 0.61) and women (quartile 1: $B = 1.08$, 95 %CI = 0.97, 1.19 vs. quartile 4: $B = 0.59$, 95 %CI: 0.47, 0.70).

Conclusions: Strategies aiming to reduce the impact of multimorbidity on mental health should promote muscle-strengthening physical activity among middle-aged and older adults.

Keywords: European; Fitness; Physical activity; Public health; SHARE project.

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Conflict of interest statement

Declaration of competing interest None to declare.

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J Multimorb Comorb



. 2024 Feb 27:14:26335565241236410.

doi: 10.1177/26335565241236410. eCollection 2024 Jan-Dec.

Variation in multimorbidity by sociodemographics and social drivers of health among patients seen at community-based health centers

[Wyatt P Bensken](#)^{1,2}, [Suparna M Navale](#)¹, [Brenda M McGrath](#)¹, [Nicole Cook](#)¹, [Yui Nishiike](#)³, [Gretchen Mertes](#)¹, [Rose Goueth](#)¹, [Matthew Jones](#)¹, [Anna Templeton](#)¹, [Stephen J Zyzanski](#)^{4,5}, [Siran M Koroukian](#)², [Kurt C Stange](#)^{2,4,5}

Affiliations expand

- PMID: 38419819
- PMCID: [PMC10901061](#)
- DOI: [10.1177/26335565241236410](#)

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Abstract

Purpose: Understanding variation in multimorbidity across sociodemographics and social drivers of health is critical to reducing health inequities.

Methods: From the multi-state OCHIN network of community-based health centers (CBHCs), we identified a cross-sectional cohort of adult (> 25 years old) patients who had a visit between 2019-2021. We used generalized linear models to examine the relationship between the Multimorbidity Weighted Index (MWI) and sociodemographics and social drivers of health (Area Deprivation Index [ADI] and social risks [e.g., food insecurity]). Each model included an interaction term between the primary predictor and age to examine if certain groups had a higher MWI at younger ages.

Results: Among 642,730 patients, 28.2% were Hispanic/Latino, 42.8% were male, and the median age was 48. The median MWI was 2.05 (IQR: 0.34, 4.87) and was higher for adults over the age of 40 and American Indians and Alaska Natives. The regression model revealed a higher MWI at younger ages for patients living in areas of higher deprivation. Additionally, patients with social risks had a higher MWI (3.16; IQR: 1.33, 6.65) than those without (2.13; IQR: 0.34, 4.89) and the interaction between age and social risk suggested a higher MWI at younger ages.

Conclusions: Greater multimorbidity at younger ages and among those with social risks and living in areas of deprivation shows possible mechanisms for the premature aging and disability often seen in community-based health centers and highlights the need for comprehensive approaches to improving the health of vulnerable populations.

Keywords: disparities; equity; multimorbidity; social drivers of health.

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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.

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

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. 2024 Feb 26;117(2):125-132.

doi: 10.1093/qjmed/hcad236.

Elevated risk of multimorbidity post-COVID-19 infection: protective effect of vaccination

[F T T Lai](#)^{1,2,3}, [W Liu](#)¹, [Y Hu](#)¹, [C Wei](#)¹, [R Y K Chu](#)¹, [D H Lum](#)¹, [J C N Leung](#)¹, [F W T Cheng](#)¹, [C S L Chui](#)^{3,4,5}, [X Li](#)^{1,3,6}, [E Y F Wan](#)^{1,2,3}, [C K H Wong](#)^{1,2,3}, [C L Cheung](#)^{1,3}, [E W Y Chan](#)^{1,3}, [I F N Hung](#)⁶, [I C K Wong](#)^{1,3,7}

Affiliations expand

- PMID: 37824396
- DOI: [10.1093/qjmed/hcad236](https://doi.org/10.1093/qjmed/hcad236)

Abstract

Background: It is unclear how the coronavirus disease 2019 (Covid-19) pandemic has affected multimorbidity incidence among those with one pre-existing chronic condition, as well as how vaccination could modify this association.

Aim: To examine the association of Covid-19 infection with multimorbidity incidence among people with one pre-existing chronic condition, including those with prior vaccination.

Design: Nested case-control study.

Methods: We conducted a territory-wide nested case-control study with incidence density sampling using Hong Kong electronic health records from public healthcare facilities and mandatory Covid-19 reports. People with one listed chronic condition (based on a list of 30) who developed multimorbidity during 1 January 2020-15 November 2022 were selected as case participants and randomly matched with up to 10 people of the same age, sex and with the same first chronic condition without having developed multimorbidity at that point. Conditional logistic regression was used to estimate adjusted odds ratios (aORs) of multimorbidity.

Results: In total, 127 744 case participants were matched with 1 230 636 control participants. Adjusted analysis showed that there were 28%-increased odds of multimorbidity following Covid-19 [confidence interval (CI) 22% to 36%] but only 3% (non-significant) with prior full vaccination with BNT162b2 or CoronaVac (95% CI -2% to 7%). Similar associations were observed in men, women, older people aged 65 or more, and people aged 64 or younger.

Conclusions: We found a significantly elevated risk of multimorbidity following a Covid-19 episode among people with one pre-existing chronic condition. Full vaccination significantly reduced this risk increase.

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SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and fundingexpand

FULL TEXT LINKS



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

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Med Int (Lond)

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. 2024 Feb 8;4(2):12.

doi: 10.3892/mi.2024.136. eCollection 2024 Mar-Apr.

[Impact of prenatal life on the risk of developing epilepsy](#)

[Nina Otinashvili](#)¹, [Saba Ahmadi](#)¹, [Luka Jordanishvili](#)¹, [Anashwara Balagopal](#)¹, [Tsothe Gvasalia](#)¹

Affiliations expand

- PMID: 38410757
- PMCID: [PMC10895459](#)
- DOI: [10.3892/mi.2024.136](#)

Free PMC article

Abstract

Epilepsy is an enduring predisposition of the brain to generate epileptic seizures and has a worldwide incidence of 21-24 per 100,000 cases among children. Epilepsy is a multifactorial disease; however, certain risk factors are predicted to increase its incidence. Abnormal brain development during prenatal life, particularly during the last trimester, is considered to play a crucial role in the development of certain neurological disorders. The present study evaluated a total of 453 children between the ages of 1 to 18 years, with or without epilepsy. The association between gestational age, birth weight, maternal age and sex, and the risk of developing epilepsy was examined in the children. It was found that children born preterm had a 2.3-fold higher risk of having epilepsy [odds ratio (OR), 2.3; 95% confidence interval (CI), 1.4-3.7], and those whose birth weight was <2,500 g had a 2-fold greater risk of developing epilepsy (OR, 2; 95% CI, 1.1-3.6). The male sex appeared to be associated with a lower risk of developing epilepsy and there was a statistically significant association between the female sex and the risk of developing epilepsy only in preterm children (OR, 3.2; 95% CI, 1.2-8.8). Maternal age was not found to be associated with the risk of developing epilepsy. On the whole, the present study demonstrates that a short gestational age, a low birth weight and the female sex are associated with an increased risk of developing epilepsy.

Keywords: birthweight; epilepsy; gestational age; premature birth; prematurity.

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Conflict of interest statement

The authors declare that they have no competing interests.

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

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Grants and fundingexpand

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Pediatrics



. 2024 Mar 1;153(3):e2023062178.

doi: 10.1542/peds.2023-062178.

[Advice to Clinicians From Expectant Parents at Extreme Prematurity: A Multimethod Study](#)

[Anne Sullivan](#)^{1,2}, [Bonnie Arzuaga](#)^{2,3}, [Donna Luff](#)^{4,2}, [Erin Ward](#)¹, [David N Williams](#)⁵, [Christy Cummings](#)^{1,2}

Affiliations expand

- PMID: 38321935
- PMCID: [PMC10904886](#)
- DOI: [10.1542/peds.2023-062178](#)

Abstract

Background and objectives: Despite recommendations for patient-centered counseling on extreme prematurity, clinicians often miss opportunities to communicate in a way that facilitates parental knowledge, decision-making, and emotional support. In this study, we aimed to determine empirical, parent-derived recommendations and advice for clinicians counseling on extreme prematurity.

Methods: Pregnant women (and their partners) admitted at 22 0/7 to 25 6/7 weeks' estimated gestation participated in postantenatal counseling semi-structured interviews or questionnaires to explore parental preferences in the counseling process, including advice to clinicians. Thematic analysis was performed.

Results: A total of 39 interviews and 47 questionnaires, representing 62 total prenatal consultations, were completed. Thematic analysis of participants' advice to clinicians from both interview and questionnaire data resulted in 14 parent-derived recommendations to clinicians who counsel expectant parents at extreme prematurity. Parental recommendations related to compassionately engaging, supporting, and communicating with families, as well as aligning teams and following up.

Conclusions: We present an empirical parent-derived, family-centered, and practical approach for clinicians counseling on extreme prematurity. Future studies should include a more diverse patient population and assess the impact of these recommendations on the counseling process and outcomes.

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Conflict of interest statement

CONFLICT OF INTEREST DISCLOSURES: The authors have indicated they have no potential conflicts of interest relevant to this article to disclose.

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Pediatrics



. 2024 Mar 1;153(3):e2023062574.

doi: 10.1542/peds.2023-062574.

Respiratory Syncytial Virus–Associated Hospitalizations Among Children <5 Years Old: 2016 to 2020

[Aaron T Curns](#)¹, [Brian Rha](#)¹, [Joana Y Lively](#)¹, [Leila C Sahni](#)², [Janet A Englund](#)³, [Geoffrey A Weinberg](#)⁴, [Natasha B Halasa](#)⁵, [Mary A Staat](#)⁶, [Rangaraj Selvarangan](#)⁷, [Marian Michaels](#)⁸, [Heidi Moline](#)¹, [Yingtao Zhou](#)^{1,9}, [Ariana Perez](#)^{1,10}, [Chelsea Rohlfs](#)⁶, [Robert Hickey](#)⁸, [Kirsten Lacombe](#)³, [Rendie McHenry](#)⁵, [Brett Whitaker](#)¹, [Jennifer Schuster](#)⁷, [Claudia Guevara Pulido](#)⁵, [Bonnie Strelitz](#)³, [Christina Quigley](#)⁶, [Gina Weddle Dnp](#)⁷, [Vasanthi Avadhanula](#)², [Christopher J Harrison](#)¹¹, [Laura S Stewart](#)⁵, [Elizabeth Schlaudecker](#)⁶, [Peter G Szilagyi](#)¹², [Eileen J Klein](#)³, [Julie Boom](#)², [John V Williams](#)⁸, [Gayle Langley](#)¹, [Susan I Gerber](#)¹, [Aron J Hall](#)¹, [Meredith L McMorrow](#)¹

Affiliations expand

- PMID: 38298053
- DOI: [10.1542/peds.2023-062574](https://doi.org/10.1542/peds.2023-062574)

Abstract

Background: Respiratory syncytial virus (RSV) is the leading cause of hospitalization in US infants. Accurate estimates of severe RSV disease inform policy decisions for RSV prevention.

Methods: We conducted prospective surveillance for children <5 years old with acute respiratory illness from 2016 to 2020 at 7 pediatric hospitals. We interviewed parents, reviewed medical records, and tested midturbinate nasal ± throat swabs by reverse transcription polymerase chain reaction for RSV and other respiratory viruses. We describe characteristics of children hospitalized with RSV, risk factors for ICU admission, and estimate RSV-associated hospitalization rates.

Results: Among 13 524 acute respiratory illness inpatients <5 years old, 4243 (31.4%) were RSV-positive; 2751 (64.8%) of RSV-positive children had no underlying condition or history of prematurity. The average annual RSV-associated hospitalization rate was 4.0 (95% confidence interval [CI]: 3.8-4.1) per 1000 children <5 years, was highest among children 0

to 2 months old (23.8 [95% CI: 22.5-25.2] per 1000) and decreased with increasing age. Higher RSV-associated hospitalization rates were found in premature versus term children (rate ratio = 1.95 [95% CI: 1.76-2.11]). Risk factors for ICU admission among RSV-positive inpatients included: age 0 to 2 and 3 to 5 months (adjusted odds ratio [aOR] = 1.97 [95% CI: 1.54-2.52] and aOR = 1.56 [95% CI: 1.18-2.06], respectively, compared with 24-59 months), prematurity (aOR = 1.32 [95% CI: 1.08-1.60]) and comorbid conditions (aOR = 1.35 [95% CI: 1.10-1.66]).

Conclusions: Younger infants and premature children experienced the highest rates of RSV-associated hospitalization and had increased risk of ICU admission. RSV prevention products are needed to reduce RSV-associated morbidity in young infants.

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Review

Crit Care Nurs Clin North Am

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. 2024 Mar;36(1):69-98.

doi: 10.1016/j.cnc.2023.08.004. Epub 2023 Sep 15.

[Monitoring SpO₂: The Basics of Retinopathy of Prematurity \(Back to Basics\) and Targeting Oxygen Saturation](#)

[Augusto Sola](#)¹, [Leslie Altimier](#)², [María Teresa Montes Bueno](#)³, [Cristian Emanuel Muñoz](#)⁴

Affiliations expand

- PMID: 38296377
- DOI: [10.1016/j.cnc.2023.08.004](https://doi.org/10.1016/j.cnc.2023.08.004)

Abstract

Oxygen (O₂) is a drug frequently used in newborn care. Adverse effects of hypoxia are well known but the damaging effects of excess oxygen administration and oxidative stress have only been studied in the last 2 decades. Many negative effects have been described, including retinopathy of prematurity . Noninvasive pulse oximetry (SpO₂) is useful to detect hypoxemia but requires careful evaluation and understanding of the frequently changing relationship between O₂ and hemoglobin to prevent hyperoxemia. Intention to treat SpO₂ ranges should be individualized for every newborn receiving supplemental O₂, according to gestational age, post-natal age, and clinical condition.

Keywords: Hyperoxemia; Hypoxemia; Intention to treat; Oxidative stress; Preterm newborn; ROP; SpO₂.

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Conflict of interest statement

Disclosure Dr A. Sola is a part-time employee of Masimo (Irvine, Ca), Medical Affairs, Neonatology Education and Research. No funding sources for any of the authors.

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Publication types, MeSH terms, Substances expand

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Crit Care Nurs Clin North Am

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. 2024 Mar;36(1):23-33.

doi: 10.1016/j.cnc.2023.08.007. Epub 2023 Sep 19.

Care from Birth to Discharge of Infants Born at 22 to 23 Weeks' Gestation

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Affiliations expand

- PMID: 38296373
- DOI: [10.1016/j.cnc.2023.08.007](https://doi.org/10.1016/j.cnc.2023.08.007)

Abstract

The clinical care of infants born at 22 weeks' gestation must be well-designed and standardized if optimal results are to be expected. Although several approaches to care in this vulnerable population are possible, protocols should be neither random nor inconsistent. We describe the approach taken at the University of Iowa Stead Family Children's Hospital neonatal intensive care unit with respect to preterm infants born at 22 weeks' gestation. We have chosen to present our standardize care plan with respect to prenatal, neurologic, nutritional, gastrointestinal, and skin management. Respiratory and cardiopulmonary care will be briefly reviewed, as these strategies have been published previously.

Keywords: Extreme prematurity; Outcomes; Precision.

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Review

Acta Paediatr

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. 2024 Mar;113(3):394-402.

doi: 10.1111/apa.17093. Epub 2024 Jan 12.

[Diuretics use in the management of bronchopulmonary dysplasia in preterm infants: A systematic review](#)

[Eoin Ó Briain](#)¹, [Aisling O Byrne](#)¹, [Jack Dowling](#)¹, [Julia Kiernan](#)¹, [James Carlo Rio Lynch](#)¹, [Lulwa Alomairi](#)¹, [Lauren Coyle](#)¹, [Lorcan Mulkerrin](#)¹, [David Mockler](#)², [Geraldine Fitzgerald](#)³, [Liqia Ur Rehman](#)⁴, [Gergana Semova](#)¹, [Eman Isweisi](#)^{1,5}, [Anne O'Sullivan](#)^{1,4}, [Pamela O'Connor](#)⁴, [Kevin Mulligan](#)⁴, [Aoife Branagan](#)^{1,4,5}, [Edna Roche](#)^{1,5,6}, [Judith Meehan](#)^{1,5}, [Eleanor Molloy](#)^{1,4,5,7,8}

Affiliations expand

- PMID: 38214373
- DOI: [10.1111/apa.17093](https://doi.org/10.1111/apa.17093)

Abstract

Aim: Bronchopulmonary dysplasia (BPD), a respiratory complication associated with neonatal prematurity, presents opportunities for pharmacological intervention due to its contributing risk factors. Despite diuretics' controversial usage in BPD treatment and varying institutional practices, this review aims to consolidate evidence from clinical trials regarding diuretic use in BPD.

Methods: We conducted a systematic review following PRISMA guidelines, searching EMBASE, Medline, Web of Science and CINAHL databases (PROSPERO 2022: CRD42022328292). Covidence facilitated screening and data extraction, followed by analysis and formatting in Microsoft Excel.

Results: Among 430 screened records, 13 were included for analysis. Three studies assessed spironolactone and chlorothiazide combinations, two studied spironolactone and hydrochlorothiazide, while eight examined furosemide. All studies evaluated drug effects on dynamic pulmonary compliance and pulmonary resistance, serving as comparative measures in our review.

Conclusion: Diuretics' effectiveness in treating bronchopulmonary dysplasia remains uncertain. The limited number of identified randomised controlled trials (RCTs) hampers high-level evidence-based conclusions when applying the Population, Intervention, Comparison, Outcome (PICO) approach. Conducting large prospective studies of good quality could provide more definitive insights, but the rarity of outcomes and eligible patients poses challenges. Further research, primarily focusing on RCTs assessing diuretics' safety and efficacy in this population, is warranted.

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Maternal and neonatal outcomes according to the timing of diagnosis of hyperglycaemia in pregnancy: a nationwide cross-sectional study of 695,912 deliveries in France in 2018

[Nolwenn Regnault](#)¹, [Elodie Lebreton](#)¹, [Luveon Tang](#)¹, [Sandrine Fosse-Edorh](#)¹, [Yaya Barry](#)¹, [Valérie Olié](#)¹, [Cécile Billionnet](#)², [Alain Weill](#)³, [Anne Vambergue](#)⁴, [Emmanuel Cosson](#)^{5,6}

Affiliations expand

- PMID: 38182910
- PMCID: [PMC10844424](#)
- DOI: [10.1007/s00125-023-06066-4](#)

Free PMC article

Abstract

Aims/hypothesis: We aimed to assess maternal-fetal outcomes according to various subtypes of hyperglycaemia in pregnancy.

Methods: We used data from the French National Health Data System (Système National des Données de Santé), which links individual data from the hospital discharge database and the French National Health Insurance information system. We included all deliveries after 22 gestational weeks (GW) in women without pre-existing diabetes recorded in 2018. Women with hyperglycaemia were classified as having overt diabetes in pregnancy or gestational diabetes mellitus (GDM), then categorised into three subgroups according to

their gestational age at the time of GDM diagnosis: before 22 GW (GDM_{<22}); between 22 and 30 GW (GDM₂₂₋₃₀); and after 30 GW (GDM_{>30}). Adjusted prevalence ratios (95% CI) for the outcomes were estimated after adjusting for maternal age, gestational age and socioeconomic status. Due to the multiple tests, we considered an association to be statistically significant according to the Holm-Bonferroni procedure. To take into account the potential immortal time bias, we performed analyses on deliveries at ≥ 31 GW and deliveries at ≥ 37 GW.

Results: The study population of 695,912 women who gave birth in 2018 included 84,705 women (12.2%) with hyperglycaemia in pregnancy: overt diabetes in pregnancy, 0.4%; GDM_{<22}, 36.8%; GDM₂₂₋₃₀, 52.4%; and GDM_{>30}, 10.4%. The following outcomes were statistically significant after Holm-Bonferroni adjustment for deliveries at ≥ 31 GW using GDM₂₂₋₃₀ as the reference. Caesarean sections (1.54 [1.39, 1.72]), large-for-gestational-age (LGA) infants (2.00 [1.72, 2.32]), Erb's palsy or clavicle fracture (6.38 [2.42, 16.8]), preterm birth (1.84 [1.41, 2.40]) and neonatal hypoglycaemia (1.98 [1.39, 2.83]) were more frequent in women with overt diabetes. Similarly, LGA infants (1.10 [1.06, 1.14]) and Erb's palsy or clavicle fracture (1.55 [1.22, 1.99]) were more frequent in GDM_{<22}. LGA infants (1.44 [1.37, 1.52]) were more frequent in GDM_{>30}. Finally, women without hyperglycaemia in pregnancy were less likely to have preeclampsia or eclampsia (0.74 [0.69, 0.79]), Caesarean section (0.80 [0.79, 0.82]), pregnancy and postpartum haemorrhage (0.93 [0.89, 0.96]), LGA neonate (0.67 [0.65, 0.69]), premature neonate (0.80 [0.77, 0.83]) and neonate with neonatal hypoglycaemia (0.73 [0.66, 0.82]). Overall, the results were similar for deliveries at ≥ 37 GW. Although the estimation of the adjusted prevalence ratio of perinatal death was five times higher (5.06 [1.87, 13.7]) for women with overt diabetes, this result was non-significant after Holm-Bonferroni adjustment.

Conclusions/interpretation: Compared with GDM₂₂₋₃₀, overt diabetes, GDM_{<22} and, to a lesser extent, GDM_{>30} were associated with poorer maternal-fetal outcomes.

Keywords: Caesarean section; Diabetes; Gestational diabetes mellitus; Macrosomia; Overt diabetes in pregnancy; Perinatal death; Preeclampsia; Pregnancy; Prematurity.

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- [4 figures](#)

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Pediatr Pulmonol



. 2024 Mar;59(3):679-687.

doi: 10.1002/ppul.26810. Epub 2023 Dec 28.

[Infants hospitalized with lower respiratory tract infections during the first two years of life have increased risk of pediatric obstructive sleep apnea](#)

[Mirtha G Gayoso-Liviac](#)¹, [Gustavo Nino](#)¹, [Agnes S Montgomery](#)¹, [Xiumei Hong](#)², [Xiaobin Wang](#)^{2,3}, [Maria J Gutierrez](#)⁴

Affiliations expand

- PMID: 38153215
- PMCID: PMC10901459 (available on 2025-03-01)
- DOI: [10.1002/ppul.26810](https://doi.org/10.1002/ppul.26810)

Abstract

Rationale: Lower respiratory tract infections (LRTI) during the first 2 years of life increase the risk of pediatric obstructive sleep apnea (OSA), but whether this risk varies by LRTI severity is unknown.

Methods: We analyzed data from 2962 children, aged 0-5 years, with early-life LRTI requiring hospitalization (severe LRTI, n = 235), treated as outpatients (mild LRTI, n = 394) and without LRTI (reference group, n = 2333) enrolled in the Boston Birth Cohort. Kaplan-Meier survival estimates and Cox proportional hazards models adjusted by pertinent covariables were used to evaluate the risk of pediatric OSA.

Results: Compared to children without LRTI, those with mild LRTI were at a higher risk of having OSA (hazard ratio [HR] 1.44, 95% confidence interval [CI]: 1.01-2.05), and those with severe LRTI were at the highest risk (HR 2.06, 95% CI: 1.41-3.02), independently of relevant covariables (including maternal age, race, gestational age, and type of delivery). Additional risk factors linked to a higher risk of OSA included prematurity (HR 1.34, 95% CI 1.01-1.77) and maternal obesity (HR 1.82, 95% CI 1.32-2.52). The time elapsed between LRTI and OSA diagnosis was similar in mild and severe LRTI cases, with medians of 23 and 25.5 months, respectively (p = .803).

Conclusion: Infants with severe early-life LRTI have a higher risk of developing OSA, and surveillance strategies to identify OSA need to be particularly focused on this group. OSA monitoring should continue throughout the preschool years as it may develop months or years after the initial LRTI hospitalization.

Keywords: hospitalized infants; lower tract respiratory infections; pediatric obstructive sleep apnea.

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Conflict of interest statement

Conflict of interest: None of the authors have conflicts of interest to disclose.

- [39 references](#)

SUPPLEMENTARY INFO

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Pediatr Pulmonol

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. 2024 Mar;59(3):540-551.

doi: 10.1002/ppul.26795. Epub 2023 Dec 5.

Bronchopulmonary dysplasia in adults: Exploring pathogenesis and phenotype

[Phillip S Wozniak](#)^{1,2,3}, [Lara Makhoul](#)³, [Mena M Botros](#)⁴

Affiliations expand

- PMID: 38050796
- DOI: [10.1002/ppul.26795](https://doi.org/10.1002/ppul.26795)

Abstract

This review highlights both the longstanding impact of bronchopulmonary dysplasia (BPD) on the health of adult survivors of prematurity and the pressing need for prospective, longitudinal studies of this population. Conservatively, there are an estimated 1,000,000 survivors of BPD in the United States alone. Unfortunately, most of the available literature regarding outcomes of lung disease due to prematurity naturally focuses on pediatric patients in early or middle childhood, and the relative amount of literature on adult survivors is scant. As the number of adult survivors of BPD continues to increase, it is essential that both adult and pediatric pulmonologists have a comprehensive understanding of the pathophysiology and underlying disease process, including the molecular signaling pathways and pro-inflammatory modulators that contribute to the pathogenesis of BPD. We summarize the most common presenting symptoms for adults with BPD and identify the critical challenges adult pulmonologists face in managing the care of survivors of prematurity. Specifically, these challenges include the wide variability of the clinical presentation of adult patients, comorbid cardiopulmonary complications, and the paucity of longitudinal data available on these patients. Adult survivors of BPD have even required lung transplantation, indicating the high burden of morbidity that can result

from premature birth and subsequent lung injury. In addition, we analyze the disparate symptoms and management approach to adults with "old" BPD versus "new" BPD. The aim of this review is to assist pulmonologists in understanding the underlying pathophysiology of BPD and to improve clinical recognition of this increasingly common pulmonary disease.

Keywords: adult survivors of prematurity; bronchopulmonary dysplasia.

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- [117 references](#)

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Review

Glia

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. 2024 Mar;72(3):475-503.

doi: 10.1002/glia.24474. Epub 2023 Nov 1.

[Key roles of glial cells in the encephalopathy of prematurity](#)

[Juliette Van Steenwinckel¹](#), [Cindy Bokobza¹](#), [Mireille Laforge¹](#), [Isabelle K Shearer²](#), [Veronique E Miron^{3,4,5}](#), [Rejane Rua⁶](#), [Samantha M Matta²](#), [Elisa L Hill-Yardin²](#), [Bobbi Fleiss^{1,2}](#), [Pierre Gressens¹](#)

Affiliations expand

- PMID: 37909340
- DOI: [10.1002/glia.24474](https://doi.org/10.1002/glia.24474)

Abstract

Across the globe, approximately one in 10 babies are born preterm, that is, before 37 weeks of a typical 40 weeks of gestation. Up to 50% of preterm born infants develop brain injury, encephalopathy of prematurity (EoP), that substantially increases their risk for developing lifelong defects in motor skills and domains of learning, memory, emotional regulation, and cognition. We are still severely limited in our abilities to prevent or predict preterm birth. No longer just the "support cells," we now clearly understand that during development glia are key for building a healthy brain. Glial dysfunction is a hallmark of EoP, notably, microgliosis, astrogliosis, and oligodendrocyte injury. Our knowledge of glial biology during development is exponentially expanding but hasn't developed sufficiently for development of effective neuroregenerative therapies. This review summarizes the current state of knowledge for the roles of glia in infants with EoP and its animal models, and a description of known glial-cell interactions in the context of EoP, such as the roles for border-associated macrophages. The field of perinatal medicine is relatively small but has worked passionately to improve our understanding of the etiology of EoP coupled with detailed mechanistic studies of pre-clinical and human cohorts. A primary finding from this review is that expanding our collaborations with computational biologists, working together to understand the complexity of glial subtypes, glial maturation, and the impacts of EoP in the short and long term will be key to the design of therapies that improve outcomes.

Keywords: astrocytes; cytokine and chemokine receptors; development; growth factor; mechanisms of glia cell injury; microglial cells; oligodendrocytes.

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- [337 references](#)

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Clin Pediatr (Phila)



. 2024 Mar;63(3):365-374.

doi: 10.1177/00099228231177286. Epub 2023 Jun 16.

[Birth History and Cardiovascular Disease Risk Among Youth With Significant Obesity](#)

[Sara K Hurley](#)¹, [Diane Vizthum](#)¹, [Kirstie Ducharme-Smith](#)², [Beena D Kamath-Rayne](#)³, [Tammy M Brady](#)^{1,4}

Affiliations expand

- PMID: 37326064
- DOI: [10.1177/00099228231177286](https://doi.org/10.1177/00099228231177286)

Abstract

Children born prematurely have greater lifetime risk for hypertension. We aimed to determine (1) the association between prematurity and cardiovascular disease (CVD) risk factors among 90 children with obesity and elevated blood pressure and (2) if dietary sodium intake modified these associations. Multivariable regression analysis explored for associations between prematurity (<37 weeks gestation; early gestational age) and low birth weight (<2.5 kg) with hypertension, left ventricular mass index (LVMI), and left ventricular hypertrophy (LVH). Effect modification by dietary sodium intake was also explored. Patients were predominately male (60%), black (78%), adolescents (13.3 years), and with substantial obesity (body mass index: 36.5 kg/m²). Early gestational age/low birth weight was not an independent predictor for hypertension, LVMI, or LVH. There was no

effect modification by sodium load. Our results suggest the increased CVD risk conferred by prematurity is less significant at certain cardiometabolic profiles. Promoting heart-healthy lifestyles to prevent pediatric obesity remains of utmost importance to foster cardiovascular health.

Keywords: cardiometabolic risk; hypertension; left ventricular hypertrophy; low birth weight; prematurity.

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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Am J Perinatol

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. 2024 Mar;41(4):439-444.

doi: 10.1055/s-0041-1740347. Epub 2021 Dec 10.

Respiratory Complications in Infants with Retinopathy of Prematurity (ROP) Requiring Laser Photocoagulation

[Novisi Arthur](#)¹, [Emma Byrne](#)², [Folasade Kehinde](#)^{1,2}, [Vineet Bhandari](#)^{1,2,3}, [Vilmaris Quinones Cardona](#)^{1,2}

Affiliations expand

- PMID: 34891193
- DOI: [10.1055/s-0041-1740347](https://doi.org/10.1055/s-0041-1740347)

Abstract

Objective: The objective of this paper was to describe peri-procedural events and complications of infants requiring laser photocoagulation for retinopathy of prematurity (ROP) in a level IV neonatal intensive care unit.

Study design: A retrospective chart review was performed of neonates requiring ROP exams from January 2017 to August 2020. Baseline maternal and neonatal characteristics, ROP exam findings, and associated treatment were analyzed. Group characteristics were compared based on the need for laser photocoagulation. Subgroup analysis of the laser group including respiratory outcomes, cardiorespiratory index (CRI) scores, and pain scores was also performed.

Results: Neonatal and maternal characteristics in the laser ($n = 27$) and non-laser ($n = 172$) groups were assessed. Of the 81.5% (22/27) that required re-intubation for laser, 36% (8/22) had >1 intubation and 18% (4/22) had >1 extubation attempt. The average duration of intubation following laser was 2.46 ± 7.13 days, with 40% (9/22) needing peri-extubation steroids and 18% (4/22) racemic epinephrine to facilitate extubation. Mean total respiratory support time post-laser was 8.65 ± 15.23 days. Mean neonatal pain, agitation, and sedation scores after laser were zero immediately after the procedure, 0.09 ± 0.33 at 12 hours, 0.11 ± 0.47 at 24 hours, and 0.11 ± 0.51 at 48 hours. The mean CRI scores were 1 ± 0 immediately after the procedure, 1.17 ± 0.4 at 12 hours, 1.41 ± 0.20 at 24 hours, and 1 ± 0 at 48 hours.

Conclusion: Nearly all infants undergoing laser photocoagulation for ROP in our cohort required intubation and continued respiratory support. Despite stability during the procedure, complications from intubation were common.

Key points: · Routine intubation for laser is associated with complications.. · Need for post-procedural respiratory support is common.. · Avoiding intubation may mitigate these neonatal complications..

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Conflict of interest statement

None declared

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Clinical Trial

Am J Perinatol

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. 2024 Mar;41(4):458-469.

doi: 10.1055/a-1692-0544. Epub 2021 Nov 9.

Factors Associated with Outpatient Therapy Utilization in Extremely Preterm Infants

[Adharsh Ponnappakkam](#)^{#1}, [Nicholas R Carr](#)^{#1,2}, [Bryan A Comstock](#)³, [Krystle Perez](#)⁴, [T Michael O'Shea](#)⁵, [Veeral N Tolia](#)^{6,7}, [Reese H Clark](#)⁷, [Patrick J Heagerty](#)³, [Sandra E Juul](#)⁴, [Kaashif A Ahmad](#)^{7,8,9,10,11}, [Preterm Erythropoietin Neuroprotection Trial Consortium](#)

Affiliations expand

- PMID: 34753183
- DOI: [10.1055/a-1692-0544](https://doi.org/10.1055/a-1692-0544)

Abstract

Objective: Factors influencing utilization of outpatient interventional therapies for extremely low gestational age newborns (ELGANs) after discharge remain poorly characterized, despite a significant risk of neurodevelopmental impairment. We sought to assess the effects of maternal, infant, and environmental characteristics on outpatient therapy utilization in the first 2 years after discharge using data from the Preterm Erythropoietin Neuroprotection (PENUT) Trial.

Study design: This is a secondary analysis of 818, 24 to 27 weeks gestation infants enrolled in the PENUT trial who survived through discharge and completed at least one follow-up call or in-person visit between 4 and 24 months of age. Utilization of a state early intervention (EI) program, physical therapy (PT), occupational therapy (OT), and speech therapy (ST) was recorded. Odds ratios and cumulative frequency curves for resource utilization were calculated for patient characteristics adjusting for gestational age, treatment group, and birth weight.

Results: EI was not accessed by 37% of infants, and 18% did not use any service (PT/OT/ST/EI). Infants diagnosed with severe morbidities (intraventricular hemorrhage, retinopathy of prematurity, bronchopulmonary dysplasia, necrotizing enterocolitis), discharged with home oxygen, or with gastrostomy placement experienced increased utilization of PT, OT, and ST compared with peers. However, substantial variation in service utilization occurred by the state of enrollment and selected maternal characteristics.

Conclusions: ELGANs with severe medical comorbidities are more likely to utilize services after discharge. Therapy utilization may be impacted by maternal characteristics and state of enrollment. Outpatient therapy services remain significantly underutilized in this high-risk cohort. Further research is required to characterize and optimize the utilization of therapy services following NICU discharge of ELGANs.

Key points: · Outpatient therapy is underutilized in ELGANs.. · Medical comorbidities may impact therapy use.. · Maternal characteristics may impact therapy use.. · State of enrollment may impact therapy use..

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Conflict of interest statement

None declared.

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Clinical Trial

BMJ Open

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. 2024 Feb 28;14(2):e076702.

doi: 10.1136/bmjopen-2023-076702.

[Effects of vitamin D levels during pregnancy on prematurity: a systematic review protocol](#)

[Olívia Barbosa](#)^{1,2,3}, [Margarida Sim-Sim](#)⁴, [Marta Pereira Silvestre](#)⁵, [Cristina Pedro](#)³, [Dulce Cruz](#)^{4,2}

Affiliations expand

- PMID: 38418231
- DOI: [10.1136/bmjopen-2023-076702](https://doi.org/10.1136/bmjopen-2023-076702)

Free article

Abstract

Introduction: Prematurity is an urgent public health problem worldwide. Recent studies associate maternal hypovitaminosis D during pregnancy with an increased risk of

prematurity. However, the evidence on this association remains inconclusive, and there is lack of consensus in the literature. The exact mechanism by which low vitamin D levels may increase the risk of preterm birth is not yet fully understood. Nevertheless, it is known that vitamin D may play a role in maintaining a healthy pregnancy by regulating inflammation and immunomodulation by acting on the maternal and fetal immune systems. Inflammation and immune dysregulation are both associated with preterm birth, and low vitamin D levels may exacerbate these processes. The results of this review may have important implications for clinical practice and public health policy, particularly regarding vitamin D supplementation during pregnancy.

Methods and analysis: A systematic review of the literature will be conducted. The search will be performed in electronic databases: CINAHL; MEDLINE; Cochrane Central Register of Controlled Trials; Cochrane Library; Academic Search Complete; Information Science and Technology Abstracts; MedicLatina; SCOPUS; PubMed; and Google Scholar, with the chronological range of January 2018 to November 2022. The search strategy will include the following Medical Subject Headings or similar terms: 'Vitamin D'; '25-hydroxyvitamin D'; 'Hypovitaminosis D'; 'Pregnancy'; 'Pregnant women'; 'Expectant mother'; 'Prematurity'; 'Premature birth'; 'Premature delivery'; 'Preterm birth'; and 'Preterm labour'. This review will include quantitative primary studies, both experimental (clinical trials) and observational (cohort, cross-sectional, and case-control). The quality of each selected study and the results obtained will be assessed by two reviewers separately, using the Cochrane risk of bias tool for evaluating randomised clinical trials or the Newcastle Ottawa Scale for non-randomised studies, following the respective checklist. In case of disagreement, a third reviewer will be consulted.

Ethics and dissemination: This study does not involve human subjects and therefore does not require ethics approval. The results will be disseminated through publication in a peer-reviewed scientific journal and through conference presentations. All changes made to the protocol will be registered in PROSPERO, with information on the nature and justification for the changes made.

Prospero registration number: CRD42022303901.

Keywords: Fetal medicine; Maternal medicine; NEONATOLOGY; OBSTETRICS; Prenatal diagnosis.

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Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS



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Review

Eur J Pediatr

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. 2024 Feb 28.

doi: 10.1007/s00431-023-05410-5. Online ahead of print.

[Impact of preterm birth on muscle mass and function: a systematic review and meta-analysis](#)

[Alyson Deprez](#)^{1,2}, [Jéssica H Poletto Bonetto](#)¹, [Daniela Ravizzoni Dartora](#)¹, [Philippe Dodin](#)¹, [Anne Monique Nuyt](#)^{1,3}, [Thuy Mai Luu](#)^{1,3}, [Nicolas A Dumont](#)^{4,5}

Affiliations expand

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- DOI: [10.1007/s00431-023-05410-5](https://doi.org/10.1007/s00431-023-05410-5)

Abstract

Individuals born preterm present lower exercise capacity. Along with the cardiopulmonary responses and activity level, muscle strength is a key determinant of exercise capacity. This systematic review aimed to summarize the current knowledge on the impact of preterm birth on skeletal muscle mass and function across the lifespan. The databases PubMed, MEDLINE, EBM, Embase, CINAHL Plus, Global Index Medicus, and Google Scholar were searched using keywords and MeSH terms related to skeletal muscle, preterm birth, and low birth weight. Two independent reviewers undertook study selection, data extraction, and quality appraisal using Covidence review management. Data were pooled to estimate the prematurity effect on muscle mass and function using the R software. From 4378 studies retrieved, 132 were full-text reviewed and 25 met the inclusion/exclusion criteria. Five studies presented a low risk of bias, and 5 had a higher risk of bias due to a lack of adjustment for confounding factors and presenting incomplete outcomes. Meta-analyses of pooled data from homogenous studies indicated a significant reduction in muscle thickness and jump test (muscle power) in individuals born preterm versus full-term with standardized mean difference and confidence interval of - 0.58 (0.27, 0.89) and - 0.45 (0.21, 0.69), respectively. Conclusion: Overall, this systematic review summarizing the existing literature on the impact of preterm birth on skeletal muscle indicates emerging evidence that individuals born preterm, display alteration in the development of their skeletal muscle mass and function. This work also highlights a clear knowledge gap in understanding the effect of preterm birth on skeletal muscle development. What is Known: • Preterm birth, which occurs at a critical time of skeletal muscle development and maturation, impairs the development of different organs and tissues leading to a higher risk of comorbidities such as cardiovascular diseases. • Preterm birth is associated with reduced exercise capacity. What is New: • Individuals born preterm display alterations in muscle mass and function compared to individuals born at term from infancy to adulthood. • There is a need to develop preventive or curative interventions to improve skeletal muscle health in preterm-born individuals.

Keywords: Exercise capacity; Muscle function; Muscle mass; Preterm birth; Skeletal muscle.

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- [93 references](#)

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Physiol Meas

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. 2024 Feb 28;45(2).

doi: 10.1088/1361-6579/ad2291.

Detecting central apneas using multichannel signals in premature infants

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Affiliations expand

- PMID: 38271714
- DOI: [10.1088/1361-6579/ad2291](https://doi.org/10.1088/1361-6579/ad2291)

Abstract

Objective. Monitoring of apnea of prematurity, performed in neonatal intensive care units by detecting central apneas (CAs) in the respiratory traces, is characterized by a high number of false alarms. A two-step approach consisting of a threshold-based apneic event detection algorithm followed by a machine learning model was recently presented in literature aiming to improve CA detection. However, since this is characterized by high complexity and low precision, we developed a new direct approach that only consists of a detection model based on machine learning directly working with multichannel signals. *Approach.* The dataset used in this study consisted of 48 h of ECG, chest impedance and peripheral oxygen saturation extracted from 10 premature infants. CAs were labeled by two clinical experts. 47 features were extracted from time series using 30 s moving windows with an overlap of 5 s and evaluated in sets of 4 consecutive moving windows, in a similar way to what was indicated for the two-step approach. An undersampling method

was used to reduce imbalance in the training set while aiming at increasing precision. A detection model using logistic regression with elastic net penalty and leave-one-patient-out cross-validation was then tested on the full dataset. *Main results.* This detection model returned a mean area under the receiver operating characteristic curve value equal to 0.86 and, after the selection of a FPR equal to 0.1 and the use of smoothing, an increased precision (0.50 versus 0.42) at the expense of a decrease in recall (0.70 versus 0.78) compared to the two-step approach around suspected apneic events. *Significance.* The new direct approach guaranteed correct detections for more than 81% of CAs with length $L \geq 20$ s, which are considered among the most threatening apneic events for premature infants. These results require additional verifications using more extensive datasets but could lead to promising applications in clinical practice.

Keywords: apnea of prematurity; central apnea; machine learning; prematurity; signal processing.

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MeSH termsexpand

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Int J Retina Vitreous

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. 2024 Feb 27;10(1):21.

doi: 10.1186/s40942-024-00536-6.

Comparative analysis of risk factors for retinopathy of prematurity in single and multiple birth neonates

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Affiliations expand

- PMID: 38414089
- PMCID: [PMC10900704](#)
- DOI: [10.1186/s40942-024-00536-6](#)

Free PMC article

Abstract

Aim: To conduct a comparative analysis of risk factors for retinopathy of prematurity (ROP) in single- and multiple-born neonates.

Methods: In a retrospective evaluation of 521 premature neonates, encompassing singletons, twins, and triplets born at or before 34 weeks of gestational age with a birthweight of less than 2000 g and who completed the ROP screening program, between 2020 and 2023, in outpatient referral ROP screening clinic affiliated by Shiraz University of Medical Sciences, were included. Neonates with the eligibility criteria were enrolled in the screening program from 28 days old age and followed up to discharge or treatment based on national ROP screening guideline. Data on ROP severity, outcome, treatment modality, and risk factors, including gestational age (GA), birth weight (BW), sex, duration of neonatal intensive care unit (NICU) admission, oxygen supplementation, mechanical ventilation, blood transfusion, method of delivery, and maternal and neonatal comorbidities, were extracted and compared between premature neonates from singleton and multiple births.

Results: The analysis of the ROP severity distribution revealed 238 neonates (45.7%) with low-risk (type 2 prethreshold ROP or less severe) ROP and 16 (3.1%) with high-risk (type I prethreshold ROP or more severe) ROP who underwent treatment. According to the comparative analysis of risk factors in neonates with ROP requiring treatment, multiple birth neonates exhibited significantly greater GA (27.50 ± 3.27 vs. 30.00 ± 2.00 vs. 31.14 ± 0.38 weeks, $p = 0.032$ for singletons, twins and triplets, respectively); greater BW (861.67 ± 274.62 vs. 1233.33 ± 347.75 vs. 1537.14 ± 208.86 g, $p = 0.002$); and shorter duration of

NICU admission (60.17 ± 21.36 vs. 34.00 ± 12.17 vs. 12.00 ± 6.32 days, $p = 0.001$) and oxygen supplementation (47.33 ± 16.57 vs. 36.00 ± 8.49 vs. 4.60 ± 2.41 days, $p = 0.001$). There was no significant difference between single-born neonates and multiple-born neonates regarding the prevalence of other risk factors. Multiple-born neonates with no ROP and low risk ROP showed significantly lower GA and BW compared to singletons ($p < 0.001$).

Conclusion: Multiple gestation neonates may develop high-risk ROP requiring treatment at a greater gestational age and birth weight and at a lower duration of oxygen supplementation and NICU admission compared to the single birth neonates. This pattern prompts a reevaluation of screening criteria, suggesting a potential need to consider multiple birth neonates with lower traditional risk factors in screening programs. This pattern should be further evaluated in larger populations of multiple born premature neonates.

Keywords: Multiple birth; Multiple gestation; ROP; Retinopathy of prematurity; Risk factor; Triplet; Twin.

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Conflict of interest statement

No conflicts of interest to declare.

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

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Grants and funding [expand](#)

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Am J Perinatol



. 2024 Feb 26.

doi: 10.1055/s-0044-1781460. Online ahead of print.

Impact of Congenital Heart Disease on the Outcomes of Very Low Birth Weight Infants

[Xuxin Chen](#)¹, [Shazia Bhombal](#)², [David M Kwiatkowski](#)³, [Michael Ma](#)⁴, [Valerie Y Chock](#)⁵

Affiliations expand

- PMID: 38408479
- DOI: [10.1055/s-0044-1781460](https://doi.org/10.1055/s-0044-1781460)

Abstract

Objective: To investigate the association of congenital heart disease (CHD) with morbidity and mortality of very low birth weight (VLBW) infants.

Study design: This matched case-control study included VLBW infants born at a single institution between 2001 and 2015. The primary outcome was mortality. Secondary outcomes included necrotizing enterocolitis, bronchopulmonary dysplasia (BPD), sepsis, retinopathy of prematurity, and intraventricular hemorrhage. These outcomes were assessed by comparing VLBW-CHDs with control VLBW infants matched by gestational age within a week, birth weight within 500 g, sex, and birth date within a year using conditional logistic regression. Multivariable logistic regression analyzed differences in outcomes in the VLBW-CHD group between two birth periods (2001-2008 and 2009-2015) to account for changes in practice.

Results: In a cohort of 44 CHD infants matched with 88 controls, the mortality rate was 27% in infants with CHD and 1% in controls ($p < 0.0001$). The VLBW-CHDs had increased BPD; (odds ratio [OR]: 7.70, 95% confidence interval [CI]: 1.96-30.29) and sepsis (OR: 10.59, 95% CI: 2.99-37.57) compared with the control VLBWs. When adjusted for preoperative ventilator use, the VLBW-CHDs still had significantly higher odds of BPD (OR: 6.97, 95% CI: 1.73-28.04). VLBW-CHDs also had significantly higher odds of both presumed and culture-positive sepsis as well as late-onset sepsis than their matched controls. There were no significant differences in outcomes between the two birth periods.

Conclusion: VLBW-CHDs showed higher odds of BPD, sepsis, and mortality than VLBW infants without CHD. Future research should focus on the increased mortality and specific complications encountered by VLBW infants with CHD and implement targeted strategies to address these risks.

Key points: · Incidence of CHD is higher in preterm infants than in term infants but the incidence of their morbidities is not well described.. · VLBW infants with CHD have higher odds of mortality, bronchopulmonary dysplasia, and sepsis.. · Future research is needed to implement targeted preventive responses..

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Conflict of interest statement

None declared.

FULL TEXT LINKS



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Review

J Perinat Med

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. 2023 Dec 8;52(2):119-125.

doi: 10.1515/jpm-2023-0454. Print 2024 Feb 26.

[Artificial intelligence in the NICU to predict extubation success in prematurely born infants](#)

[Allan C Jenkinson](#)¹, [Theodore Dassios](#)^{1,2}, [Anne Greenough](#)^{1,2}

Affiliations expand

- PMID: 38059494
- DOI: [10.1515/jpm-2023-0454](https://doi.org/10.1515/jpm-2023-0454)

Free article

Abstract

Objectives: Mechanical ventilation in prematurely born infants, particularly if prolonged, can cause long term complications including bronchopulmonary dysplasia. Timely extubation then is essential, yet predicting its success remains challenging. Artificial intelligence (AI) may provide a potential solution.

Content: A narrative review was undertaken to explore AI's role in predicting extubation success in prematurely born infants. Across the 11 studies analysed, the range of reported area under the receiver operator characteristic curve (AUC) for the selected prediction models was between 0.7 and 0.87. Only two studies implemented an external validation procedure. Comparison to the results of clinical predictors was made in two studies. One group reported a logistic regression model that outperformed clinical predictors on decision tree analysis, while another group reported clinical predictors outperformed their artificial neural network model (AUCs: ANN 0.68 vs. clinical predictors 0.86). Amongst the studies there was an heterogenous selection of variables for inclusion in prediction models, as well as variations in definitions of extubation failure.

Summary: Although there is potential for AI to enhance extubation success, no model's performance has yet surpassed that of clinical predictors.

Outlook: Future studies should incorporate external validation to increase the applicability of the models to clinical settings.

Keywords: artificial intelligence; deep learning; extubation; machine learning; prematurity.

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- [39 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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

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Osteoporos Int

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. 2024 Mar 2.

doi: 10.1007/s00198-024-07037-0. Online ahead of print.

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

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

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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2

Allergy

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. 2024 Mar 2.

doi: 10.1111/all.16052. Online ahead of print.

House dust mite SCIT reduces asthma risk and significantly improves long-term rhinitis and asthma control-A RWE study

[Marek Jutel](#)^{1,2}, [Ludger Klimek](#)³, [Hartmut Richter](#)⁴, [Bernd Brüggenjürgen](#)⁵, [Christian Vogelberg](#)⁶

Affiliations expand

- PMID: 38429981
- DOI: [10.1111/all.16052](https://doi.org/10.1111/all.16052)

Abstract

Background: The German Therapy Allergen Ordinance (TAO) triggered an ongoing upheaval in the market for house dust mite (HDM) allergen immunotherapy (AIT) products. Three HDM subcutaneous AIT (SCIT) products hold approval in Germany and therefore will be available after the scheduled completion of the TAO procedure in 2026. In general, data from clinical trials on the long-term effectiveness of HDM AIT are rare. We evaluated real-world data (RWD) in a retrospective, observational cohort study based on a longitudinal claims database including 60% of all German statutory healthcare prescriptions to show the long-term effectiveness of one of these products in daily life. Aim of this analysis was to provide a per product analysis on effectiveness of mite AIT as it is demanded by international guidelines on AIT.

Methods: Subjects between 5 and 70 years receiving their first (index) prescription of SCIT with a native HDM product (SCIT group) between 2009 and 2013 were included. The

exactly 3:1 matched control group received prescriptions for only symptomatic AR medication (non-AIT group); the evaluation period for up to 6 years of follow-up ended in February 2017. Study endpoints were the progression of allergic rhinitis (AR) and asthma, asthma occurrence and time to the onset of asthma after at least 2 treatment years.

Results: In total, 892 subjects (608 adults and 284 children/adolescents) were included in the SCIT group and 2676 subjects (1824 adults and 852 children/adolescents) in the non-AIT group. During the follow-up period after at least 2 years of SCIT, the number of prescriptions in the SCIT group was reduced by 62.8% ($p < .0001$) for AR medication and by 42.4% for asthma medication ($p = .0003$). New-onset asthma risk was significantly reduced in the SCIT vs non-AIT group by 27.0% ($p = .0212$). The asthma-preventive effect of SCIT occurred 15 months after start of the treatment. In the SCIT group, the time to onset of asthma was prolonged compared to the non-AIT group ($p = .0010$).

Conclusion: In this first product based RWD analysis on SCIT with a native HDM product, patients aged 5 to 70 years benefited from AIT in the long term in terms of reduced progression of AR and asthma after at least 2 years of treatment. The effects seemed to last for up to 6 years after treatment termination. A significantly reduced risk of asthma onset was observed, starting after 15 months of treatment.

Keywords: allergen immunotherapy; house dust mite; long-term effect; real-world evidence; subcutaneous immunotherapy.

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- [59 references](#)

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3

Review

Clin Transl Allergy



. 2024 Mar;14(3):e12344.

doi: 10.1002/ct2.12344.

Non-pharmacological interventions for asthma prevention and management across the life course: Umbrella review

[Xunliang Tong](#)¹, [Xinyue Zhang](#)², [Mengyuan Wang](#)³, [Zijun Wang](#)⁴, [Fawu Dong](#)², [Enying Gong](#)^{5,6}, [Torsten Zuberbier](#)⁷, [Yanming Li](#)¹

Affiliations expand

- PMID: 38423800
- PMCID: [PMC10904350](#)
- DOI: [10.1002/ct2.12344](#)

Abstract

Background: The impact of non-pharmacological interventions (NPIs) on asthma prevention and management is insufficiently examined. We aim to comprehensively evaluate and synthesize existing evidence regarding the effectiveness of various NPIs throughout the life course.

Methods: We conducted a systematic search and screening of reviews that examined the effectiveness of various NPIs on asthma prevention and control in the Cochrane Library, PubMed, Embase, and Ovid databases. Data extraction was performed by considering the type of NPIs and the life course stages of the target population. Recommendations were provided by considering the quality of review assessed using the AMSTAR2 tool and the consistency of findings across reviews.

Results: We identified 145 reviews and mapped the evidence on the impact of 25 subtypes of NPIs on asthma prevention and control based on five stages of life course. Reviews indicated a shift of focus and various impacts of major NPIs on asthma prevention and control across life courses, while a few types of NPIs, such as physical exercise, appeared to be beneficial in children, adolescents and adults. Consistent and high-level evidence was observed only for psychological intervention on asthma control and quality of life among adults and older adults. Potential benefit with high-level evidence was reported on certain NPIs, such as vitamin D in reducing risk of developing asthma in offsprings in the prenatal stage, digital health interventions in improving asthma control from childhood to older adulthood, and breathing exercise in improving quality of life, asthma-related symptoms and lung function in adulthood and older adulthood.

Conclusion: This study emphasizes the significance of delivering NPIs to improve asthma prevention and management and highlights the heterogeneity regarding the impact of NPIs across life courses. High-quality research is urgently needed to further strengthen the evidence base of NPIs and tailored interventions should be considered in guideline development.

Keywords: asthma; life course; non-pharmacological interventions; umbrella review.

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Conflict of interest statement

The authors have none to declare.

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

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

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Respirol Case Rep

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. 2024 Feb 27;12(3):e01311.

doi: 10.1002/rcr2.1311. eCollection 2024 Mar.

[Efficacy of tezepelumab against uncontrolled severe non-type 2 asthma refractory to bronchial thermoplasty, benralizumab, dupilumab and mepolizumab](#)

[Yoshiro Kai](#)¹, [Kentaro Suzuki](#)¹, [Ryosuke Kataoka](#)¹, [Ichiro Sato](#)², [Shinji Tamaki](#)³, [Shigeo Muro](#)²

Affiliations expand

- PMID: 38420113
- PMCID: [PMC10898956](#)
- DOI: [10.1002/rcr2.1311](#)

Free PMC article

Abstract

Severe asthma affects approximately 5%-10% of patients with asthma. Herein, we describe a case of non-type 2 asthma that progressively worsened over the years. An 80-year-old woman was diagnosed with asthma 11 years back. She experienced repeated exacerbations requiring treatment with systemic corticosteroid despite therapy with medications including high-dose inhaled corticosteroids/long-acting beta-agonists plus

long-acting muscarinic antagonist. The patient presented with non-eosinophilic asthma. Therefore, the patient was initially treated with bronchial thermoplasty, which was effective for 1 year only. Treatment with bronchial thermoplasty, benralizumab, dupilumab, and mepolizumab was ineffective. The fourth treatment, which included tezepelumab, was initiated. The patient's symptoms and quality of life improved significantly. This is the first case of a patient who did not respond to sequential bronchial thermoplasty, benralizumab, dupilumab, and mepolizumab but who presented with good clinical response to tezepelumab. Therefore, tezepelumab may be useful for patients with non-type 2 asthma.

Keywords: benralizumab; bronchial thermoplasty; dupilumab; mepolizumab; tezepelumab.

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Conflict of interest statement

None declared.

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

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[Practice Guideline](#)

Otolaryngol Head Neck Surg

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Clinical Practice Guideline: Immunotherapy for Inhalant Allergy

[Richard K Gurgel](#)¹, [Fuad M Baroody](#)², [Cecelia C Damask](#)³, [James Whit Mims](#)⁴, [Stacey L Ishman](#)⁵, [Dole P Baker Jr](#)⁶, [Kevin J Contrera](#)⁷, [Fariha S Farid](#)⁸, [John A Fornadley](#)⁹, [Donna D Gardner](#)¹⁰, [LaKeisha R Henry](#)¹¹, [Jean Kim](#)¹², [Joshua M Levy](#)¹³, [Christine M Reger](#)¹⁴, [Howard J Ritz](#)¹⁵, [Robert J Stachler](#)¹⁶, [Tulio A Valdez](#)¹⁷, [Joe Reyes](#)¹⁸, [Nui Dhepyasuwan](#)¹⁸

Affiliations expand

- PMID: 38408152
- DOI: [10.1002/ohn.648](https://doi.org/10.1002/ohn.648)

Abstract

Objective: Allergen immunotherapy (AIT) is the therapeutic exposure to an allergen or allergens selected by clinical assessment and allergy testing to decrease allergic symptoms and induce immunologic tolerance. Inhalant AIT is administered to millions of patients for allergic rhinitis (AR) and allergic asthma (AA) and is most commonly delivered as subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Despite its widespread use, there is variability in the initiation and delivery of safe and effective immunotherapy, and there are opportunities for evidence-based recommendations for improved patient care.

Purpose: The purpose of this clinical practice guideline (CPG) is to identify quality improvement opportunities and provide clinicians trustworthy, evidence-based recommendations regarding the management of inhaled allergies with immunotherapy. Specific goals of the guideline are to optimize patient care, promote safe and effective therapy, reduce unjustified variations in care, and reduce the risk of harm. The target patients for the guideline are any individuals aged 5 years and older with AR, with or without AA, who are either candidates for immunotherapy or treated with immunotherapy for their inhalant allergies. The target audience is all clinicians involved in the administration of immunotherapy. This guideline is intended to focus on evidence-based quality improvement opportunities judged most important by the guideline development group (GDG). It is not intended to be a comprehensive, general guide regarding the management of inhaled allergies with immunotherapy. The statements in this guideline are not intended to limit or restrict care provided by clinicians based on their experience and assessment of individual patients.

Action statements: The GDG made a strong recommendation that (Key Action Statement [KAS] 10) the clinician performing allergy skin testing or administering AIT must be able to diagnose and manage anaphylaxis. The GDG made recommendations for the following KASs: (KAS 1) Clinicians should offer or refer to a clinician who can offer immunotherapy for patients with AR with or without AA if their patients' symptoms are inadequately controlled with medical therapy, allergen avoidance, or both, or have a preference for immunomodulation. (KAS 2A) Clinicians should not initiate AIT for patients who are pregnant, have uncontrolled asthma, or are unable to tolerate injectable epinephrine. (KAS 3) Clinicians should evaluate the patient or refer the patient to a clinician who can evaluate for signs and symptoms of asthma before initiating AIT and for signs and symptoms of uncontrolled asthma before administering subsequent AIT. (KAS 4) Clinicians should educate patients who are immunotherapy candidates regarding the differences between SCIT and SLIT (aqueous and tablet) including risks, benefits, convenience, and costs. (KAS 5) Clinicians should educate patients about the potential benefits of AIT in (1) preventing new allergen sensitizations, (2) reducing the risk of developing AA, and (3) altering the natural history of the disease with continued benefit after discontinuation of therapy. (KAS 6) Clinicians who administer SLIT to patients with seasonal AR should offer pre- and co-seasonal immunotherapy. (KAS 7) Clinicians prescribing AIT should limit treatment to only those clinically relevant allergens that correlate with the patient's history and are confirmed by testing. (KAS 9) Clinicians administering AIT should continue escalation or maintenance dosing when patients have local reactions (LRs) to AIT. (KAS 11) Clinicians should avoid repeat allergy testing as an assessment of the efficacy of ongoing AIT unless there is a change in environmental exposures or a loss of control of symptoms. (KAS 12) For patients who are experiencing symptomatic control from AIT, clinicians should treat for a minimum duration of 3 years, with ongoing treatment duration based on patient response to treatment. The GDG offered the following KASs as options: (KAS 2B) Clinicians may choose not to initiate AIT for patients who use concomitant beta-blockers, have a history of anaphylaxis, have systemic immunosuppression, or have eosinophilic esophagitis (SLIT only). (KAS 8) Clinicians may treat polysensitized patients with a limited number of allergens.

Keywords: allergen immunotherapy; allergic asthma; allergic rhinitis; anaphylaxis; inhalant allergy; subcutaneous immunotherapy; sublingual immunotherapy.

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- [264 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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EClinicalMedicine



. 2024 Feb 17:69:102500.

doi: 10.1016/j.eclinm.2024.102500. eCollection 2024 Mar.

[Long-term risks of respiratory diseases in patients infected with SARS-CoV-2: a longitudinal, population-based cohort study](#)

[Meijun Meng](#)^{1,2,3}, [Rui Wei](#)², [YanJun Wu](#)^{2,3}, [Ruijie Zeng](#)^{2,4}, [Dongling Luo](#)¹, [Yuying Ma](#)^{2,3}, [Lijun Zhang](#)^{2,5}, [Wentao Huang](#)^{2,3}, [Hanshi Zeng](#)⁶, [Felix W Leung](#)^{7,8}, [Xinqi Qiu](#)⁹, [Weihong Sha](#)^{1,2,3,4,5}, [Hao Chen](#)^{1,2,3,4,5}

Affiliations expand

- PMID: 38389713
- PMCID: [PMC10882104](#)
- DOI: [10.1016/j.eclinm.2024.102500](#)

Free PMC article

Abstract

Background: In the post-pandemic era, growing apprehension exists regarding the potential sequelae of COVID-19. However, the risks of respiratory diseases following SARS-CoV-2 infection have not been comprehensively understood. This study aimed to investigate whether COVID-19 increases the long-term risk of respiratory illness in patients with COVID-19.

Methods: In this longitudinal, population-based cohort study, we built three distinct cohorts age 37-73 years using the UK Biobank database; a COVID-19 group diagnosed in medical records between January 30th, 2020 and October 30th, 2022, and two control groups, a contemporary control group and a historical control group, with cutoff dates of October 30th, 2022 and October 30th, 2019, respectively. The follow-up period of all three groups was 2.7 years (the median (IQR) follow-up time was 0.8 years). Respiratory outcomes diagnosed in medical records included common chronic pulmonary diseases (asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), pulmonary vascular disease (PVD), and lung cancer. For the data analysis, we calculated hazard ratios (HRs) along with their 95% CIs using Cox regression models, following the application of inverse probability weights (IPTW).

Findings: A total of 3 cohorts were included in this study; 112,311 individuals in the COVID-19 group with a mean age (\pm SDs) of 56.2 (8.1) years, 359,671 in the contemporary control group, and 370,979 in the historical control group. Compared with the contemporary control group, those infected with SARS-CoV-2 exhibited elevated risks for developing respiratory diseases. This includes asthma, with a HR of 1.49 and a 95% CI 1.28-1.74; bronchiectasis (1.30; 1.06-1.61); COPD (1.59; 1.41-1.81); ILD (1.81; 1.38-2.21); PVD (1.59; 1.39-1.82); and lung cancer (1.39; 1.13-1.71). With the severity of the acute phase of COVID-19, the risk of pre-described respiratory outcomes increases progressively. Besides, during the 24-months follow-up, we observed an increasing trend in the risks of asthma and bronchiectasis over time. Additionally, the HR of lung cancer for 0-6 month follow-up was 3.07 (CI 1.73-5.44), and the association of lung cancer with COVID-19 disease disappeared at 6-12 month follow-up (1.06; 0.43-2.64) and at 12-24 months (1.02; 0.45-2.34). Compared to those with one SARS-CoV-2 infection, reinfected patients were at a higher risk of asthma (3.0; 1.32-6.84), COPD (3.07; 1.42-6.65), ILD (3.61; 1.11-11.8), and lung cancer (3.20; 1.59-6.45). Similar findings were noted when comparing with a historical cohort serving as a control group, including asthma (1.31; 1.13-1.52); bronchiectasis (1.53; 1.23-1.89); COPD (1.41; 1.24-1.59); ILD (2.53; 2.05-3.13); PVD (2.30; 1.98-2.66); and lung cancer (2.23; 1.78-2.79).

Interpretation: Our research suggests that patients with COVID-19 may have an increased risk of developing respiratory diseases, and the risk increases with the severity of infection and reinfection. Even during the 24-month follow-up, the risk of asthma and bronchiectasis continued to increase. Hence, implementing appropriate follow-up strategies for these individuals is crucial to monitor and manage potential long-term respiratory health issues. Additionally, the increased risk in lung cancer in the COVID-19 individuals was probably due to the diagnostic tests conducted and incidental diagnoses.

Funding: The National Natural Science Foundation of China of China Regional Innovation and Development Joint Foundation; National Natural Science Foundation of China; Program for High-level Foreign Expert Introduction of China; Natural Science Foundation for Distinguished Young Scholars of Guangdong Province; Guangdong Basic and Applied Basic Research Foundation; Climbing Program of Introduced Talents and High-level Hospital Construction Project of Guangdong Provincial People's Hospital; VA Clinical Merit and ASGE clinical research funds.

Keywords: COVID-19 (coronavirus disease 2019); Epidemiological study; Respiratory diseases; SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).

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Conflict of interest statement

All authors declare no competing interests.

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

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World Allergy Organ J

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. 2024 Feb 15;17(3):100879.

doi: 10.1016/j.waojou.2024.100879. eCollection 2024 Mar.

Diagnostic biomarkers for chronic rhinosinusitis in adult asthmatics in real-world practice

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Affiliations [expand](#)

- PMID: 38380106
- PMCID: [PMC10877182](#)
- DOI: [10.1016/j.waojou.2024.100879](#)

Free PMC article

Abstract

Background: Chronic rhinosinusitis (CRS) is a common comorbid condition of asthma that affects the long-term outcome of asthmatic patients. CRS is a heterogeneous disease requiring multiple biomarkers to explain its pathogenesis. This study aimed to develop potential biomarkers for predicting CRS in adult asthmatic patients in a real-world clinical setting.

Methods: This study enrolled 108 adult asthmatic patients who had maintained anti-asthmatic medications, including medium-to-high doses of inhaled corticosteroid plus long-acting β 2-agonists, and compared clinical characteristics between patients with CRS (CRS group) and those without CRS (non-CRS group). CRS was diagnosed based on the results of paranasal sinus X-ray and/or osteomeatal-unit CT as well as clinical symptoms. Type-2 parameters, including blood eosinophil count, serum levels of periostin/dipeptidyl peptidase 10 (DPP10) and clinical parameters, such as FEV1% and fractional exhaled nitric oxide (FeNO), were analyzed. All biomarkers were evaluated by logistic regression and classification/regression tree (CRT) analyses.

Results: The CRS group had higher blood eosinophil counts/FeNO levels and prevalence of aspirin-exacerbated respiratory disease (AERD) than the non-CRS group ($n = 57, 52.8\%$ vs. $n = 75, 47.2\%$; $P < 0.05$), but no differences in sex/smoking status or asthma control status were noted. The CRS group had higher serum periostin/DPP10 levels than the non-CRS group. Moreover, logistic regression demonstrated that serum periostin/DPP10 and the AERD phenotype were significant factors for predicting CRS in

asthmatic patients (adjusted odds ratio, 2.14/1.94/12.39). A diagnostic algorithm and the optimal cutoff values determined by CRT analysis were able to predict CRS with 86.27% sensitivity (a 0.17 negative likelihood ratio).

Conclusion: Serum periostin, DPP10 and the phenotype of AERD are valuable biomarkers for predicting CRS in adult asthmatic patients in clinical practice.

Keywords: Asthma; Biomarkers; Dipeptidyl-peptidases and tripeptidyl-peptidases; Eosinophils; Fractional exhaled nitric oxide testing; Periostin; Rhinitis; Sinusitis.

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Conflict of interest statement

None.

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

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Randomized Controlled Trial

Respir Med

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. 2024 Mar;223:107539.

doi: 10.1016/j.rmed.2024.107539. Epub 2024 Feb 5.

Improving asthma control and quality of life via a smartphone self-management app: A randomized controlled trial

[Mehrdad Farzandipour¹](#), [Marzieh Heidarzadeh Arani²](#), [Reihane Sharif³](#), [Ehsan Nabovati¹](#), [Hossein Akbari⁴](#), [Shima Anvari¹](#)

Affiliations expand

- PMID: 38325663
- DOI: [10.1016/j.rmed.2024.107539](https://doi.org/10.1016/j.rmed.2024.107539)

Abstract

Background: Mobile phone applications (apps) show promise for enhancing asthma self-management, but their effectiveness varies. This study examined the effect of a smartphone asthma app on asthma control and quality of life.

Methods: Using block randomization, 60 patients with asthma were allocated to an intervention group (n = 30) or control group (n = 30) for this single-blind randomized controlled trial. At baseline, both groups completed the Asthma Control Test (ACT) and Asthma Quality of Life Questionnaire-Marks (AQLQ-M). The intervention group used a smartphone-based asthma self-management app plus their regular treatment, while the control group received only usual care. Follow-up ACT and AQLQ-M assessments occurred at 3 and 6 months. SPSS version 26 was used for analysis, including descriptive statistics, non-parametric tests (Wilcoxon and Mann-Whitney U), and analysis of variance with repeated measurements.

Results: Both groups showed improved asthma control and quality of life at 3 and 6 months compared to baseline. However, after 6 months the intervention group had significantly greater improvement than controls ($p < 0.05$). Repeated measures ANOVA revealed divergent changes in ACT and AQLQ-M scores over time, with the intervention group demonstrating greater enhancement of asthma control and quality of life ($p < 0.001$).

Conclusion: This study demonstrated that use of a smartphone-based asthma self-management app improved asthma control and quality of life after 6 months compared to

usual care alone. These findings indicate that guideline-based asthma apps can positively impact outcomes.

Keywords: Asthma; Asthma control; Mobile applications; Quality of life; mHealth.

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Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

Adv Ther

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. 2024 Mar;41(3):1262-1283.

doi: 10.1007/s12325-023-02746-0. Epub 2024 Feb 4.

[The Association Between Short-Acting \$\beta_2\$ -Agonist Over-Prescription, and Patient-Reported Acquisition and Use](#)

on Asthma Control and Exacerbations: Data from Australia

[David Price](#)^{1,2,3,4}, [Christine Jenkins](#)⁵, [Kerry Hancock](#)^{6,7}, [Rebecca Vella](#)⁸, [Florian Heraud](#)⁹, [Porsche Le Cheng](#)⁸, [Ruth Murray](#)¹⁰, [Maarten Beekman](#)¹¹, [Sinthia Bosnic-Anticevich](#)^{12,13}, [Fabio Botini](#)⁸, [Victoria Carter](#)¹⁰, [Angelina Catanzariti](#)¹⁴, [Joe Doan](#)¹⁵, [Kirsty Fletton](#)¹⁰, [Ata Kichkin](#)¹⁶, [Thao Le](#)¹⁷, [Chantal Le Lievre](#)⁸, [Chi Ming Lau](#)¹⁸, [Dominique Novic](#)¹⁹, [John Pakos](#)²⁰, [Kanchanamala Ranasinghe](#)^{21,22}, [Alexander Roussos](#)⁸, [Josephine Samuel-King](#)²³, [Anita Sharma](#)²⁴, [Deb Stewart](#)²⁵, [Bruce Willet](#)²⁶, [Eric Bateman](#)²⁷; [OPCA Improving Asthma Outcomes in Australia Research Group](#)

Collaborators, Affiliations expand

- PMID: 38310584
- PMCID: [PMC10879376](#)
- DOI: [10.1007/s12325-023-02746-0](#)

Free PMC article

Abstract

Introduction: In Australia, short-acting β_2 -agonists (SABA) are available both over the counter (OTC) and on prescription. This ease of access may impact SABA use in the Australian population. Our aim was to assess patterns and outcome associations of prescribed, acquired OTC and reported use of SABA by Australians with asthma.

Methods: This was a cross-sectional study, using data derived from primary care electronic medical records (EMRs) and patient completed questionnaires within Optimum Patient Care Research Database Australia (OPCRDA). A total of 720 individuals aged ≥ 12 years with an asthma diagnosis in their EMRs and receiving asthma therapy were included. The annual number of SABA inhalers authorised on prescription, acquired OTC and reported, and the association with self-reported exacerbations and asthma control were investigated.

Results: 92.9% (n = 380/409) of individuals issued with SABA prescription were authorised ≥ 3 inhalers annually, although this differed from self-reported usage. Of individuals reporting SABA use (n = 546) in the last 12 months, 37.0% reported using ≥ 3 inhalers. These patients who reported SABA overuse experienced 2.52 (95% confidence interval [CI] 1.73-3.70) times more severe exacerbations and were 4.51 times (95% CI 3.13-6.55) more likely to have poor asthma control than those who reported using 1-2 SABA inhalers. Patients who did not receive SABA on prescription (43.2%; n = 311/720) also experienced

2.71 (95% CI 1.07-7.26) times more severe exacerbations than those prescribed 1-2 inhalers. Of these patients, 38.9% reported using OTC SABA and other prescription medications, 26.4% reported using SABA OTC as their only asthma medication, 13.2% were prescribed other therapies but not SABA OTC and 14.5% were not using any medication.

Conclusion: Both self-reported SABA overuse and zero SABA prescriptions were associated with poor asthma outcomes. The disconnect between prescribing authorisation, OTC availability and actual use, make it difficult for clinicians to quantify SABA use.

Keywords: Asthma management; Asthma outcomes; Over-the-counter medication; Prescription patterns; Short-acting β 2-agonists.

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Conflict of interest statement

Kerry L. Hancock has received speakers' fees, consulting honoraria and/or travel grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Menarini Australia, Mylan and Novartis. Sinthia Bosnic-Anticevich has received honorarium for participation in expert advisory boards and given lectures for Teva Pharmaceuticals, AstraZeneca, GSK, Meda, Mundipharma, Sanofi, Mylan and received unrestricted research grants from Mylan, AstraZeneca, Teva and Mundipharma International. Angelina Catanzariti is an employee of AstraZeneca. Christine Jenkins, Joe Doan, Ata Kichkin, Chi Ming Lau, Dominique Novic, John Pakos, Kanchanamala Ranasinghe, Josephine Samuel-King, Bruce Willet, and Thao Le declares no conflict of interest. Anita Sharma is a practising Primary Care Physician and Senior Lecturer, School of Clinical Medicine-Primary Care Clinical Unit, University of Queensland. She supervises clinical training of primary care doctors and serves on advisory boards for Diabetes, Heart Failure and Osteoporosis for Novartis, Merck Sharp & Dohme and Boehringer Ingelheim, Eli Lilly and Amgen. Eric Bateman has received honorarium for participation in advisory boards from ALK, AstraZeneca, Novartis, Regeneron and Sanofi Aventis, and for giving lectures for AstraZeneca, Chiesi, Menarini, Novartis, Orion, Regeneron and Sanofi Aventis. He is a member of the Board and Science Committee of GINA. Maarten JHI Beekman was an employee of AstraZeneca at time of study conduct. Rebecca Vella, Florian Heraud, Porsche Le Cheng, Fabio Botini, Thao Le, Chantal Le Lievre, Alex Roussos are employees of Optimum Patient Care Australia. Ruth Murray is a consultant for the Observational and Pragmatic Research Institute. Victoria Carter is an employee of Optimum Patient Care Global and has 5% shareholding of Optimum Patient Care Australia. Kirsty Fletton is an employee of Optimum Patient Care United Kingdom. David Price has advisory board membership with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatrix, Teva Pharmaceuticals; consultancy agreements with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatrix, Teva Pharmaceuticals; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Chiesi, Viatrix, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, and UK

National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Inside Practice, GlaxoSmithKline, Medscape, Viatrix, Novartis, Regeneron Pharmaceuticals and Sanofi Genzyme, Teva Pharmaceuticals; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Novartis, Medscape, Teva Pharmaceuticals.; stock/stock options from AKL Research and Development Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); 5% shareholding in Timestamp which develops adherence monitoring technology; is peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation programme, and Health Technology Assessment; and was an expert witness for GlaxoSmithKline.

- [32 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Randomized Controlled Trial

Adv Ther

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. 2024 Mar;41(3):1201-1225.

doi: 10.1007/s12325-023-02774-w. Epub 2024 Feb 1.

Effect of Individual Patient Characteristics and Treatment Choices on Reliever Medication Use in Moderate–Severe Asthma: A Poisson Analysis of Randomised Clinical Trials

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Affiliations expand

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- PMCID: [PMC10879282](#)
- DOI: [10.1007/s12325-023-02774-w](#)

Free PMC article

Abstract

Introduction: Even though increased use of reliever medication, including short-acting beta agonists (SABA), provides an indirect measure of symptom worsening, there have been limited efforts to assess how different patterns of reliever use correlate with symptom control and future risk of exacerbations. Here, we evaluate the effect of individual baseline characteristics on reliever use in patients with moderate-severe asthma on regular maintenance therapy with fluticasone propionate (FP) or combination therapy with fluticasone propionate/salmeterol (FP/SAL) or budesonide/formoterol (BUD/FOR).

Methods: A drug-disease model describing the number of 24-h puffs and overnight occasions was developed with data from five clinical studies (N = 6212). The model was implemented using a nonlinear mixed effects approach and a Poisson function, considering clinical and demographic baseline characteristics. Goodness of fit and model predictive performance were assessed. Heatmaps were created to summarise the effect of concurrent baseline factors on reliever utilisation.

Results: The final model accurately described individual patterns of reliever use, which is significantly increased with time since diagnosis, smoking, higher Asthma Control

Questionnaire (ACQ-5) score and higher body mass index (BMI) at baseline. Whilst the number of puffs decreases slowly after an initial drop relative to the start of treatment, exacerbating patients utilise significantly more reliever than those who do not exacerbate. The mean effect of FP/SAL (median dose: 250/50 µg BID) on reliever use was slightly higher than that of BUD/FOR (median dose: 160/4.5 µg BID), i.e. a 75.3% vs 69.3% reduction in reliever use, respectively.

Conclusions: The availability of individual-level patient data in conjunction with a parametric approach enabled the characterisation of interindividual differences in the patterns of reliever use in patients with moderate-severe asthma. Taken together, individual demographic and clinical characteristics, as well as exacerbation history, can be considered an indicator of the degree of asthma control. High SABA reliever use suggests suboptimal clinical management of patients on maintenance therapy.

Keywords: Asthma symptom control; Drug-disease modelling; Exacerbation; ICS/LABA combination therapy; Inhaled corticosteroids; Reliever medication; Rescue medication; SABA; Short-acting beta agonists.

Plain language summary

In this study, we tried to understand how patients with moderate to severe asthma use their quick-relief inhalers (like albuterol), how it relates to their symptoms and the risk of having asthma attacks. To evaluate whether differences in reliever inhaler use between patients are associated with factors like smoking or their asthma symptoms at the beginning of treatment, we gathered data from five clinical studies (n = 6212 patients). These data allowed us to create a model that predicts how often patients use their reliever inhalers (expressed as number of puffs in 24 h) during maintenance therapy with inhaled corticosteroids alone or in combination with long-acting beta agonists. The final model showed that reliever inhaler use is higher in patients who have been diagnosed with asthma for > 10 years, are smokers, have higher asthma symptom scores, and are obese or extremely obese. Patients who had asthma attacks also used their reliever inhalers more often. In addition, to understand how relief inhalers are used in real-life situations, we also created heatmaps that include a wide range of patient characteristics. By using individual patient data together with this model, we have learned that smoking, asthma control, BMI, long history of asthma and previous asthma attacks significantly influence reliever use. This information can help physicians and healthcare professionals understand how well someone's asthma is managed. A patient who uses their reliever inhaler often is likely not to have their asthma well controlled by their regular medications.

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Conflict of interest statement

Ian Pavord has received honoraria for speaking at sponsored meetings from AstraZeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK, and payments for organising educational events from AstraZeneca, GSK, Sanofi/Regeneron and Teva; he has received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi and Knopp and payments to support FDA approval meetings from GSK; he has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, AstraZeneca, Teva and Chiesi; he has received a grant from Chiesi to support a Phase 2 clinical trial in Oxford; he is co-patent holder of the rights to the Leicester Cough Questionnaire and has received payments for its use in clinical trials from Merck, Bayer and Insmmed; and in 2014–2015 he was an expert witness for a patent dispute involving AstraZeneca and Teva; Guy Brusselle has acted as a speaker/consultant for AstraZeneca, Boehringer-Ingelheim, Chiesi, GSK, Novartis, Sanofi and Teva; Arzu Yorgancıoğlu has received research grants from Novartis, MSD, AstraZeneca and Sanofi, and has acted as a speaker/consultant for AstraZeneca, Abdi İbrahim, GSK, Novartis, Chiesi and Bilim; Paulo Pitrez has acted as a speaker/consultant for AstraZeneca, GSK, Novartis, Boehringer Ingelheim and Sanofi; Sven van Dijkman, Sean Oosterholt, Sourabh Fulmali, Anurita Majumdar and Oscar Della Pasqua are GSK employees and hold stocks/shares in GSK.

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

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Publication types, MeSH terms, Substancesexpand

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Am J Physiol Lung Cell Mol Physiol

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. 2024 Mar 1;326(3):L280-L291.

Early-life pulmonary viral infection leads to long-term functional and lower airway structural changes in the lungs

[Carrie-Anne Malinczak](#)¹, [Wendy Fonseca](#)¹, [Steven M Hrycaj](#)², [Susan B Morris](#)¹, [Andrew J Rasky](#)¹, [Kazuma Yagi](#)¹, [Deneen M Wellik](#)³, [Steven F Ziegler](#)⁴, [Rachel L Zemans](#)², [Nicholas W Lukacs](#)^{1,5}

Affiliations expand

- PMID: 38290164
- DOI: [10.1152/ajplung.00300.2023](https://doi.org/10.1152/ajplung.00300.2023)

Abstract

Early-life respiratory virus infections have been correlated with enhanced development of childhood asthma. In particular, significant numbers of respiratory syncytial virus (RSV)-hospitalized infants go on to develop lung disease. It has been suggested that early-life viral infections may lead to altered lung development or repair that negatively impacts lung function later in life. Our data demonstrate that early-life RSV infection modifies lung structure, leading to decreased lung function. At 5 wk postneonatal RSV infection, significant defects are observed in baseline pulmonary function test (PFT) parameters consistent with decreased lung function as well as enlarged alveolar spaces. Lung function changes in the early-life RSV-infected group continue at 3 mo of age. The altered PFT and structural changes induced by early-life RSV were mitigated in *TSLPR*^{-/-} mice that have previously been shown to have reduced immune cell accumulation associated with a persistent Th2 environment. Importantly, long-term effects were demonstrated using a secondary RSV infection 3 mo following the initial early-life RSV infection and led to significant additional defects in lung function, with severe mucus deposition within the airways, and consolidation of the alveolar spaces. These studies suggest that early-life respiratory viral infection leads to alterations in lung structure/repair that predispose to diminished lung function later in life. **NEW & NOTEWORTHY** These studies outline a novel finding that early-life respiratory virus infection can alter lung structure and function long-term. Importantly, the data also indicate that there are critical links between inflammatory responses and subsequent events that produce a more severe pathogenic response later in

life. The findings provide additional data to support that early-life infections during lung development can alter the trajectory of airway function.

Keywords: RSV; lung function.

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

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12

Respir Med



. 2024 Mar;223:107543.

doi: 10.1016/j.rmed.2024.107543. Epub 2024 Jan 28.

[The diagnostic value of bronchial provocation testing combined with fractional exhaled nitric oxide \(FeNO\) in children with chest tightness - variant asthma \(CTVA\)](#)

[Tengteng Zhang](#)¹, [Lijuan Xu](#)², [Yingqian Zhang](#)¹, [Lina Zhen](#)³

Affiliations expand

- PMID: 38286340

- DOI: [10.1016/j.rmed.2024.107543](https://doi.org/10.1016/j.rmed.2024.107543)

Abstract

Background: Chest tightness-variant asthma (CTVA) is a novel atypical asthma characterized by chest tightness as the sole or primary symptom.

Objectives: To investigate the value of bronchial provocation testing combined with fractional exhaled nitric oxide (FeNO) in the diagnosis of CTVA in children.

Methods: This study included 95 children aged 6-14 years with chest tightness as the sole symptom, with a duration of symptoms exceeding 4 weeks. All subjects underwent FeNO measurement, pulmonary function testing, and bronchial provocation testing using the Astograph method. Subjects with positive bronchial provocation testing were classified as the CTVA group, while those with negative results served as the non-CTVA control group.

Results: The lung function of children in both groups was normal. The FeNO level in the CTVA group was (22.35 ± 9.91) ppb, significantly higher than the control group (14.85 ± 5.63) ppb, with a statistically significant difference ($P < 0.05$). The value of FeNO in diagnosing CTVA was analyzed using an ROC curve, with an area under the curve of 0.073 ($P < 0.05$). The optimal cutoff point for diagnosing CTVA using FeNO was determined to be 18.5 ppb, with a sensitivity of 60.3 % and specificity of 77.8 %. There was a negative correlation between FeNO and Dmin as well as PD15 ($P = 0.006$).

Conclusion: FeNO can serve as an adjunctive diagnostic tool for CTVA, with the optimal cutoff point for diagnosing CTVA being 18.5 ppb. However, FeNO is not a specific diagnostic marker for CTVA and should be used in conjunction with bronchial provocation testing to enhance its diagnostic value.

Keywords: Bronchial provocation testing; CTVA; Chest tightness-variant asthma; Fractional exhaled nitric oxide.

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Conflict of interest statement

Declaration of competing interest None.

SUPPLEMENTARY INFO

MeSH terms, Substances expand

FULL TEXT LINKS



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13

Meta-Analysis

Allergy



. 2024 Mar;79(3):643-655.

doi: 10.1111/all.16000. Epub 2024 Jan 23.

Plasma protein signatures of adult asthma

[Gordon J Smilnak](#)¹, [Yura Lee](#)², [Abhijnan Chattopadhyay](#)¹, [Annah B Wyss](#)¹, [Julie D White](#)^{1,3}, [Sinjini Sikdar](#)^{1,4}, [Jianping Jin](#)⁵, [Andrew J Grant](#)⁶, [Alison A Motsinger-Reif](#)⁷, [Jian-Liang Li](#)⁸, [Mikyeong Lee](#)¹, [Bing Yu](#)², [Stephanie J London](#)¹

Affiliations expand

- PMID: 38263798
- DOI: [10.1111/all.16000](https://doi.org/10.1111/all.16000)

Abstract

Background: Adult asthma is complex and incompletely understood. Plasma proteomics is an evolving technique that can both generate biomarkers and provide insights into disease mechanisms. We aimed to identify plasma proteomic signatures of adult asthma.

Methods: Protein abundance in plasma was measured in individuals from the Agricultural Lung Health Study (ALHS) (761 asthma, 1095 non-case) and the Atherosclerosis Risk in Communities study (470 asthma, 10,669 non-case) using the SOMAScan 5K array. Associations with asthma were estimated using covariate adjusted logistic regression and

meta-analyzed using inverse-variance weighting. Additionally, in ALHS, we examined phenotypes based on both asthma and seroatopy (asthma with atopy (n = 207), asthma without atopy (n = 554), atopy without asthma (n = 147), compared to neither (n = 948)).

Results: Meta-analysis of 4860 proteins identified 115 significantly (FDR<0.05) associated with asthma. Multiple signaling pathways related to airway inflammation and pulmonary injury were enriched (FDR<0.05) among these proteins. A proteomic score generated using machine learning provided predictive value for asthma (AUC = 0.77, 95% CI = 0.75-0.79 in training set; AUC = 0.72, 95% CI = 0.69-0.75 in validation set). Twenty proteins are targeted by approved or investigational drugs for asthma or other conditions, suggesting potential drug repurposing. The combined asthma-atopy phenotype showed significant associations with 20 proteins, including five not identified in the overall asthma analysis.

Conclusion: This first large-scale proteomics study identified over 100 plasma proteins associated with current asthma in adults. In addition to validating previous associations, we identified many novel proteins that could inform development of diagnostic biomarkers and therapeutic targets in asthma management.

Keywords: allergy; area under curve; biomarkers; precision medicine; proteomics.

© 2024 The Authors. Allergy published by John Wiley & Sons Ltd and European Academy of Allergy and Clinical Immunology. This article has been contributed to by U.S. Government employees and their work is in the public domain in the USA.

- [73 references](#)

SUPPLEMENTARY INFO

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

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[Review](#)

Acta Physiol (Oxf)



. 2024 Mar;240(3):e14092.

doi: 10.1111/apha.14092. Epub 2024 Jan 22.

The gut–lung axis and asthma susceptibility in early life

[Fariz G Kahhaleh](#)¹, [Gabriela Barrientos](#)^{2,3}, [Melanie L Conrad](#)¹

Affiliations expand

- PMID: 38251788
- DOI: [10.1111/apha.14092](https://doi.org/10.1111/apha.14092)

Abstract

Asthma is the most common chronic disease among children, with more than 300 million cases worldwide. Over the past several decades, asthma incidence has grown, and epidemiological studies identify the modernized lifestyle as playing a strong contributing role in this phenomenon. In particular, lifestyle factors that modify the maternal gut microbiome during pregnancy, or the infant microbiome in early life, can act as developmental programming events which determine health or disease susceptibility later in life. Microbial colonization of the gut begins at birth, and factors such as delivery mode, breastfeeding, diet, antibiotic use, and exposure to environmental bacteria influence the development of the infant microbiome. Colonization of the gut microbiome is crucial for proper immune system development and disruptions to this process can predispose a child to asthma development. Here, we describe the importance of early-life events for shaping immune responses along the gut-lung axis and why they may provide a window of opportunity for asthma prevention.

Keywords: DOHaD; antibiotic; asthma; early life; gut-lung axis; hygiene hypothesis; microbiome.

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- [142 references](#)

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Pediatr Infect Dis J



. 2024 Mar 1;43(3):234-241.

doi: 10.1097/INF.0000000000004193. Epub 2024 Jan 18.

[Risk Factors for Severe and Critical Coronavirus Disease 2019 in Children](#)

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Affiliations expand

- PMID: 38241652
- DOI: [10.1097/INF.0000000000004193](https://doi.org/10.1097/INF.0000000000004193)

Abstract

Background: Coronavirus disease 2019 (COVID-19) is generally mild in children; however, severe or critical cases may occur. In this nationwide study, we analyzed clinical manifestations in children diagnosed with severe acute respiratory syndrome coronavirus 2

to identify high-risk groups for severe or critical disease and compared the clinical features between the Delta- and Omicron-dominant periods.

Methods: Data were retrieved from the National Health Insurance Service (NHIS) database and merged with the Korea Disease Control and Prevention Agency-COVID-19-NHIS cohort, which includes information on COVID-19 cases and vaccination records. We included individuals <20 years old diagnosed with COVID-19 during both periods (Delta: July 25, 2021-January 15, 2022; Omicron: January 16, 2022-March 31, 2022).

Results: Proportion of severe or critical cases was higher during the Delta period than during the Omicron period. The Omicron period saw increased hospitalization for pneumonia and croup and increased likelihood of hospitalization for neurological manifestations. The risk of severe COVID-19 depended on age group (Delta: highest for 12-19 years; Omicron: 0-4 years). This risk was high in children with multiple complex chronic conditions during both periods and with obesity or asthma during the Delta but not during the Omicron period. Two-dose COVID-19 vaccination provided strong protection against severe disease in the Delta period (adjusted odds ratio: 0.20), with reduced effectiveness in the Omicron period (adjusted odds ratio: 0.91). However, it significantly reduced the risk of critical illness (adjusted odds ratio: 0.14).

Conclusions: These findings can facilitate identification of children at high risk of severe or critical COVID-19, who may require intensive medical support, and development of vaccination policies.

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Conflict of interest statement

The authors have no funding or conflicts of interest to disclose.

- [37 references](#)

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MeSH terms, Substancesexpand

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16

Clinical Trial

Respir Investig

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. 2024 Mar;62(2):216-222.

doi: 10.1016/j.resinv.2023.12.009. Epub 2024 Jan 10.

Safety and efficacy of sirolimus in hospitalised patients with COVID-19 pneumonia

[Abhishek Singla](#)¹, [Nusrat Harun](#)², [Daniel F Dilling](#)³, [Karim Merchant](#)⁴, [Susan McMahan](#)¹, [Rebecca Ingledue](#)¹, [Alexandria French](#)¹, [Josefina A Corral](#)⁵, [Leslie Korbee](#)⁶, [Elizabeth J Kopras](#)¹, [Nishant Gupta](#)⁷

Affiliations expand

- PMID: 38211546
- DOI: [10.1016/j.resinv.2023.12.009](https://doi.org/10.1016/j.resinv.2023.12.009)

Abstract

Background: There is a critical need to develop novel therapies for COVID-19.

Methods: We conducted a phase 2, multicentre, placebo-controlled, double-blind, randomised trial; hospitalised patients with hypoxemic respiratory failure due to COVID-19 and at least one poor prognostic biomarker, were given sirolimus (6 mg on Day 1 followed by 2 mg daily for 14 days or hospital discharge, whichever happens first) or placebo, in a 2:1 randomization scheme favouring sirolimus. Primary outcome was the proportion of patients alive and free from advanced respiratory support measures at Day 28.

Results: Between April 2020 and April 2021, 32 patients underwent randomization and 28 received either sirolimus (n = 18) or placebo (n = 10). Mean age was 57 years and 75 % of

the subjects were men. Twenty-two subjects had at least one co-existing condition (Diabetes, hypertension, obesity, CHF, or asthma/COPD) associated with worse prognosis. Mean FiO₂ requirement was 0.35. There was no difference in the proportion of patients who were alive and free from advanced respiratory support measures in the sirolimus group (n = 15, 83 %) compared with the placebo group (n = 8, 80 %). Although patients in the sirolimus group demonstrated faster improvement in oxygenation and spent less time in the hospital, these differences were not statistically significant. There was no between-group difference in the rate of change in serum biomarkers such as LDH, ferritin, d-dimer or lymphocyte count. There was a decreased risk of thromboembolic complications in patients on sirolimus compared with placebo.

Conclusions: Larger studies are warranted to evaluate the role sirolimus in COVID-19 infection.

Keywords: Clinical trial; Rapamycin; SARS-CoV-2; SCOPE; mTOR.

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Conflict of interest statement

Declaration of competing interest The authors report no conflict of interest.

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Publication types, MeSH terms, Substancesexpand

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[Review](#)

Respir Investig

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. 2024 Mar;62(2):206-215.

doi: 10.1016/j.resinv.2023.12.015. Epub 2024 Jan 10.

Efficacy and safety of macrolide therapy for adult asthma: A systematic review and meta-analysis

[Yosuke Fukuda](#)¹, [Nobuyuki Horita](#)², [Masaharu Aga](#)³, [Fumihiro Kashizaki](#)⁴, [Yu Hara](#)⁵, [Yasushi Obase](#)⁶, [Akio Niimi](#)⁷, [Takeshi Kaneko](#)⁵, [Hiroshi Mukae](#)⁶, [Hironori Sagara](#)⁸

Affiliations expand

- PMID: 38211545
- DOI: [10.1016/j.resinv.2023.12.015](https://doi.org/10.1016/j.resinv.2023.12.015)

Free article

Abstract

Background: The evidence for macrolide therapy in adult asthma is not properly established and remains controversial. We conducted a systematic review and meta-analysis to examine the efficacy and safety of macrolide therapy for adult asthma.

Methods: We searched randomized controlled trials from MEDLINE via the PubMed, CENTRAL, and Ichushi Web databases. The primary outcome was asthma exacerbation. The secondary outcomes were serious adverse events (including mortality), asthma-related quality of life (symptom scales, Asthma Control Questionnaire, and Asthma Quality of Life Questionnaire), rescue medication (puffs/day), respiratory function (morning peak expiratory flow, evening peak flow, and forced expiratory volume in 1 s), bronchial hyperresponsiveness, and minimum oral corticosteroid dose. Of the 805 studies, we selected seven studies for the meta-analysis, which was conducted using a random-effects model.

Systematic review registration: University Hospital Medical Information Network Clinical Trials Registry (UMIN000050824).

Results: No significant difference between macrolide and placebo for asthma exacerbations was observed (risk ratio 0.71, 95 % confidence interval [CI] 0.46-1.09; $p = 0.12$). Macrolide therapy for adult asthma showed a significant improvement in rescue medication with short-acting beta-agonists (mean difference -0.41, 95 % CI -0.78 to -0.04;

$p = 0.03$). Macrolide therapy did not show more serious adverse events (odds ratio 0.61, 95% CI 0.34-1.10; $p = 0.10$) than those with placebo. The other secondary outcomes were not significantly different between the macrolide and placebo groups.

Conclusions: Macrolide therapy for adult asthma may be more effective than placebo and could be a treatment option.

Keywords: Adult; Asthma; Azithromycin; Clarithromycin; Exacerbation; Macrolide.

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Conflict of interest statement

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

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Am J Physiol Lung Cell Mol Physiol

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. 2024 Mar 1;326(3):L266-L279.

doi: 10.1152/ajplung.00419.2022. Epub 2023 Dec 27.

[Small airway fibroblasts from patients with chronic obstructive pulmonary disease exhibit cellular senescence](#)

[Catherine L Wrench](#)^{1,2}, [Jonathan R Baker](#)¹, [Sue Monkley](#)³, [Peter S Fenwick](#)¹, [Lynne Murray](#)², [Louise E Donnelly](#)¹, [Peter J Barnes](#)¹

Affiliations expand

- PMID: 38150543
- DOI: [10.1152/ajplung.00419.2022](https://doi.org/10.1152/ajplung.00419.2022)

Free article

Abstract

Small airway disease (SAD) is a key early-stage pathology of chronic obstructive pulmonary disease (COPD). COPD is associated with cellular senescence whereby cells undergo growth arrest and express the senescence-associated secretory phenotype (SASP) leading to chronic inflammation and tissue remodeling. Parenchymal-derived fibroblasts have been shown to display senescent properties in COPD, however small airway fibroblasts (SAFs) have not been investigated. Therefore, this study investigated the role of these cells in COPD and their potential contribution to SAD. To investigate the senescent and fibrotic phenotype of SAF in COPD, SAFs were isolated from nonsmoker, smoker, and COPD lung resection tissue ($n = 9-17$ donors). Senescence and fibrotic marker expressions were determined using iCELLigence (proliferation), qPCR, Seahorse assay, and ELISAs. COPD SAFs were further enriched for senescent cells using FACS Aria Fusion based on cell size and autofluorescence (10% largest/autofluorescent vs. 10% smallest/nonautofluorescent). The phenotype of the senescence-enriched population was investigated using RNA sequencing and pathway analysis. Markers of senescence were observed in COPD SAFs, including senescence-associated β -galactosidase, SASP release, and reduced proliferation. Because the pathways driving this phenotype were unclear, we used cell sorting to enrich senescent COPD SAFs. This population displayed increased p21^{CIP1} and p16^{INK4a} expression and mitochondrial dysfunction. RNA sequencing suggested these senescent cells express genes involved in oxidative stress response, fibrosis, and mitochondrial dysfunction pathways. These data suggest COPD SAFs are senescent and may be associated with fibrotic properties and mitochondrial dysfunction. Further understanding of cellular senescence in SAFs may lead to potential therapies to limit SAD progression. **NEW & NOTEWORTHY** Fibroblasts and senescence are thought to play key roles in the pathogenesis of small airway disease and COPD; however, the characteristics of small airway-derived fibroblasts are not well explored. In this study we isolate and enrich the senescent small airway-derived fibroblast (SAF) population from COPD lungs and explore the pathways driving this phenotype using bulk RNA-seq.

Keywords: COPD; fibroblast; senescence; small airway disease.

- [Cited by 1 article](#)

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MeSH terms, Supplementary concepts, Grants and fundingexpand

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Pediatr Pulmonol

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. 2024 Mar;59(3):798-800.

doi: 10.1002/ppul.26825. Epub 2023 Dec 27.

[Asthma care: The need for evidence-based, equitable, and affordable approaches](#)

[Kavita Jyoti Prakash](#)¹, [Anand Gourishankar](#)²

Affiliations expand

- PMID: 38149486
- DOI: [10.1002/ppul.26825](https://doi.org/10.1002/ppul.26825)

No abstract available

Keywords: asthma and early wheeze; asthma care; equity; social dimensions of pulmonary medicine.

- [11 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Meta-Analysis

Arch Gerontol Geriatr

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. 2024 Mar;118:105310.

doi: 10.1016/j.archger.2023.105310. Epub 2023 Dec 12.

Causal relationship between frailty and chronic obstructive pulmonary disease or asthma: A two sample bidirectional Mendelian randomization study

[Jingge Qu](#)¹, [Ying Liang](#)¹, [Yafei Rao](#)¹, [Yuqiang Pei](#)¹, [Danyang Li](#)¹, [Yue Zhang](#)¹, [Yahong Chen](#)¹, [Yongchang Sun](#)²

Affiliations expand

- PMID: 38128266
- DOI: [10.1016/j.archger.2023.105310](https://doi.org/10.1016/j.archger.2023.105310)

Abstract

Background: Observational studies have established a strong association between frailty and obstructive lung diseases. However, the causal nature of this association remains unclear. To address this gap, we conducted a bidirectional Mendelian randomization (MR) study to investigate the causal relationship between frailty, as measured by the frailty index (FI), and chronic obstructive pulmonary disease (COPD) or asthma.

Methods: The latest meta-analysis of genome-wide association studies for FI, which included individuals of European ancestry from UK Biobank and TwinGene (N = 175,226), yielded the genetic instruments for frailty and outcome summary statistics. The genetic instrument for COPD and asthma, as well as the outcome summary data, were derived from the GWAS conducted on individuals of European ancestry from the FinnGen, with a sample size of 16,410 cases and 283,589 controls for COPD, and 37,253 cases and 187,112 controls for asthma. The analysis of MR was conducted employing the inverse-variance weighted (IVW) method, complemented by the weighted median method, MR-Egger regression, and MR pleiotropy residual sum and outlier (MR-PRESSO) test.

Results: Our results showed that genetically predicted higher FI was significantly associated with increased risk of COPD (odds ratio [OR] 1.75, 95 % confidence interval [CI] 1.29-2.36) and asthma (OR 2.10, 95 % CI 1.44-3.16). In the reverse direction analysis, genetic liability to both COPD (beta 0.06, 95 % CI 0.01-0.10) and asthma (beta 0.08, 95 % CI 0.06-0.11) showed significant associations with a higher FI.

Conclusions: Our research has reinforced the existing evidence supporting a reciprocal causal relationship between frailty and obstructive lung diseases. A deeper comprehension of this interconnection is imperative for the prevention and treatment of obstructive lung diseases.

Keywords: Asthma; Chronic obstructive pulmonary disease; Frailty; Mendelian randomization study.

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Conflict of interest statement

Declaration of Competing Interest The authors have declared no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

Pediatr Pulmonol



. 2024 Mar;59(3):743-749.

doi: 10.1002/ppul.26824. Epub 2023 Dec 20.

[Palivizumab prophylaxis in preterm infants and subsequent wheezing/asthma: 10-year follow-up study](#)

[Masahiko Kato](#)^{1,2}, [Hiroyuki Mochizuki](#)^{1,2}, [Yuichi Kama](#)¹, [Satoshi Kusuda](#)³, [Kenji Okada](#)⁴, [Shigemi Yoshihara](#)⁵, [Hiroyuki Furuya](#)⁶, [Eric A F Simões](#)⁷; [Scientific Committee for Elucidation of Infantile Asthma \(SCELIA\)](#)

Affiliations [expand](#)

- PMID: 38116923
- DOI: [10.1002/ppul.26824](https://doi.org/10.1002/ppul.26824)

Abstract

Background: Respiratory syncytial virus (RSV) causes not only infantile recurrent wheezing but also the development of asthma. To investigate whether palivizumab, an anti-RSV

monoclonal antibody, prophylaxis given to preterm infants during the first RSV season reduces the incidence of subsequent recurrent wheezing and/or development of asthma, at 10 years of age.

Methods: We conducted an observational prospective multicenter (52 registered hospitals in Japan) case-control study in preterm infants with a gestational age between 33 and 35 weeks followed for 6 years. During the 2007-2008 RSV season, the decision to administer palivizumab was made based on standard medical practice (SCELIA study). Here, we followed these subjects until 10 years of age. Parents of study subjects reported the patients' physician's assessment of recurrent wheezing/asthma, using a report card and a novel mobile phone-based reporting system using the internet. The relationship between RSV infection and asthma development, as well as the relationship between other factors and asthma development, were investigated.

Results: Of 154 preterm infants enrolled, 113 received palivizumab during the first year of life. At 10 years, although both recurrent wheezing and development of asthma were not significantly different between the treated and untreated groups, maternal smoking with aeroallergen sensitization of the patients was significantly correlated with physician-diagnosed asthma.

Conclusions: In contrast to the prior study results at 6 years, by 10 years palivizumab prophylaxis had no impact on recurrent wheezing or asthma, but there was a significant correlation between maternal passive smoking with aeroallergen sensitization and development of asthma by 10 years of age.

Keywords: aeroallergen sensitization; asthma development; palivizumab; passive smoking; respiratory syncytial virus.

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- [33 references](#)

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Publication types, MeSH terms, Substances, Grants and fundingexpand

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. 2024 Mar;20(3):335-344.

doi: 10.1016/j.sapharm.2023.12.002. Epub 2023 Dec 10.

The association of depressive symptoms and medication adherence in asthma patients: The mediation effect of medication beliefs

[Ruiying Dong](#)¹, [Shanwen Sun](#)¹, [Yajun Sun](#)¹, [Yali Wang](#)¹, [Xiaochun Zhang](#)²

Affiliations expand

- PMID: 38110324
- DOI: [10.1016/j.sapharm.2023.12.002](https://doi.org/10.1016/j.sapharm.2023.12.002)

Free article

Abstract

Background: The significant role of depression in influencing medication beliefs, which are pivotal cognitive factors that strongly influence medication adherence, has been established. Poor adherence to asthma-controlled medication poses an significant barrier to achieving optimal asthma management.

Objective: To explore the potential mediating effects of medication beliefs on the relationship between depressive symptoms and medication adherence in patients with asthma.

Methods: Demographic and clinical characteristics, depressive symptoms, medication adherence, and medication beliefs were collected using questionnaires. Structural equation modeling, was utilized to model medication beliefs as mediators in the relationship between depressive symptoms and medication adherence. Bootstrapping was performed

to analyze the mediation- and contrast-specific indirect effects of the two medication beliefs.

Results: Among the patients who participated in the study, 29.6 % with depressive symptoms were more prone to poor adherence and exhibited skepticism toward asthma medications. Depression had a direct effect (direct effect = -0.275, 95%CI: -0.369 to -0.190) and an indirect effect on adherence mediated by medication beliefs (indirect effect = -0.168, 95%CI: -0.224 to -0.121). The specific mediation effect of concern belief was stronger than that of necessity belief (difference = -0.076, 95%CI: -0.132 to -0.029).

Conclusion: Depressive symptoms have a direct impact on medication adherence as well as an indirect effect mediated by beliefs about medication, particularly concerns belief.

Keywords: Adherence; Asthma; Depressive symptoms; Medication beliefs.

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MeSH termsexpand

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Randomized Controlled Trial

J Pediatr

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. 2024 Mar;266:113867.

doi: 10.1016/j.jpeds.2023.113867. Epub 2023 Dec 6.

Effect of the Telemedicine Enhanced Asthma Management Through the Emergency Department (TEAM-ED) Program on Asthma Morbidity: A Randomized Controlled Trial

[Jill S Halterman](#)¹, [Maria Fagnano](#)², [Paul Tremblay](#)², [Arlene Butz](#)³, [Tamara T Perry](#)⁴, [Hongyue Wang](#)⁵

Affiliations expand

- PMID: 38065280
- DOI: [10.1016/j.jpeds.2023.113867](https://doi.org/10.1016/j.jpeds.2023.113867)

Abstract

Objective: To test the effectiveness of a telemedicine-based program in reducing asthma morbidity among children who present to the emergency department (ED) for asthma, by facilitating primary care follow-up and promoting delivery of guideline-based care.

Study design: We included children (3-12 years of age) with persistent asthma who presented to the ED for asthma, who were then randomly assigned to Telemedicine Enhanced Asthma Management through the Emergency Department (TEAM-ED) or enhanced usual care. TEAM-ED included (1) school-based telemedicine follow-ups, completed by a primary care provider, (2) point-of-care prompting to promote guideline-based care, and 3) an opportunity for 2 additional telemedicine follow-ups. The primary outcome was the mean number of symptom-free days (SFDs) over 2 weeks at 3, 6, 9, and 12 months.

Results: We included 373 children from 2016 through 2021 (participation rate 68%; 54% Black, 32% Hispanic, 77% public insurance; mean age, 6.4 years). Demographic characteristics and asthma severity were similar between groups at baseline. Most (91%) TEAM-ED children had ≥ 1 telemedicine visit and 41% completed 3 visits. At 3 months, caregivers of children in TEAM-ED reported more follow-up visits (66% vs 48%; aOR, 2.07; 95% CI, 1.28-3.33), preventive asthma medication actions (90% vs 79%; aOR, 3.28; 95% CI, 1.56-6.89), and use of a preventive medication (82% vs 69%; aOR, 2.716; 95% CI, 1.45-5.08), compared with enhanced usual care. There was no difference between groups in medication adherence or asthma morbidity. When only prepandemic data were included,

there was greater improvement in SFDs over time for children in TEAM-ED vs enhanced usual care.

Conclusions: TEAM-ED significantly improved follow-up and preventive care after an ED visit for asthma. We also saw improved SFDs with pre-pandemic data. The lack of overall improvement in morbidity and adherence indicates the need for additional ongoing management support.

Trial registration: [NCT02752165](https://www.clinicaltrials.gov/ct2/show/study/NCT02752165).

Keywords: asthma; child; emergency department; prevention; telemedicine.

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Conflict of interest statement

Declaration of Competing Interest The authors declare no conflicts of interest. Funded by a grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health (R01HL091835). The funder had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated data, Grants and funding expand

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Case Reports

J Diabetes Investig

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. 2024 Mar;15(3):388-390.

[A case of type 2 diabetes mellitus with weight gain and worsening of glycemic management after tezepelumab administration for severe bronchial asthma](#)

[Kotaro Umamoto](#)¹, [Ryotaro Bouchi](#)^{1,2}, [Noriko Ihana-Sugiyama](#)^{1,2}, [Noriko Kodani](#)¹, [Mitsuru Ohsugi](#)^{1,2}, [Masayuki Hojo](#)³, [Kohjiro Ueki](#)^{1,4}, [Hiroshi Kajio](#)¹

Affiliations expand

- PMID: 38064175
- PMCID: [PMC10906019](#)
- DOI: [10.1111/jdi.14127](#)

Free PMC article

Abstract

Some cases of bronchial asthma are refractory to conventional therapies. As the pathogenesis of bronchial asthma has been clarified, new treatments, such as bronchial thermoplasty and biological drugs, have been developed. Tezepelumab, an anti-thymic stromal lymphopoietin antibody, has been reported to inhibit the exacerbation of severe asthma; however, its adverse effects on glucose metabolism have not yet been reported. We encountered a case of weight gain and worsening glycemic management in a patient with type 2 diabetes and refractory bronchial asthma after the initiation of tezepelumab treatment. It has been reported that the overexpression of thymic stromal lymphopoietin in mice resulted in an enhanced release of free fatty acids from adipose tissues and the liver; thus, the administration of anti-thymic stromal lymphopoietin antibodies in the present case might have caused obesity, fatty liver and lower glucose tolerance.

Keywords: Asthma; Obesity; Tezepelumab.

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

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Pulm Ther

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. 2024 Mar;10(1):53-67.

doi: 10.1007/s41030-023-00245-9. Epub 2023 Dec 8.

[Effect of Tezepelumab on the Humoral Immune Response to Seasonal Quadrivalent Influenza Vaccination in Patients with Moderate to Severe Asthma: The Phase 3b VECTOR Study](#)

[Jeremy Cole](#)¹, [Iwona Capała-Szczurko](#)², [Stephanie Roseti](#)³, [Claudia Chen](#)⁴, [Scott Caveney](#)⁵, [Anastasia A Aksyuk](#)⁶, [Katie Streicher](#)⁶, [Sandhia Ponnarambil](#)^{7,8}, [Gene Colice](#)³

Affiliations [expand](#)

- PMID: 38064153

- PMID: [PMC10881940](#)
- DOI: [10.1007/s41030-023-00245-9](#)

Free PMC article

Abstract

Introduction: Annual influenza vaccinations are recommended for adolescents and adults with moderate to severe asthma. This study investigated the effect of tezepelumab, a human monoclonal antibody that blocks the activity of thymic stromal lymphopoietin, on the humoral immune response to the quadrivalent seasonal influenza vaccine in patients with moderate to severe asthma.

Methods: VECTOR was a phase 3b, randomized, multicenter, double-blind, parallel-group, placebo-controlled study. Adolescents (aged 12-17 years) and young adults (aged 18-21 years) with moderate to severe asthma were enrolled across 15 centers in the USA. Patients received tezepelumab 210 mg or placebo subcutaneously at weeks 0, 4, 8, and 12, and a single dose of inactivated quadrivalent seasonal influenza vaccine at week 12 before receiving study treatment. Immediately before vaccination and at 4 weeks postvaccination (week 16), strain-specific antibody responses were assessed for four influenza antigens by hemagglutination inhibition (HAI) and microneutralization (MN) assays. Safety was assessed.

Results: Seventy patients were randomized to tezepelumab (n = 35) or placebo (n = 35). There were no meaningful differences in HAI or MN antibody responses between treatment groups at week 16. HAI assay geometric mean fold rises (GMFRs) for influenza strains were 1.76-7.34 for tezepelumab and 1.46-4.75 for placebo. MN assay GMFRs were 4.00-14.56 for tezepelumab and 3.56-10.62 for placebo. In the HAI assay, a fourfold or larger rise in antibody titer from weeks 12 to 16 occurred in 15.2-78.8% and 15.2-51.5% of tezepelumab and placebo recipients, respectively, and 97.0-100% of patients in both treatment groups achieved an antibody titer of at least 40 at week 16. No unexpected safety findings occurred.

Conclusion: There was no observed suppression of the humoral immune response after influenza vaccination in adolescents and young adults with moderate to severe asthma treated with tezepelumab. Therefore, the influenza vaccine can be administered to this patient population during tezepelumab treatment.

Gov identifier: [NCT05062759](#).

Keywords: Airway obstruction; Hemagglutinin; Inflammatory disorders; Microneutralization; Thymic stromal lymphopoietin.

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Conflict of interest statement

Jeremy Cole has nothing to declare. Iwona Cąpała-Szczurko, Stephanie Roseti, Claudia Chen, Anastasia A Aksyuk, Katie Streicher, and Sandhia Ponnarambil are employees of AstraZeneca and may own stock or stock options in AstraZeneca. Scott Caveney is an employee of Amgen and owns stock in Amgen. Gene Colice was an employee of AstraZeneca at the time of the study.

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

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26

J Infect Dis

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. 2024 Mar 1;229(Supplement_1):S70-S77.

doi: 10.1093/infdis/jiad510.

Respiratory Syncytial Virus–Associated Hospitalization in Adults With

Comorbidities in 2 European Countries: A Modeling Study

[Richard Osei-Yeboah](#)¹, [Caroline Klint Johannesen](#)², [Amanda Marie Egeskov-Cavling](#)³, [Junru Chen](#)⁴, [Toni Lehtonen](#)⁵, [Arantxa Urchueguía Fornes](#)⁶, [John Paget](#)⁷, [Thea K Fischer](#)², [Xin Wang](#)^{1,4}, [Harish Nair](#)¹, [Harry Campbell](#)¹

Affiliations expand

- PMID: 37970679
- DOI: [10.1093/infdis/jiad510](https://doi.org/10.1093/infdis/jiad510)

Abstract

Background: Individuals with comorbidities are at increased risk of severe respiratory syncytial virus (RSV) infection. We estimated RSV-associated respiratory hospitalization among adults aged ≥ 45 years with comorbidities in Denmark and Scotland.

Methods: By analyzing national hospital and virologic data, we estimated annual RSV-associated hospitalizations by 7 selected comorbidities and ages between 2010 and 2018. We estimated rate ratios of RSV-associated hospitalization for adults with comorbidity than the overall population.

Results: In Denmark, annual RSV-associated hospitalization rates per 1000 adults ranged from 3.1 for asthma to 19.4 for chronic kidney disease (CKD). In Scotland, rates ranged from 2.4 for chronic liver disease to 9.0 for chronic obstructive pulmonary disease (COPD). In both countries, we found a 2- to 4-fold increased risk of RSV hospitalization for adults with COPD, ischemic heart disease, stroke, and diabetes; a 1.5- to 3-fold increased risk for asthma; and a 3- to 7-fold increased risk for CKD. RSV hospitalization rates among adults aged 45 to 64 years with COPD, asthma, ischemic heart disease, or CKD were higher than the overall population.

Conclusions: This study provides important evidence for identifying risk groups and assisting health authorities in RSV vaccination policy making.

Keywords: adults; comorbidity; hospitalization; respiratory syncytial virus.

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Conflict of interest statement

Potential conflicts of interest. H. C. reports grants, personal fees, and nonfinancial support from the World Health Organization; grants and personal fees from Sanofi Pasteur; and grants from the Bill and Melinda Gates Foundation, outside this submitted work. H. C. is a shareholder in the Journal of Global Health Ltd. H. N. reports grants from Pfizer and Icosavax and consulting fees from the World Health Organization, Pfizer, Bill and Melinda Gates Foundation, Abbvie, and Sanofi, outside the submitted work. H. N. reports participation on a data safety monitoring board or advisory board for GSK, Sanofi, Merck, the World Health Organization, Janssen, Novavax, Resvinct, Icosavax, and Pfizer. X. W. reports grants from GlaxoSmithKline and consultancy fees from Pfizer, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

SUPPLEMENTARY INFO

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27

Review

Br J Pharmacol

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. 2024 Mar;181(5):610-639.

doi: 10.1111/bph.16272. Epub 2023 Dec 20.

[Use of human airway smooth muscle in vitro and ex vivo to investigate drugs](#)

for the treatment of chronic obstructive respiratory disorders

[Luigino Calzetta](#)¹, [Clive Page](#)², [Maria Gabriella Matera](#)³, [Mario Cazzola](#)⁴, [Paola Rogliani](#)⁴

Affiliations expand

- PMID: 37859567
- DOI: [10.1111/bph.16272](https://doi.org/10.1111/bph.16272)

Abstract

Isolated airway smooth muscle has been extensively investigated since 1840 to understand the pharmacology of airway diseases. There has often been poor predictability from murine experiments to drugs evaluated in patients with asthma or chronic obstructive pulmonary disease (COPD). However, the use of isolated human airways represents a sensible strategy to optimise the development of innovative molecules for the treatment of respiratory diseases. This review aims to provide updated evidence on the current uses of isolated human airways in validated in vitro methods to investigate drugs in development for the treatment of chronic obstructive respiratory disorders. This review also provides historical notes on the pioneering pharmacological research on isolated human airway tissues, the key differences between human and animal airways, as well as the pivotal differences between human medium bronchi and small airways. Experiments carried out with isolated human bronchial tissues in vitro and ex vivo replicate many of the main anatomical, pathophysiological, mechanical and immunological characteristics of patients with asthma or COPD. In vitro models of asthma and COPD using isolated human airways can provide information that is directly translatable into humans with obstructive lung diseases. Regardless of the technique used to investigate drugs for the treatment of chronic obstructive respiratory disorders (i.e., isolated organ bath systems, videomicroscopy and wire myography), the most limiting factors to produce high-quality and repeatable data remain closely tied to the manual skills of the researcher conducting experiments and the availability of suitable tissue.

Keywords: COPD; airway smooth muscle; asthma; epithelium damage; in vitro models; isolated human airways.

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- [314 references](#)

SUPPLEMENTARY INFO

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J Asthma

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. 2024 Mar;61(3):194-202.

doi: 10.1080/02770903.2023.2260868. Epub 2024 Feb 8.

[The relationships between Physical activity and asthma control and Body Mass Index \(BMI\) in patients with asthma](#)

[Bonny Rockette-Wagner](#)¹, [Juan P Wisnivesky](#)², [Fernando Holguin](#)³, [Jyoti Ankam](#)², [Arushi Arora](#)², [Emily Federmann](#)², [Vongphone Smith](#)³, [Alex D Federman](#)², [Molly B Conroy](#)⁴

Affiliations expand

- PMID: 37847059
- DOI: [10.1080/02770903.2023.2260868](https://doi.org/10.1080/02770903.2023.2260868)

Abstract

Objective: Asthma is one of the most common chronic conditions in developed countries. We examined whether physical activity (PA) is related to asthma control and body mass index (BMI) in asthma patients.

Methods: Cross-sectional data collected on PA (ActiGraph GT3X-BT), asthma control (the Asthma Control Questionnaire; ACQ), and BMI were examined in 206 adults (mean[*sd*] age 47.2[13.8] years; 49.5% had an obese BMI) with clinically diagnosed asthma. Relationships between PA and continuous BMI and asthma control were assessed using linear regression. Differences in PA across obesity (non-obese: <30 Kg/m²/obese: ≥30 Kg/m²) and asthma control categories (controlled: ≤0.75/uncontrolled: >0.75 ACQ score) were also examined.

Results: Median (*p*₂₅, *p*₇₅) steps counts and peak cadence were 6035 (4248, 8461) steps/day and 123 (115, 133) steps in a minute, respectively. There were nearly 2000 fewer steps/day among those with uncontrolled asthma versus controlled and among those with obese BMI versus nonobese, respectively (both *p* < 0.05). In regression models adjusted for relevant covariates each 1-unit increase in ACQ score was associated with -686 [95%CI -997, -13] (*p* ≤ 0.05) average steps/day. The statistical significance of these findings was attenuated (*p* ≥ 0.05) when BMI was added to the model. However, the point estimate was not reduced (-766 [95%CI -1060, 34]).

Conclusions: Overall step counts were low in this population despite peak cadence values suggesting that most participants could perform moderate intensity activity. Increasing step counts should be considered an important lifestyle intervention goal in obese and non-obese asthma patients with low PA levels.

Keywords: Overweight; accelerometry; cadence; obesity; steps.

SUPPLEMENTARY INFO

MeSH termsexpand

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Allergy

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. 2024 Mar;79(3):656-666.

doi: 10.1111/all.15918. Epub 2023 Oct 17.

Tezepelumab decreases airway epithelial IL-33 and T2-inflammation in response to viral stimulation in patients with asthma

[A Sverrild](#)¹, [S Cerps](#)², [J J Nieto-Fontarigo](#)^{2,3,4}, [S Ramu](#)², [M Hvidtfeldt](#)¹, [M Menzel](#)², [J Kearley](#)⁵, [J M Griffiths](#)⁶, [J R Parnes](#)⁷, [C Porsbjerg](#)¹, [L Uller](#)²

Affiliations expand

- PMID: 37846599
- DOI: [10.1111/all.15918](https://doi.org/10.1111/all.15918)

Abstract

Background: Respiratory virus infections are main triggers of asthma exacerbations. Tezepelumab, an anti-TSLP mAb, reduces exacerbations in patients with asthma, but the effect of blocking TSLP on host epithelial resistance and tolerance to virus infection is not known.

Aim: To examine effects of blocking TSLP in patients with asthma on host resistance (IFN β , IFN λ , and viral load) and on the airway epithelial inflammatory response to viral challenge.

Methods: Bronchoalveolar lavage fluid (BALF, n = 39) and bronchial epithelial cells (BECs) were obtained from patients with uncontrolled asthma before and after 12 weeks of tezepelumab treatment (n = 13) or placebo (n = 13). BECs were cultured in vitro and exposed to the viral infection mimic poly(I:C) or infected by rhinovirus (RV). Alarmins, T2- and pro-inflammatory cytokines, IFN β IFN λ , and viral load were analyzed by RT-qPCR and multiplex ELISA before and after stimulation.

Results: IL-33 expression in unstimulated BECs and IL-33 protein levels in BALF were reduced after 12 weeks of tezepelumab. Further, IL-33 gene and protein levels decreased in BECs challenged with poly(I:C) after tezepelumab whereas TSLP gene expression remained unaffected. Poly(I:C)-induced IL-4, IL-13, and IL-17A release from BECs was also

reduced with tezepelumab whereas IFN β and IFN λ expression and viral load were unchanged.

Conclusion: Blocking TSLP with tezepelumab in vivo in asthma reduced the airway epithelial inflammatory response including IL-33 and T2 cytokines to viral challenge without affecting anti-viral host resistance. Our results suggest that blocking TSLP stabilizes the bronchial epithelial immune response to respiratory viruses.

Keywords: airway epithelium; asthma; tezepelumab; virus.

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- [33 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and fundingexpand

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Multicenter Study

J Asthma

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. 2024 Mar;61(3):232-237.

doi: 10.1080/02770903.2023.2263078. Epub 2024 Feb 8.

[Safety and efficacy of benralizumab in elderly subjects with severe asthma](#)

[Marcela Valverde-Monge](#)^{1,2}, [Remedios Cárdenas](#)³, [Ismael García-Moguel](#)^{4,5}, [Ana Rosado](#)⁶, [Mar Gandolfo-Cano](#)^{7,8}, [Teresa Robledo Echarren](#)^{9,10}, [María Del Mar Moro-Moro](#)¹¹, [María Del Mar Reaño Martos](#)¹², [Rafael Pineda-Pineda](#)¹³, [Cristina Martín-Arriscado Arroba](#)¹⁴, [Javier Domínguez-Ortega](#)¹⁵; [AIRE Group](#)

Affiliations [expand](#)

- PMID: 37737844
- DOI: [10.1080/02770903.2023.2263078](https://doi.org/10.1080/02770903.2023.2263078)

Abstract

Introduction: The prevalence of asthma in adults >65 years old is approximately 12-14%, and 10% have severe asthma. A higher mortality rate is observed in subjects with asthma >65 years old and especially >80 years old.

Objective: To analyze the effectiveness and safety of at least three doses of benralizumab in a subgroup of elderly subjects (>65 years old) with uncontrolled severe eosinophilic asthma in real-life conditions.

Methods: This was a retrospective multicenter study (AUTOBENRA study) conducted in 9 hospitals that included 72 patients aged >18 years old with uncontrolled severe asthma based on the Spanish Asthma Guidelines who were treated with at least three doses of benralizumab, self-administered at home since before April 30, 2021. The recruitment period ended on October 1, 2021. Written consent was obtained before the study commencement. In this subanalysis, we compared the results between patients >65 years old and patients <65 years old.

Results: A total of 72 subjects with severe asthma were screened, and 54 were included (*MD*: 57.3 ± 10 years old). There were 12 subjects aged >65 years old [*MD*: 69.8 ± 4.3 years old (minimum: 65 years old; maximum: 83 years old)]. Subjects >65 years old experienced statistically significant improvement in lung function, ACT and mini-AQLQ with benralizumab. Additionally, 9 patients (75%) experienced no asthma exacerbation ($p = 0.0047$), half (3/6) were able to stop OCS ($p = 0.08$), and no adverse effects with benralizumab were reported during the 20 months of follow-up.

Conclusions: In patients aged >65 years old, benralizumab was an effective and safe therapy for severe eosinophilic asthma in our study, with no significant differences from the younger subgroup. This is especially important since they are a group with numerous comorbidities, medications and worse quality of life.

Keywords: >65 years old; Benralizumab; elderly; safety; self-administration; severe eosinophilic asthma.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

FULL TEXT LINKS



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Cite

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31

J Asthma

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. 2024 Mar;61(3):238-248.

doi: 10.1080/02770903.2023.2263090. Epub 2024 Feb 8.

[Adherence to the asthma pathway, including pre-triage bronchodilator history, reduces hospitalizations](#)

[Suttipong Ittiporn](#)^{1,2}, [Kanlaya Prajongdee](#)³

Affiliations expand

- PMID: 37737546
- DOI: [10.1080/02770903.2023.2263090](https://doi.org/10.1080/02770903.2023.2263090)

Abstract

Objective: To determine if adherence to an asthma treatment pathway is associated with a decrease in hospitalizations. **Methods:** A prospective cohort design was conducted of Thai children aged 2-15 years who visited the emergency department with severe asthma

exacerbations, defined as a Buddhasothorn Asthma Severity Score ≥ 8 . Patients who received systemic corticosteroids and nebulized short-acting beta-2 agonists combined with ipratropium bromides were classified as the adherence group. The timing of steroid and bronchodilator administration, length of hospital stay, and hospitalization rate were examined in relation to adherence to the asthma pathway. Multivariable logistic regression models and adjusted odds ratios were used to assess associations. **Results:** A total of 118 episodes of asthma exacerbations (EAEs) from 59 participants were included. Patients who adhered to the pathway had a significantly higher rate of systemic corticosteroid administration within 1 h of arrival at triage (88.6% vs. 41.9%, adjusted Odds Ratio: aOR 10.21; 95%CI 3.52-29.62). A higher proportion of the patients who adhered to the pathway also received inhaled ipratropium bromide ≥ 2 doses within 1 h of arrival at triage (72.7% vs. 12.2%, aOR 23.51; 95%CI 7.73-71.54) and it was administered significantly faster by 31 min (5 min vs. 36 min, $p < 0.001$) compared to non-adherence group. The hospitalization rate was significantly lower by almost half of EAEs for adherence group (36.4% vs. 63.5%, aOR 0.41; 95%CI 0.18-0.93). **Conclusions:** Accurate assessment of severity and adherence to the clinical pathway can reduce hospitalization in pediatric patients with severe asthma exacerbations.

Keywords: Asthma; clinical pathway; emergency department; hospital admissions; pediatrics.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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32

J Asthma

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. 2024 Mar;61(3):203-211.

doi: 10.1080/02770903.2023.2260881. Epub 2024 Feb 8.

Predicting pediatric severe asthma exacerbations: an administrative claims-based predictive model

[Mandana Rezaeiahari](#)¹, [Clare C Brown](#)¹, [Arina Eyimina](#)¹, [Tamara T Perry](#)^{2,3}, [Anthony Goudie](#)¹, [Melanie Boyd](#)¹, [J Mick Tilford](#)¹, [Akilah A Jefferson](#)^{2,3}

Affiliations expand

- PMID: 37725084
- DOI: [10.1080/02770903.2023.2260881](https://doi.org/10.1080/02770903.2023.2260881)

Abstract

Objective: Previous machine learning approaches fail to consider race and ethnicity and social determinants of health (SDOH) to predict childhood asthma exacerbations. A predictive model for asthma exacerbations in children is developed to explore the importance of race and ethnicity, rural-urban commuting area (RUCA) codes, the Child Opportunity Index (COI), and other ICD-10 SDOH in predicting asthma outcomes.

Methods: Insurance and coverage claims data from the Arkansas All-Payer Claims Database were used to capture risk factors. We identified a cohort of 22,631 children with asthma aged 5-18 years with 2 years of continuous Medicaid enrollment and at least one asthma diagnosis in 2018. The goal was to predict asthma-related hospitalizations and asthma-related emergency department (ED) visits in 2019. The analytic sample was 59% age 5-11 years, 39% White, 33% Black, and 6% Hispanic. Conditional random forest models were used to train the model.

Results: The model yielded an area under the curve (AUC) of 72%, sensitivity of 55% and specificity of 78% in the OOB samples and AUC of 73%, sensitivity of 58% and specificity of 77% in the training samples. Consistent with previous literature, asthma-related hospitalization or ED visits in the previous year (2018) were the two most important variables in predicting hospital or ED use in the following year (2019), followed by the total number of reliever and controller medications.

Conclusions: Predictive models for asthma-related exacerbation achieved moderate accuracy, but race and ethnicity, ICD-10 SDOH, RUCA codes, and COI measures were not important in improving model accuracy.

Keywords: Random forest; claims data; conditional random forest; machine learning; variable importance.

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

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33

Review

J Asthma

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. 2024 Mar;61(3):260-264.

doi: 10.1080/02770903.2023.2260884. Epub 2023 Sep 16.

[Dual biologics therapy in a patient with severe asthma and chronic urticaria: a case report and review of the literature](#)

[Ozge Can Bostan](#)¹, [Gul Karakaya](#)¹, [Ali Fuat Kalyoncu](#)¹, [Ebru Damadoglu](#)¹

Affiliations expand

- PMID: 37715663
- DOI: [10.1080/02770903.2023.2260884](https://doi.org/10.1080/02770903.2023.2260884)

Abstract

Introduction: The data on the use of dual biologics are scant, but a topic of current interest.

Case study: In this report, the treatment regimen of a patient with two T helper 2 pathway-related comorbidities, severe asthma, and chronic spontaneous urticaria, was presented.

Results: Both urticaria and asthma symptoms of the patient could not be controlled entirely with monotherapy while both diseases could be controlled after omalizumab-mepolizumab dual treatment. No adverse events were observed after 6 months of dual biologics use.

Conclusion: This report supports other publications in the literature involving the use of dual biologics and provides a summary of the literature.

Keywords: Severe asthma; chronic spontaneous urticarial; dual biologics; mepolizumab; omalizumab.

- [Cited by 1 article](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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34

J Asthma

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. 2024 Mar;61(3):177-183.

doi: 10.1080/02770903.2023.2255277. Epub 2023 Sep 14.

Breathing pattern disorder in chronic rhinosinusitis with severe asthma: nasal obstruction and polyps do not increase prevalence

[Rebecca Livingston](#)^{1,2}, [Helene Bellas](#)^{1,2}, [Jagdeep Sahota](#)^{2,3}, [Therese Bidder](#)^{2,4}, [Florian Vogt](#)², [Valerie J Lund](#)^{3,5}, [Simon B Gane](#)^{3,5}, [Douglas S Robinson](#)², [Harsha H Kariyawasam](#)^{2,4,5}

Affiliations expand

- PMID: 37668326
- DOI: [10.1080/02770903.2023.2255277](https://doi.org/10.1080/02770903.2023.2255277)

Abstract

Objectives: Chronic rhinosinusitis (CRS) with severe asthma are associated with breathing pattern disorder (BPD). Mouth breathing is a sign of breathing pattern disorder, and nose breathing a fundamental part of breathing pattern retraining for BPD. The prevalence of BPD in relation to CRS subtypes and the relationship of nasal obstruction to BPD in CRS and associated severe asthma is unknown. The breathing pattern assessment tool (BPAT) can identify BPD. Our objective was to thus investigate the prevalence of BPD, nasal airflow obstruction and measures of airway disease severity in CRS with (CRSwNP) and without nasal polyps (CRSsNP) in severe asthma.

Methods: We determined whether CRS status, peak nasal inspiratory flow (PNIF) or polyp disease increased BPD prevalence. Demographic factors, measures of airway function and breathlessness in relation to BPD status and CRS subtypes were also evaluated.

Results: 130 Patients were evaluated ($n = 69$ had BPD). The prevalence of BPD in CRS with severe asthma was 53.1%. There was no difference between BPD occurrence between CRSwNP and CRSsNP. The mean polyp grade and PNIF were not statistically different between the BPD and non-BPD group. The presence of nasal polyps did not increase breathlessness.

Conclusions: BPD and CRS are commonly co-associated. CRS status and nasal obstruction per se does not increase BPD prevalence.

Keywords: Chronic rhinosinusitis; breathing pattern disorder; nasal obstruction; severe asthma.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Review

Laryngoscope



. 2024 Mar;134(3):1005-1013.

doi: 10.1002/lary.30992. Epub 2023 Aug 24.

[Non-Type 2 and Mixed Inflammation in Chronic Rhinosinusitis and Lower Airway Disease](#)

[Austin Heffernan](#)¹, [Amir Shafiee](#)¹, [Teffran Chan](#)¹, [Sydney Sparanese](#)¹, [Andrew Thamboo](#)¹

Affiliations expand

- PMID: 37615304
- DOI: [10.1002/lary.30992](https://doi.org/10.1002/lary.30992)

Abstract

Objective: The aim was to discuss the role of non-type 2 inflammation in patients diagnosed with chronic rhinosinusitis (CRS) and comorbid lower airway disease.

Data sources: Medline, Embase, National Institute for Health and Care Excellence, TRIP Database, ProQuest, Clinicaltrials.gov, Cochrane Central Registry of Controlled Trials, Web of Science, government and health organizations, and graduate-level theses.

Review methods: This scoping review followed PRISMA-ScR guidelines. Search strategy was peer-reviewed by medical librarians. Studies were included if they utilized airway sampling, non-type 2 cytokines, and patients with CRS and lower airway disease.

Results: Twenty-seven from 7060 articles were included. In patients with CRS and comorbid asthma, aspirin-exacerbated respiratory disease (AERD), and chronic obstructive pulmonary disease (COPD)/bronchiectasis, 60% (n = 12), 33% (n = 2), and 100% (n = 1), respectively, demonstrated mixed or non-type 2 endotypes. Comorbid CRS and asthma produced type 1 (n = 1.5), type 2 (n = 8), type 3 (n = 1), mixed type 1/2 (n = 1), and mixed type 1/2/3 (n = 8.5) endotype shifts. AERD demonstrated type 2 (n = 4), mixed type 2/3 (n = 1), and mixed type 1/2/3 (n = 1) endotype shifts. CRS with COPD or bronchiectasis demonstrated a mixed 1/2 (n = 1) endotype shift.

Conclusion: Type 2 disease has been extensively reviewed due to advent biologics targeting type 2 inflammation, but outcomes may be suboptimal due to the presence of non-type 2 inflammation. A proportion of patients with CRS and comorbid lower airway disease demonstrated mixed and non-type 2 endotype shifts. This emphasizes that patients with unified airway disease may have forms of inflammation beyond classical type 2 disease which could inform biologic development. *Laryngoscope*, 134:1005-1013, 2024.

Keywords: chronic rhinosinusitis; endotypes; mixed inflammation; non-type 2 inflammation; unified airway disease.

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SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Allergy

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-
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. 2024 Feb 29.

doi: 10.1111/all.16082. Online ahead of print.

Immunoglobulin free light chains in severe asthma patient: Could they be a new biomarker?

[C Caruso](#)¹, [G Ciasca](#)², [I Baglivo](#)³, [R Di Santo](#)², [A Gasbarrini](#)³, [D Firinu](#)⁴, [D Bagnasco](#)⁵, [G Passalacqua](#)⁵, [M Schiappoli](#)⁶, [M Caminati](#)⁷, [G W Canonica](#)^{8,9}, [E Heffler](#)^{8,9}, [C Crimi](#)¹⁰, [R Intravaia](#)¹¹, [V Basile](#)¹², [M Marino](#)¹³, [S Colantuono](#)¹, [S Del Giacco](#)⁴

Affiliations expand

- PMID: 38425088
- DOI: [10.1111/all.16082](https://doi.org/10.1111/all.16082)

Abstract

Background: Increasing evidence is available about the presence of increased serum concentration of immunoglobulin (Ig) free light chains (FLCs) in both atopic and non-atopic inflammatory diseases, including severe asthma, providing a possible new biomarker of disease.

Methods: We analyzed clinical and laboratory data, including FLCs, obtained from a cohort of 79 asthmatic subjects, clinically classified into different GINA steps. A control group of 40 age-matched healthy donors (HD) was considered. Particularly, HD have been selected according to the absence of monoclonal components (in order to exclude paraproteinemias), were tested for total IgE (that were in the normal ranges) and were negative for aeroallergens specific IgE. Moreover, no abnormality of common inflammatory markers (i.e., erythrocyte sedimentation rate and C-reactive protein) was detectable.

Results: FLC- κ levels were significantly increased in the asthmatic population, compared to the control group. Despite the absence of statistically significant differences in FLC- λ levels, the FLC- κ /FLC- λ ratio displayed remarkable differences between the two groups. A positive correlation between FLC- κ and FLC- λ levels was found. FLC- λ level displayed a significant negative correlation with the FEV1 value. Moreover, the FLC- κ /FLC- λ ratio was negatively correlated with the SNOT-22 score and a positive correlation was observed between FLCs and Staphylococcus Aureus IgE enterotoxins sensitization.

Conclusions: Our findings confirmed the role of FLCs in asthma as a potential biomarker in an inflammatory disease characterized by different endotypes and phenotypes. In particular, FLC- κ and FLC- κ /FLC- λ ratio could be a qualitative indicator for asthma, while FLC- λ levels could be a quantitative indicator for clinical severity parameters.

Keywords: biomarker; free light chains; severe asthma; type 2 inflammation.

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Allergy

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. 2024 Feb 29.

doi: 10.1111/all.16093. Online ahead of print.

[Blood basophils and asthma among participants from CONSTANCES, the French population-based cohort](#)

[Rachel Nadif](#)¹, [Joseph Henny](#)², [Tajidine Tsiavia](#)¹, [Céline Ribet](#)², [Marcel Goldberg](#)², [Marie Zins](#)^{2,3}, [Laurent Orsi](#)¹, [Nicolas Roche](#)^{1,4}

Affiliations expand

- PMID: 38425050
- DOI: [10.1111/all.16093](https://doi.org/10.1111/all.16093)

No abstract available

- [6 references](#)

SUPPLEMENTARY INFO

Publication types, Grants and funding expand

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Curr Opin Pulm Med

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. 2024 Feb 29.

doi: 10.1097/MCP.0000000000001062. Online ahead of print.

[Recent developments in occupational asthma](#)

[Claudia Blouin](#)^{1,2}, [Catherine Lemièr](#)^{1,2}

Affiliations expand

- PMID: 38415698
- DOI: [10.1097/MCP.0000000000001062](https://doi.org/10.1097/MCP.0000000000001062)

Abstract

Purpose of this review: Occupational asthma (OA) is a complex condition that can be difficult to diagnose. The purpose of this review is to describe some recent findings regarding the epidemiology of OA, the occupational sensitizing agents, the prognosis of OA, and its primary prevention.

Recent findings: The risk of developing OA varies according to the geographic localization of the worker, the type of industry and the type of sensitizing agents. New findings have been reported for several known sensitizing agents, such as isocyanates, seafood & cleaning agents, and their related industries, such as hairdressing salons and schools. Moreover, a few new sensitizing agents, such as cannabis, have been identified in the past few years. The prognosis of OA seems worse than that of nonwork-related asthma. It is mainly determined by the duration and the level of exposure. Primary prevention is crucial to reduce the number of new cases of OA. Complete avoidance of exposure to the causal agent remains the optimal treatment of sensitizer-induced OA.

Summary: Improving our knowledge regarding OA and its causative agents is key to enable an early recognition of this condition and improve its prognosis. Further research is still needed to improve primary prevention.

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[Review](#)

FASEB J



. 2024 Feb 29;38(4):e23485.

doi: 10.1096/fj.202302584RR.

Th2 cells in rapid immune responses and protective avoidance reactions

[Edward J Goetzl](#)¹

Affiliations expand

- PMID: 38372961
- DOI: [10.1096/fj.202302584RR](https://doi.org/10.1096/fj.202302584RR)

Abstract

Type 2 helper cells (Th2 cells) differentiate from CD4 helper T cells under the influence of IL-4 and conventional or monocyte-derived CD11b⁺ dendritic cells. Th2 cells are capable of generating IL-4, IL-5, and IL-13, as well as evoking immunoglobulin class-switch to IgE. Three types of rapid immune responses are Th2 cell-dependent: (1) mast cell-IgE mediated allergic reactions, (2) Th2 cell-derived cytokine-mediated reactions that complement allergic reactions and protect the host from toxins, xenobiotics, environmental irritants, and helminthic parasites, and (3) IgE-stimulated mast cell-derived cysteinyl-leukotriene mediated avoidance of toxins. The contributions of Th2 cell-derived cytokines to eosinophilia (IL-5), IgE class-switch, and epithelial barrier activation, mucous secretion, and metaplasia (IL-4 and IL-13) in asthma, allergic rhinitis with polyps and atopic dermatitis have led to anti-cytokine monoclonal antibody treatments. Anti-IL-5 neutralizing monoclonal antibody in asthma and anti-IL-4/IL-13 receptor neutralizing monoclonal antibody in asthma and atopic dermatitis are proven successful therapies in appropriately selected patients who are not sufficiently improved by conventional treatments.

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- [17 references](#)

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Review

Life Sci

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. 2024 Feb 28:122538.

doi: 10.1016/j.lfs.2024.122538. Online ahead of print.

Targeting type I PRMTs as promising targets for the treatment of pulmonary disorders: Asthma, COPD, lung cancer, PF, and PH

[Shuyan Zhou](#)¹, [Qiangsheng Zhang](#)¹, [Honglin Yang](#)¹, [Yongxia Zhu](#)², [Xiang Hu](#)¹, [Guoquan Wan](#)¹, [Luoting Yu](#)³

Affiliations expand

- PMID: 38428571
- DOI: [10.1016/j.lfs.2024.122538](https://doi.org/10.1016/j.lfs.2024.122538)

Abstract

Pulmonary disorders, including asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis (PF), pulmonary hypertension (PH), and lung cancer, seriously impair the quality of lives of patients. A deeper understanding of the occurrence and development of the above diseases may inspire new strategies to remedy the scarcity of treatments. Type I protein arginine methyltransferases (PRMTs) can affect processes of inflammation, airway remodeling, fibroblast proliferation, mitochondrial mass, and epithelial dysfunction through substrate methylation and non-enzymatic activity, thus affecting the occurrence and development of asthma, COPD, lung cancer, PF, and PH. As potential therapeutic targets, inhibitors of type I PRMTs are developed, moreover, representative compounds such as GSK3368715 and MS023 have also been used for early research. Here, we collated structures of type I PRMTs inhibitors and compared their activity. Finally, we highlighted the physiological and pathological associations of type I PRMTs with asthma, COPD, lung cancer, PF, and PH. The developing of type I PRMTs modulators will be beneficial for the treatment of these diseases.

Keywords: Asthma; COPD; Epigenetics; Lung cancer; Pulmonary fibrosis; Pulmonary hypertension; Type I PRMTs.

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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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[Practice Guideline](#)



The 1st EoETALY Consensus on the Diagnosis and Management of Eosinophilic Esophagitis - Definition, Clinical Presentation and Diagnosis

[Nicola de Bortoli](#)¹, [Pierfrancesco Visaggi](#)¹, [Roberto Penagini](#)², [Bruno Annibale](#)³, [Federica Baiano Svizzero](#)¹, [Giovanni Barbara](#)⁴, [Ottavia Bartolo](#)⁵, [Edda Battaglia](#)⁶, [Antonio Di Sabatino](#)⁷, [Paola De Angelis](#)⁸, [Ludovico Docimo](#)⁹, [Marzio Frazzoni](#)¹⁰, [Manuele Furnari](#)¹¹, [Andrea Iori](#)¹², [Paola Iovino](#)¹³, [Marco Vincenzo Lenti](#)¹⁴, [Elisa Marabotto](#)¹¹, [Giovanni Marasco](#)⁴, [Aurelio Mauro](#)¹⁵, [Salvatore Oliva](#)¹⁶, [Gaia Pellegatta](#)¹⁷, [Marcella Pesce](#)¹⁸, [Antonino Carlo Privitera](#)¹⁹, [Ilaria Puxeddu](#)²⁰, [Francesca Racca](#)²¹, [Mentore Ribolsi](#)²², [Erminia Ridolo](#)²³, [Salvatore Russo](#)²⁴, [Giovanni Sarnelli](#)¹⁸, [Salvatore Tolone](#)²⁵, [Patrizia Zentilin](#)²⁶, [Fabiana Zingone](#)²⁷, [Brigida Barberio](#)²⁷, [Matteo Ghisa](#)²⁷, [Edoardo Vincenzo Savarino](#)²⁸

Affiliations expand

- PMID: 38423918
- DOI: [10.1016/j.dld.2024.02.005](https://doi.org/10.1016/j.dld.2024.02.005)

Abstract

Eosinophilic esophagitis (EoE) is a chronic type 2-mediated inflammatory disease of the esophagus that represents the most common eosinophilic gastrointestinal disease. Experts in the field of EoE across Italy (i.e., EoETALY Consensus Group) including gastroenterologists, endoscopists, allergologists/immunologists, and paediatricians conducted a Delphi process to develop updated consensus statements for the management of patients with EoE and update the previous position paper of the Italian Society of Gastroenterology (SIGE) in light of recent evidence. Grading of the strength and quality of the evidence of the recommendations was performed using accepted GRADE criteria. The guideline is divided in two documents: Part 1 includes three chapters, namely 1) definition, epidemiology, and pathogenesis; 2) clinical presentation and natural history, and 3) diagnosis, while Part 2 includes two chapters: 4) treatment and 5) monitoring and

follow-up. This document has received the endorsement of three Italian national societies including the SIGE, the Italian Society of Neurogastroenterology and Motility (SINGEM), and the Italian Society of Allergology, Asthma, and Clinical Immunology (SIAAIC). With regards to patients' involvement, these guidelines involved the contribution of members of ESEO Italia, the Italian Association of Families Against EoE.

Keywords: EoE; EoETALY; Eosinophilic esophagitis; Guidelines.

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Conflict of interest statement

Declaration of competing interest Nicola de Bortoli: Advisory board member for: AlfaSigma, Sanofi Genzyme, Dr Falk; Lecture grants from Reckitt-Benckiser, Malesci, Dr. Flak, Sofar, Alfa-Sigma, Pharma-Line. Pierfrancesco Visaggi: Has served as speaker for Dr Falk, JB Pharmaceuticals, Malesci. Roberto Penagini: Has served as speaker for Dr Falk, Sanofi. Edda Battaglia: has served as consultant for NZP, GUNA Gaia Pellegatta has served as speaker for Dr Falk, Sanofi Genzyme, Malesci. Paola Iovino: Has served as consultant for Dr Falk Giovanni Marasco: Served as an advisory board member for AlfaSigma, EG Pharma, MontereSearch srl, Recordati, Cineca. Received lecture grants from Agave, AlfaSigma, Bromatech, Clorofilla, Echosens, Ferring, Mayoly Spindler, Menarini and Schwabe Pharma. Salvatore Oliva: Has served as speaker for Sanofi, Medtronic; Has served as consultant for: Sanofi, Medtronic, Bristol; Has received research support from Alfa Sigma, Medtronic. Francesca Racca: has served as speaker for Sanofi; has served as consultant for Dr Falk, Sanofi, GSK Erminia Ridolo: has served as consultant for Dr Falk Edoardo Vincenzo Savarino: has served as speaker for Abbvie, Agave, AGPharma, Alfasigma, Aurora Pharma, CaDiGroup, Celltrion, Dr Falk, EG Stada Group, Fenix Pharma, Fresenius Kabi, Galapagos, Janssen, JB Pharmaceuticals, Innovamedica/Adacyte, Malesci, Mayoly Biohealth, Omega Pharma, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda, Tillots, Unifarco; has served as consultant for Abbvie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, Diadema Farmaceutici, Dr. Falk, Fenix Pharma, Fresenius Kabi, Janssen, JB Pharmaceuticals, Merck & Co, Nestlè, Reckitt Benckiser, Regeneron, Sanofi, SILA, Sofar, Synformulas GmbH, Tssakeda, Unifarco; he received research support from Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, Zeta Farmaceutici. Bruno Annibale, Federica Baiano Svizzero, Giovanni Barbara, Brigida Barberio, Ottavia Bartolo, Antonio Di Sabatino, Ludovico Docimo, Marzio Frazzoni, Manuele Furnari, Matteo Ghisa, Andrea Iori, Marco Vincenzo Lenti, Elisa Marabotto, Aurelio Mauro, Marcella Pesce, Antonino Carlo Privitera, Ilaria Puxeddu, Mentore Ribolsi, Salvatore Russo, Giovanni Sarnelli, Salvatore Tolone, Patrizia Zentilin, Fabiana Zingone: None.

SUPPLEMENTARY INFO

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Respir Res

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. 2024 Feb 28;25(1):104.

doi: 10.1186/s12931-024-02710-8.

[The effect of combining an inhaled corticosteroid and a long-acting muscarinic antagonist on human airway epithelial cells in vitro](#)

[Maria Gabriella Matera](#)¹, [Barbara Rinaldi](#)², [Cecilia Calabrese](#)³, [Carmela Belardo](#)², [Luigino Calzetta](#)⁴, [Mario Cazzola](#)⁵, [Clive Page](#)⁶

Affiliations expand

- PMID: 38419021
- PMCID: [PMC10902985](#)
- DOI: [10.1186/s12931-024-02710-8](#)

Free PMC article

Abstract

Background: Airway epithelial cells (AECs) are a major component of local airway immune responses. Direct effects of type 2 cytokines on AECs are implicated in type 2 asthma, which is driven by epithelial-derived cytokines and leads to airway obstruction. However, evidence suggests that restoring epithelial health may attenuate asthmatic features.

Methods: We investigated the effects of passive sensitisation on IL-5, NF- κ B, HDAC-2, ACh, and ChAT in human bronchial epithelial cells (HBEpCs) and the effects of fluticasone furoate (FF) and umeclidinium (UME) alone and in combination on these responses.

Results: IL-5 and NF- κ B levels were increased, and that of HDAC-2 reduced in sensitised HBEpCs. Pretreatment with FF reversed the effects of passive sensitisation by concentration-dependent reduction of IL-5, resulting in decreased NF- κ B levels and restored HDAC-2 activity. Addition of UME enhanced these effects. Sensitized HBEpCs also exhibited higher ACh and ChAT levels. Pretreatment with UME significantly reduced ACh levels, and addition of FF caused a further small reduction.

Conclusion: This study confirmed that passive sensitisation of AECs results in an inflammatory response with increased levels of IL-5 and NF- κ B, reduced levels of HDAC-2, and higher levels of ACh and ChAT compared to normal cells. Combining FF and UME was found to be more effective in reducing IL-5, NF- κ B, and ACh and restoring HDAC-2 compared to the individual components. This finding supports adding a LAMA to established ICS/LABA treatment in asthma and suggests the possibility of using an ICS/LAMA combination when needed.

Keywords: Airway epithelial cells; Asthma; Inflammation; Inhaled corticosteroid; Long-acting muscarinic antagonists.

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Conflict of interest statement

MGM participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of ABC Farmaceutici, Almirall, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline and Novartis, was a consultant to Chiesi Farmaceutici and GSK, and her department was funded by GSK and Novartis. CC received honoraria for lectures from AstraZeneca, GSK, Sanofi and Novartis, and support for attending meetings and/or travel received from AstraZeneca, GSK, Sanofi and Novartis. LC has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis, received nonfinancial support from AstraZeneca, received a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; has been a consultant to ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon. MC participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of Abdi Ibrahim, Alkem, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, Eurodrug, GSK, Glenmark, Lallemand, Mankind

Pharma, Menarini Group, Mundipharma, Novartis, Pfizer, Recipharm, Sanofi, Teva, Verona Pharma and Zambon, and is or was a consultant to ABC Farmaceutici, AstraZeneca, Chiesi Farmaceutici, GSK, Lallemand, Novartis, Ockham Biotech, Recipharm, Verona Pharma and Zambon. CP has acted as a consultant to Eurodrug, Recipharm, Glycosynnovation and PrEP Biopharma, and also holds equity in Verona Pharma. BR and CB declare no conflict of interest.

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

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Occup Environ Med

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. 2024 Feb 28:oemed-2023-109100.

doi: 10.1136/oemed-2023-109100. Online ahead of print.

[Chronic occupational exposures to irritants and asthma in the CONSTANCES cohort](#)

[Guillaume Sit](#)¹, [Laurent Orsi](#)¹, [Yuriko Iwatsubo](#)², [Brigitte Dananché](#)¹, [Florence Orsi](#)¹, [Marcel Goldberg](#)^{3,4}, [Benedicte Leynaert](#)¹, [Rachel Nadif](#)¹, [Céline Ribet](#)^{3,4}, [Nicolas Roche](#)⁵, [Yves Roquelaure](#)⁶, [Raphäelle Varraso](#)¹, [Marie Zins](#)^{3,4}, [Corinne Pilorget](#)², [Nicole Le Moual](#)¹, [Orianne Dumas](#)⁷

Affiliations expand

- PMID: 38418224
- DOI: [10.1136/oemed-2023-109100](https://doi.org/10.1136/oemed-2023-109100)

Abstract

Objectives: The impact of chronic occupational exposures to irritants on asthma remains discussed. We studied the associations between occupational exposures and asthma, with specific interest for chronic exposure to irritants, including disinfectants and cleaning products (DCPs) and solvents.

Methods: Cross-sectional analyses included 115 540 adults (55% women, mean age 43 years, 10% current asthma) working at inclusion in the French population-based CONSTANCES cohort (2012-2020). Current asthma was defined by ever asthma with symptoms, medication or asthma attacks (past 12 months), and the asthma symptom score by the sum of 5 respiratory symptoms (past 12 months). Both lifetime and current occupational exposures were assessed by the Occupational Asthma-specific Job-Exposure Matrix. Associations were evaluated by gender using logistic and binomial negative regressions adjusted for age, smoking status and body mass index.

Results: In women, associations were observed between current asthma and lifetime exposure to irritants (OR 1.05, 95% CI 1.00 to 1.11), DCPs (1.06, 95% CI 1.00 to 1.12) and solvents (1.06, 95% CI 0.98 to 1.14). In men, only lifetime exposure to DCPs (1.10, 95% CI 1.01 to 1.20) was associated with current asthma. Lifetime exposure to irritants was associated with higher asthma symptom score both in women (mean score ratio: 1.08, 95% CI 1.05 to 1.11) and men (1.11, 95% CI 1.07 to 1.15), especially for DCPs (women: 1.09, 95% CI 1.06 to 1.13, men: 1.21, 95% CI 1.15 to 1.27) and solvents (women 1.14, 95% CI 1.10 to 1.19, men: 1.10, 95% CI 1.05 to 1.15). For current exposures, no consistent associations were observed with current asthma and asthma symptom score.

Conclusions: Lifetime occupational exposures to irritants were associated with current asthma and higher asthma symptom score. These exposures should be carefully considered in asthma management.

Keywords: Asthma; Cross-Sectional Studies; Epidemiology; Occupational Health; Solvents.

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Conflict of interest statement

Competing interests: None declared.

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Review

Eur Respir Rev

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. 2024 Feb 28;33(171):230174.

doi: 10.1183/16000617.0174-2023. Print 2024 Jan 31.

[Preclinical models of maternal asthma and progeny outcomes: a scoping review](#)

[Joshua L Robinson](#)^{1,2,3}, [Kathryn L Gatford](#)^{1,4}, [Danielle N Bailey](#)¹, [Andrea J Roff](#)^{1,4}, [Vicki L Clifton](#)⁵, [Janna L Morrison](#)³, [Michael J Stark](#)^{6,2,7}

Affiliations expand

- PMID: 38417970
- PMCID: [PMC10900068](#)
- DOI: [10.1183/16000617.0174-2023](#)

Abstract

There is an increased risk of adverse perinatal outcomes in the ~17% of women with asthma during pregnancy. The mechanisms linking maternal asthma and adverse outcomes are largely unknown, but reflect joint effects of genetics and prenatal exposure to maternal asthma. Animal models are essential to understand the underlying mechanisms independent of genetics and comorbidities, and enable safe testing of interventions. This scoping review aimed to explore the methodology, phenotype, characteristics, outcomes and quality of published studies using preclinical maternal asthma models. MEDLINE (PubMed), Embase (Elsevier) and Web of Science were systematically searched using previously validated search strings for maternal asthma and for animal models. Two reviewers independently screened titles and abstracts, full texts, and then extracted and assessed the quality of each study using the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) 2.0 guidelines. Out of 3618 studies identified, 39 were eligible for extraction. Most studies were in rodents (86%) and all were models of allergic asthma. Maternal and progeny outcomes included airway hyperresponsiveness, airway resistance, inflammation, lung immune cells, lung structure and serum immunoglobulins and cytokines. Experimental design (100%), procedural details (97%) and rationale (100%) were most often reported. Conversely, data exclusion (21%), blinding (18%) and adverse events (8%) were reported in a minority of studies. Species differences in physiology and timing of development, the use of allergens not relevant to humans and a lack of comparable outcome measures may impede clinical translation. Future studies exploring models of maternal asthma should adhere to the minimum core outcomes set presented in this review.

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Conflict of interest statement

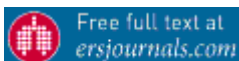
Conflict of interest: The authors declare no conflicts of interest.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respiration



. 2024 Feb 28.

doi: 10.1159/000537918. Online ahead of print.

[Associations of depressive and anxiety disorders with pulmonary disorders in the community – the PneumoLaus and PsyCoLaus studies](#)

[Brice Touilloux](#), [Alessio Casutt](#), [Marie-Pierre F Strippoli](#), [Alexandra Lenoir](#), [Simone Janett](#), [Peter Vollenweider](#), [Julien Vaucher](#), [Laurent Nicod](#), [Martin Preisig](#), [Christophe Von Garnier](#)

- PMID: 38417406
- DOI: [10.1159/000537918](https://doi.org/10.1159/000537918)

Abstract

Introduction: Mental health disorders figure among the many comorbidities of obstructive respiratory diseases. The multisystemic characteristics of chronic respiratory disease and its impact on quality of life could affect depressive and/or anxiety disorders. We aimed to evaluate the association of spirometric indices, ventilatory disorders and self-reported respiratory diseases with psychiatric disorders considering potential confounders.

Methods: We analysed data from CoLaus|PsyCoLaus, a Swiss population-based cohort study, consisting of 2'774 participants (56% women; mean age: 62.3 (SD=±9.9) years) who performed spirometry and completed semi-structured psychiatric interviews. We defined

ventilatory disorders using GLI-2012 references. Major depressive episode (MDE) and anxiety disorders were defined using the DSM-IV (Diagnostic and Statistical Manual).

Results: 630 subjects (22.7%) presented a recent MDE. Reversible obstructive ventilatory disorders were associated with recent MDE (OR=1.94, 95% CI 1.10-3.43) and recent anxiety disorders (2.21 [1.16-4.22]) only in unadjusted model. Self-reported COPD and asthma were associated with MDE with ORs of 2.49 (95%CI, 1.19-5.27) and 1.56 (95% CI, 1.04-2.35) after adjustment, respectively. Possible restrictive ventilatory impairment was positively associated with recent anxiety disorders (OR=2.46, 1.10-5.51). Z-scores of FEV₁, FVC and maximum mid expiratory flow (MMEF) were not associated with psychiatric disorders. There was no association between ventilatory disorders and MDE in adjusted models.

Conclusions: In this cross-sectional population-based study, the association between respiratory disorders and depressive disorders was observed for self-reported COPD and asthma, but not with objective diagnoses based on spirometry. Lung volumes are not associated with psychiatric disorders. Further prospective studies will be necessary to understand the significance of the association.

The Author(s). Published by S. Karger AG, Basel.

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[Review](#)

J Asthma

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. 2024 Feb 28:1-14.

doi: 10.1080/02770903.2024.2324862. Online ahead of print.

[A Comprehensive Review of the Intersection Between Asthma and Depression](#)

[Tahoorah Abdul Nasir Surve](#)¹, [Dhruvi Kumari D Sharma](#)², [Kiyan Ghani Khan](#)³, [Neisha Ghanie](#)⁴, [Riley Charanrak](#)⁵, [Mouhammad Sharifa](#)⁶, [Samreen Begum](#)⁷, [Maria Jose Auz](#)⁸, [Nozima Akbarova](#)⁹, [Maneeth Mylavarapu](#)¹⁰

Affiliations expand

- PMID: 38415695
- DOI: [10.1080/02770903.2024.2324862](https://doi.org/10.1080/02770903.2024.2324862)

Abstract

Objective To emphasize the necessity for increased research in this field, incorporating depression into the preventative, diagnostic, and therapeutic considerations for asthma. Additionally, we seek to highlight upcoming advancements that can be applied to simultaneously address these comorbidities, ultimately improving the overall well-being and quality of life for individuals coping with these conditions. **Methods** A rigorous search in PubMed using the MeSH terms "asthma" and "depression" was performed, and papers were screened by the authors in view of their eligibility to contribute to the study. **Results** There exists a correlation between these two conditions, with specific biological mechanisms and genetic factors playing a crucial role in their concurrent occurrence. In this review, we present preclinical and clinical research data, shed light on the possible mechanisms contributing to the co-occurrence of symptoms associated with both asthma and depression, and explore the intricate relationship between both conditions. **Conclusion** The evidence presented here supports the existence of a correlation between asthma and depression. By acknowledging these shared biological mechanisms, genetic factors, and epidemiological trends, we can formulate more efficacious strategies for addressing the dual impact of asthma and depression.

Keywords: Health Related Quality of Life (HRQoL); Hospital Anxiety and Depression Scale (HADS) Scores; Major Depressive Disorder (MDD); NF- κ B; oxidative stress.

SUPPLEMENTARY INFO

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Randomized Controlled Trial

Respir Care

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. 2024 Feb 28;69(3):345-348.

doi: 10.4187/respcare.10980.

[Randomized Controlled Trial Assessing a Vibrating Mesh Nebulizer Compared to a Jet Nebulizer in Severe Asthma Exacerbations](#)

[Haval Chweich](#)¹, [Najia Idrees](#)¹, [Jesse Rideout](#)¹, [Brien Barnewolt](#)¹, [Lauren Rice](#)¹, [Nicholas S Hill](#)²

Affiliations expand

- PMID: 37816543
- DOI: [10.4187/respcare.10980](https://doi.org/10.4187/respcare.10980)

No abstract available

Keywords: asthma; emergency department; exacerbation; nebulizer; vibrating mesh.

Conflict of interest statement

The authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Allergy Clin Immunol Pract

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. 2024 Feb 27:S2213-2198(24)00203-4.

doi: 10.1016/j.jaip.2024.02.029. Online ahead of print.

[Comparative Impact of Asthma Biologics - A Nationwide US Claim-Based Analysis](#)

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Affiliations expand

- PMID: 38423294
- DOI: [10.1016/j.jaip.2024.02.029](https://doi.org/10.1016/j.jaip.2024.02.029)

Abstract

Background: Biologic modifiers targeting type-2 (T2) airway inflammation are effective in reducing asthma exacerbation, however real-world and comparative effectiveness studies remain limited.

Objective: to examine and compare the real-world impact of anti-T2 asthma biologics
METHODS: In this retrospective new user cohort study, we used the MarketScan, a Commercial Claims and Encounters Database, to identify adult patients with asthma who were started on an anti-T2 biologic agent (anti-IL-5s, dupilumab or omalizumab). We examined the influence of the biologic class on asthma exacerbation by comparing the average number of asthma exacerbation 1-year pre- and post-biologic initiation. We conducted multivariable regression analyses to compare the effectiveness of these asthma biologics on reducing the incidence of asthma exacerbations within 18-month of initial administration of biologics while controlling for demographic variables, comorbidities, and asthma severity.

Results: We identified 5,538 asthma patients who were initiated on an anti-T2 biologic [mean age (\pm SD); 45.6 (12.78) years; % females, 65.8%]. Asthma biologics reduced asthma exacerbation by 11-47%, particularly among patients with 2+ asthma exacerbations in the year preceding biologic initiation (31-65% reduction). Biologics were especially effective in reducing asthma-related hospitalizations (44.6-60%). After adjusting for baseline demographics, asthma medication, and co-morbidities, dupilumab was associated with a lower estimated mean number of asthma exacerbation per year and lower adjusted OR for developing asthma exacerbation relative to other biologics (50-80% less likely).

Conclusion: Anti-T2 asthma biologics reduced asthma exacerbation in real-world settings. Evidence supports growing literature that dupilumab might have a more favorable impact on asthma exacerbation relative to other asthma biologics.

Keywords: T2 high asthma; benralizumab; comparative efficacy; dupilumab; eosinophilic asthma; mepolizumab; omalizumab; reslizumab; severe asthma.

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BMJ Open Respir Res

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Real-world treatment trajectories of adults with newly diagnosed asthma or COPD

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Affiliations expand

- PMID: 38413124
- PMCID: [PMC10900306](#)
- DOI: [10.1136/bmjresp-2023-002127](#)

Free PMC article

Abstract

Background: There is a lack of knowledge on how patients with asthma or chronic obstructive pulmonary disease (COPD) are globally treated in the real world, especially with regard to the initial pharmacological treatment of newly diagnosed patients and the different treatment trajectories. This knowledge is important to monitor and improve clinical practice.

Methods: This retrospective cohort study aims to characterise treatments using data from four claims (drug dispensing) and four electronic health record (EHR; drug prescriptions) databases across six countries and three continents, encompassing 1.3 million patients with asthma or COPD. We analysed treatment trajectories at drug class level from first diagnosis and visualised these in sunburst plots.

Results: In four countries (USA, UK, Spain and the Netherlands), most adults with asthma initiate treatment with short-acting β_2 agonists monotherapy (20.8%–47.4% of first-line treatments). For COPD, the most frequent first-line treatment varies by country. The largest percentages of untreated patients (for asthma and COPD) were found in claims databases

(14.5%-33.2% for asthma and 27.0%-52.2% for COPD) from the USA as compared with EHR databases (6.9%-15.2% for asthma and 4.4%-17.5% for COPD) from European countries. The treatment trajectories showed step-up as well as step-down in treatments.

Conclusion: Real-world data from claims and EHRs indicate that first-line treatments of asthma and COPD vary widely across countries. We found evidence of a stepwise approach in the pharmacological treatment of asthma and COPD, suggesting that treatments may be tailored to patients' needs.

Keywords: Asthma Pharmacology; COPD Pharmacology.

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Conflict of interest statement

Competing interests: AFM, PRR, JAK and KMV work for a department that receives/received unconditional research grants from Amgen, Chiesi, Johnson and Johnson, UCB Biopharma, the European Medicines Agency and the Innovative Medicines Initiative. DP-A's department has received grants from Amgen, Chiesi-Taylor, Lilly, Johnson and Johnson, Novartis, UCB Biopharma, the European Medicines Agency, and the Innovative Medicines Initiative. DP-A's research group has received consultancy fees from Astra Zeneca and UCB Biopharma. DP-A's department has organised training programmes funded or supported by Amgen, Astellas, Johnson and Johnson, Synapse Management Partners, and UCB Biopharma. JK's institute has received grants from the American Lung Association, COPD Foundation, National Heart Lung and Blood institute, PCORI, Regeneron, Sergey Brin Family Foundation and US National Institutes of Health. JK has received consultancy fees from AstraZeneca, BData and GlaxoSmithKline. JK has received honoraria from University of Chicago, University of Washington/VA Puget Sound and travel support from the Global Initiative for Asthma, American Thoracic Society. GBB's institute has received grants from Merck Sharp & Dohme. GBB has received honoraria from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Sanofi. All other authors declare no competing interests.

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. 2024 Feb 27;11(1):e002006.

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[Risk of exacerbation and mortality in asthma: a 10-year retrospective financial database analysis of the Hungarian Health Insurance Fund](#)

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Affiliations expand

- PMID: 38413122
- PMCID: [PMC10900350](#)
- DOI: [10.1136/bmjresp-2023-002006](#)

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Abstract

Introduction: Asthma is the most prevalent obstructive pulmonary disease, with drastically improved treatment options over the past decades. However, there is still a proportion of patients with suboptimal level of asthma control, leading to multiple hospitalisation due to severe acute exacerbation (SAE) and earlier death. In our study, we aimed to assess the risk of SAEs and mortality in patients who suffered an SAE.

Methods: The database of the National Health Insurance Fund was used to retrospectively analyse the data of all asthmatic patients who had been hospitalised for an SAE between 2009 and 2019. We used a competing risk model to analyse the effect of each exacerbation on the risk of further SAEs with age, sex, Charlson index and the number of severe and moderate exacerbations included as covariates.

Result: Altogether, 9257 asthmatic patients suffered at least one exacerbation leading to hospitalisation during the study time. The majority (75.8%) were women, and the average age was 58.24 years. Most patients had at least one comorbidity. 3492 patients suffered at least one further exacerbation and 1193 patients died of any cause. In the competing risk model, each SAE increased the risk of further exacerbations (HR=2.078-7.026; $p < 0.0001$ for each case) but not death. The risk of SAEs was also increased by age (HR=1.008) female sex (HR=1.102) and with the number of days of the first SAE (HR=1.007).

Conclusions: Even though asthma is generally a well-manageable disease, there still are many patients who suffer SAEs that significantly increase the risk of further similar SAEs.

Keywords: asthma; asthma epidemiology; clinical epidemiology.

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Conflict of interest statement

Competing interests: The authors report that they have no conflicts of interest related to the submitted work. LT has received lecture or consultancy fees and/or support for conference attendance from Berlin-Chemie, Orion Corporation, Novartis, Chiesi, Teva Pharmaceutical and AstraZeneca. NE has received lecture or consultancy fees and/or support for conference attendance from Berlin-Chemie, Orion Corporation, Novartis, Chiesi, Teva Pharmaceutical and AstraZeneca. GG has accepted reports personal fees from Astra-Zeneca, Chiesi, BMS, MSD, Berlin Chemie, Boehringer Ingelheim, Roche, Novartis, Pfizer, Ipsen, Mylen, Orion outside the submitted work. Santa, G. Tomisa and A. Horváth are all employees of Chiesi Hungary.

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Inflamm Bowel Dis



. 2024 Feb 27:izae027.

doi: 10.1093/ibd/izae027. Online ahead of print.

[Comorbidity Between Inflammatory Bowel Disease and Asthma and Allergic Diseases: A Genetically Informed Study](#)

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Affiliations expand

- PMID: 38412344
- DOI: [10.1093/ibd/izae027](https://doi.org/10.1093/ibd/izae027)

Abstract

Background: Little is known about shared origins between inflammatory bowel disease (IBD) and allergic diseases (asthma, allergic rhinitis, and eczema). We aimed to expand current knowledge on the etiological sources of comorbidities between these disorders using a range of genetically informed methods.

Methods: Within-individual and familial co-aggregation analysis was applied to 2 873 445 individuals born in Sweden from 1987 to 2014 and their first- and second-degree relatives. Quantitative genetic modeling was applied to 38 723 twin pairs to decompose the genetic and environmental sources for comorbidity. Polygenic risk score analysis between IBD and

allergic diseases was conducted in 48 186 genotyped twins, and linkage disequilibrium score regression was applied using publicly available data to explore the genetic overlap.

Results: IBD was associated with asthma (adjusted odds ratio [aOR], 1.35; 95% confidence interval [CI], 1.30 to 1.40), allergic rhinitis (aOR, 1.27; 95% CI, 1.20 to 1.34), and eczema (aOR, 1.47; 95% CI, 1.38 to 1.56), with similar estimates for ulcerative colitis or Crohn's disease. The ORs for familial co-aggregation decreased with decreasing genetic relatedness. Quantitative genetic modeling revealed little evidence of common genetic factors between IBD and allergic diseases (eg, IBD and allergic rhinitis; genetic correlation $r_g = 0.06$; 95% CI, -0.03 to 0.15) but did reveal some evidence of unique environmental factors between IBD and eczema ($r_e = 0.16$; 95% CI, 0.00 to 0.32). Molecular genetic analyses were similarly null for IBD and allergic diseases, except for a slight association between Crohn's disease polygenic risk score and eczema (OR, 1.09; 95% CI, 1.06 to 1.12).

Conclusions: We found little evidence to support a shared origin between IBD and any allergic disease but weak evidence for shared genetic and unique environmental components for IBD and eczema.

Keywords: Crohn's disease; allergic rhinitis; asthma; eczema; familial co-aggregation; genetic correlation; ulcerative colitis.

Plain language summary

Comorbidities between inflammatory bowel disease (IBD) with asthma and allergic diseases have been documented, but shared origin remains unknown. Using multiple genetically informed approaches, we found little evidence of a shared origin explaining the comorbidities of IBD with asthma and allergic rhinitis but weak evidence for IBD and eczema.

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Curr Opin Pulm Med



. 2024 Feb 27.

doi: 10.1097/MCP.0000000000001065. Online ahead of print.

[Examining the impact of air pollution, climate change, and social determinants of health on asthma and environmental justice](#)

[Felicia T Canaday](#)¹, [Steve N Georas](#), [Daniel P Croft](#)

Affiliations expand

- PMID: 38411188
- DOI: [10.1097/MCP.0000000000001065](https://doi.org/10.1097/MCP.0000000000001065)

Abstract

Purpose of review: In this review, we discuss the current literature examining the impact air pollution and climate change has on asthma onset, control, and exacerbation. This review also addresses the risk of exposure to specific disproportionately affected communities, highlighting health disparities in exposure and asthma outcomes.

Recent findings: Recent studies have shifted from highlighting the associations between asthma exacerbations and indoor and outdoor air pollution. Studies are now focused on confirming the association of asthma incidence from these same exposures. Many studies have linked particulate matter to adverse asthma outcomes, however, the pollutant exposures that pose the greatest risk and the effect of natural disasters fueled by climate change are under current study. Some studies have observed that the true burden that pollutant exposures have on asthma outcomes occurs at the intersection of exposure and vulnerability. Future studies in this area will address social determinants of health, societal factors such as redlining and other systemic racism practices.

Summary: Although decades of research support the causal link between gaseous and particulate air pollution and the exacerbation of preexisting asthma, recent studies suggest air pollution can cause incident (new onset) asthma. Studies have started to focus on the underlying drivers of poor outcomes in asthma. Many of the structural impediments to high quality asthma care at the society level (e.g. poverty, redlining, systemic racism) also are risk factors for worsened climate events and air pollution exposure. The individuals in these disproportionately affected groups are doubly affected by worsened exposure and worsened access to care for the resultant asthma exacerbations or incident asthma. More research is needed to understand the specific climate and air pollution mitigation efforts where disproportionately affected communities would derive the most benefit.

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Curr Opin Pulm Med

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. 2024 Feb 27.

doi: 10.1097/MCP.0000000000001061. Online ahead of print.

[Viral infections causing asthma exacerbations in the age of biologics and the COVID-19 pandemic](#)

[Pedro A Lamothe](#)¹, [Violeta Capric](#), [F Eun-Hyung Lee](#)

Affiliations expand

- PMID: 38411178
- DOI: [10.1097/MCP.0000000000001061](https://doi.org/10.1097/MCP.0000000000001061)

Abstract

Purpose of review: Asthma exacerbations are associated with substantial symptom burden and healthcare costs. Viral infections are the most common identified cause of asthma exacerbations. The epidemiology of viral respiratory infections has undergone a significant evolution during the COVID-19 pandemic. The relationship between viruses and asthmatic hosts has long been recognized but it is still incompletely understood. The use of newly approved asthma biologics has helped us understand this interaction better.

Recent findings: We review recent updates on the interaction between asthma and respiratory viruses, and we address how biologics and immunotherapies could affect this relationship by altering the respiratory mucosa cytokine milieu. By exploring the evolving epidemiological landscape of viral infections during the different phases of the COVID-19 pandemic, we emphasize the early post-pandemic stage, where a resurgence of pre-pandemic viruses with atypical seasonality patterns occurred. Finally, we discuss the newly developed RSV and SARS-CoV-2 vaccines and how they reduce respiratory infections.

Summary: Characterizing how respiratory viruses interact with asthmatic hosts will allow us to identify tailored therapies to reduce the burden of asthma exacerbations. New vaccination strategies are likely to shape the future viral asthma exacerbation landscape.

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. 2024 Feb 26:107581.

doi: 10.1016/j.rmed.2024.107581. Online ahead of print.

No remission in 60% of those with childhood-onset asthma - A population-based cohort followed from 8 to 28 years of age

[Linnéa Almqvist](#)¹, [Martin Andersson](#)², [Helena Backman](#)², [Eva Rönmark](#)², [Linnéa Hedman](#)²

Affiliations expand

- PMID: 38417585
- DOI: [10.1016/j.rmed.2024.107581](https://doi.org/10.1016/j.rmed.2024.107581)

Abstract

Background: Although remission occur, childhood-onset asthma may persist until adulthood. Since few longitudinal population-based studies have followed a cohort from childhood until adulthood, the knowledge on predictors of persistence of asthma is sparse.

Aim: To estimate persistence of asthma from 8 to 28 years and its associated factors.

Methods: Within the OLIN (Obstructive Lung Disease in Northern Sweden) studies, a cohort was recruited in 1996 (age 8y, n = 3430) and followed annually with questionnaires about asthma and risk factors until 19y. Clinical examinations included skin prick tests (at 8, 12 and 19y) and lung function tests (17 and 19y) whereof a subsample performed bronchial hyperreactivity test. We identified n = 248 with asthma at 8y whereof 170 (69%) participated in a follow-up at 28y (73% of possible to invite).

Results: Of the 170 participants at 28y, 105 (61.8%) had persistent asthma (women: 49/76, 64.5%; men: 56/94, 59.6%, p = 0.513). Factors collected at recruitment: allergic sensitization (OR7.8, 95%CI 3.0-20.2), severe respiratory infection (OR2.6, 95%CI 1.1-6.3) and higher

asthma severity score (OR1.6, 95%CI 1.1-2.4) were associated with asthma at 28y after adjustment for sex, family history of asthma, breastfeeding <3 months and eczema. Replacing allergic sensitization with rhinoconjunctivitis in the model yielded OR3.4 (95%CI 1.5-8.0). Bronchial hyperreactivity at age 17y associated with asthma at 28y (OR9.0, 95%CI 1.7-47.0).

Conclusions: Among children with asthma onset by 8y, 62% still had asthma at age 28 years. Persistent asthma was associated with allergic sensitization, rhinoconjunctivitis, severe respiratory infection, a more severe asthma and bronchial hyperreactivity.

Keywords: Asthma; Epidemiology; Longitudinal; Relapse; Remission; Risk factors.

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Conflict of interest statement

Declaration of competing interest HB: Personal fees for presentation at scientific meeting outside the submitted work from AstraZeneca, Boehringer Ingelheim and GlaxoSmithKline. None of the other authors have any conflicts of interest.

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Curr Opin Pediatr

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. 2024 Feb 26.

doi: 10.1097/MOP.0000000000001343. Online ahead of print.

Precision care in the treatment of pediatric asthma

[Lina Mahmood](#)¹, [Sevdenuur Keskin](#), [Akilah A Jefferson](#)

Affiliations expand

- PMID: 38411592
- 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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ERJ Open Res



. 2024 Feb 26;10(1):00853-2023.

doi: 10.1183/23120541.00853-2023. eCollection 2024 Jan.

[ERS International Congress 2023: highlights from the Paediatrics Assembly](#)

[Susanne J H Vijverberg](#)^{1,2}, [Asterios Kampouras](#)³, [Halime Nayir Büyüksahin](#)⁴, [Heidi Makrinioti](#)⁵, [Laura Petrarca](#)^{6,7}, [Mehtap Schmidt](#)⁸, [Leonie D Schreck](#)^{9,10}, [Ruth M Urbantat](#)^{11,12,13}, [Nicole Beydon](#)^{14,15}, [Myrofora Goutaki](#)^{9,16}, [Anna Lavizzari](#)¹⁷, [Marijke Proesmans](#)¹⁸, [Dirk Schramm](#)¹⁹, [Mirjam Stahl](#)^{11,12,13}, [Angela Zacharasiewicz](#)⁸, [Alexander Moeller](#)²⁰, [Marielle W Pijnenburg](#)²¹

Affiliations expand

- PMID: 38410713
- PMCID: [PMC10895434](#)
- DOI: [10.1183/23120541.00853-2023](#)

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Abstract

Respiratory health in children is essential for general wellbeing and healthy development in the short and long term. It is well known that many respiratory diseases in adulthood have their origins in early life, and therefore research on prevention of respiratory diseases and management of children with respiratory diseases will benefit patients during the full life course. Scientific and clinical advances in the field of respiratory health are moving at a fast pace. This article summarises some of the highlights in paediatric respiratory medicine

presented at the hybrid European Respiratory Society (ERS) International Congress 2023 which took place in Milan (Italy). Selected sessions are summarised by Early Career Members of the Paediatrics Assembly (Assembly 7) under the supervision of senior ERS officers, and cover a wide range of research areas in children, including respiratory physiology and sleep, asthma and allergy, cystic fibrosis, respiratory infection and immunology, neonatology and intensive care, respiratory epidemiology and bronchology.

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Conflict of interest statement

Conflict of interest: S.J.H. Vijverberg received support from the ERS for attending meetings and is the Early Career Member Representative of the Paediatrics Assembly of the ERS. L. Petrarca received funding from Sanofi to attend the ERS Congress 2023. L.D. Schreck is supported by the Swiss National Science Foundation (320030B_192804/1). R.M. Urbantat received a travel grant from the Gesellschaft für Pädiatrische Pneumologie to attend the ERS Congress 2023. N. Beydon is chair of group 7.01 of the ERS and has received support from the ERS for attending meetings. M. Goutaki is chair of group 7.06 of the ERS and is supported by the Swiss National Science Foundation (PZ00P3_185923). A. Lavizzari is chair of group 7.05 and reports consulting fees from Chiesi SpA, Vyair medical and Getinge, and support from Accademia Techniche Nuove. M. Proesmans is chair of group 7.04 and has received support from the ERS for attending meetings. D. Schramm is past chair of group 7.07 of the ERS and has received support from the ERS for attending meetings. M. Stahl is secretary of group 7.03 and has been supported by the German Research Foundation (Deutsche Forschungsgemeinschaft); furthermore, she has received an independent RIA grant from Vertex Pharmaceuticals. A. Zacharasiewicz is chair of group 7.02, and has received payment for lectures and support to attend meetings from Vertex, AstraZeneca, Chiesi, Gilead and Novartis. A. Moeller is the current chair of the Paediatrics Assembly and reports to have received a research grant from Vertex Inc. and funding to attend the Vertex symposium at the annual conference of the Swiss Respiratory Society. M.W. Pijnenburg received support from the ERS for attending the ERS Congress and ERS meetings, and is the past chair of the Paediatrics Assembly. The other authors report no conflict of interests for this manuscript.

- [84 references](#)
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ERJ Open Res



. 2024 Feb 26;10(1):00935-2023.

doi: 10.1183/23120541.00935-2023. eCollection 2024 Jan.

Articular manifestations related to anti-interleukin-5 therapies in severe asthma: a case series

[Clairelyne Dupin](#)^{1,2,3}, [Solène Valéry](#)^{1,3}, [Laurent Guilleminault](#)^{2,4,5}, [Gilles Devouassoux](#)^{2,6}, [Marine Merveilleau](#)⁶, [Maud Russier](#)⁷, [Gisèle Mourin](#)⁸, [Johana Pradelli](#)⁹, [Philippe Bonniaud](#)¹⁰, [Mathilde Le Brun](#)^{1,2}, [Esther Ebstein](#)¹¹, [Pierre-Antoine Juge](#)¹¹, [Agnès Lillo-Lelouet](#)¹², [Camille Taillé](#)^{1,2}

Affiliations expand

- PMID: 38410709
- PMCID: [PMC10895420](#)
- DOI: [10.1183/23120541.00935-2023](#)

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Abstract

Articular manifestations should be screened before and during anti-IL-5/5R biologic treatment in severe asthma. Rigorous multidisciplinary team discussion should be carried out to assess the risk-benefit balance of withholding effective treatment. <https://bit.ly/3vfPn4k>.

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Conflict of interest statement

Conflict of interest: C. Dupin reports consulting fees from AstraZeneca, Sanofi and GSK; lecture honoraria from AstraZeneca, GSK, Sanofi, Novartis, Chiesi, OPA Pratique, Pneumoscoop and La Lettre du Pneumologue; and travel support from AstraZeneca, Sanofi, Novartis, Chiesi and GSK; all outside the submitted work. Conflict of interest: L. Guilleminault reports grants from AstraZeneca; consulting fees from Bayer, MSD, AstraZeneca, GSK, Novartis, Sanofi and Chiesi; lecture honoraria from MSD, AstraZeneca, GSK, Novartis, Sanofi and Chiesi; payment for expert testimony from Bayer, MSD and Sanofi; and travel support from MSD, AstraZeneca, GSK, Novartis and Sanofi; all outside the submitted work. Conflict of interest: G. Devouassoux reports lecture or consulting fees from GSK, Menarini, ALK, AstraZeneca, Novartis, Chiesi and Sanofi; payment for expert testimony from GSK, AstraZeneca, Sanofi and Chiesi; and travel support from AstraZeneca, GSK, Sanofi, Novartis, Chiesi; all outside the submitted work. Conflict of interest: M. Le Brun reports grants from GSK, AstenSante and Novartis; lecture honoraria from GSK and La Revue du Praticien; and travel support from Asten Santé and Novartis; all outside the submitted work. Conflict of interest: G. Mourin reports lecture honoraria from AstraZeneca and GSK; and travel support from AstraZeneca, Sanofi, Menarini and GSK; all outside the submitted work. Conflict of interest: P. Bonniaud reports grants from AstraZeneca; lecture honoraria from Sanofi and AstraZeneca; travel support from AstraZeneca, Novartis and Sanofi; advisory board participation from AstraZeneca, Novartis, Sanofi and GSK; all outside the submitted work. Conflict of interest: E. Ebstein reports consulting fees from Abbvie, Novartis and BMS; lecture honoraria from UCB and Galapagos; and travel support from UCB and Novartis; all outside the submitted work. Conflict of interest: C. Taillé reports grants from GSK; consulting fees from AstraZeneca, GSK and Sanofi; lecture honoraria from AstraZeneca, GSK, Sanofi, Novartis, Stallergenes and Chiesi; and travel support from AstraZeneca and GSK; all outside the submitted work. Conflict of interest: S. Valéry, M. Merveilleau, M. Russier, J. Pradelli, P-A. Juge all have nothing to disclose.

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Int Forum Allergy Rhinol



. 2024 Feb 26.

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Medication utilization for patients with chronic rhinosinusitis with nasal polyposis and asthma in 12 months pre- and post-dupilumab initiation

[Emily Garvey](#)¹, [Bita Naimi](#)¹, [Alexander Duffy](#)¹, [Chase Kahn](#)¹, [Douglas Farquhar](#)¹, [Marc Rosen](#)¹, [Mindy Rabinowitz](#)¹, [Damaris Pena Evertz](#)², [Jessica Most](#)², [Elina Toskala](#)¹, [Gurston G Nyquist](#)¹

Affiliations expand

- PMID: 38409897
- DOI: [10.1002/alr.23340](https://doi.org/10.1002/alr.23340)

Abstract

This study examines the impact of dupilumab on medication use for chronic rhinosinusitis with nasal polyposis (CRSwNP) and asthma patients. Patients on dupilumab had a reduction in oral/inhaled/topical steroids, antibiotics, and leukotriene receptor antagonists (LTRAs). The reduction in medication use had no impact on total polyp or SNOT-22 scores.

Keywords: asthma; chronic rhinosinusitis; quality of life; steroid therapy.

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Review

Int Arch Allergy Immunol

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. 2024 Feb 26:1-16.

doi: 10.1159/000536335. Online ahead of print.

[The Role of Regulatory T Cells in Allergic Diseases: Collegium Internationale Allergologicum \(CIA\) Update 2024](#)

[Leticia Martín-Cruz](#)^{1,2}, [Cristina Benito-Villalvilla](#)^{1,3}, [Sofía Sirvent](#)¹, [Alba Angelina](#)¹, [Oscar Palomares](#)¹

Affiliations expand

- PMID: 38408438
- DOI: [10.1159/000536335](https://doi.org/10.1159/000536335)

Abstract

Background: Allergy represents a major health problem of increasing prevalence worldwide with a high socioeconomic impact. Our knowledge on the molecular mechanisms underlying allergic diseases and their treatments has significantly improved over the last years. The generation of allergen-specific regulatory T cells (Tregs) is crucial in

the induction of healthy immune responses to allergens, preventing the development and worsening of allergic diseases.

Summary: In the last decades, intensive research has focused on the study of the molecular mechanisms involved in Treg development and Treg-mediated suppression. These mechanisms are essential for the induction of sustained tolerance by allergen-specific immunotherapy (AIT) after treatment discontinuation. Compelling experimental evidence demonstrated altered suppressive capacity of Tregs in patients suffering from allergic rhinitis, allergic asthma, food allergy, or atopic dermatitis, as well as the restoration of their numbers and functionality after successful AIT.

Key message: The better understanding of the molecular mechanisms involved in Treg generation during allergen tolerance induction might well contribute to the development of novel strategies for the prevention and treatment of allergic diseases.

Keywords: Allergen-specific immunotherapy; Allergic asthma; Allergic rhinitis; Atopic dermatitis; Food allergy; Regulatory T cells.

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Brain Behav Immun

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. 2024 Feb 25:S0889-1591(24)00272-1.

doi: 10.1016/j.bbi.2024.02.028. Online ahead of print.

Maternal asthma symptoms during pregnancy on child behaviour and executive function: A Bayesian phenomics approach

[Syeda Fabeha Husain¹](#), [Andrea Cremaschi²](#), [Noor Hidayatul Aini Suaini²](#), [Maria De Iorio³](#), [Evelyn X L Loo⁴](#), [Lynette P Shek⁵](#), [Anne E N Goh⁶](#), [Michael J Meaney⁷](#), [Elizabeth H Tham⁵](#), [Evelyn C Law⁸](#)

Affiliations expand

- PMID: 38412907
- DOI: [10.1016/j.bbi.2024.02.028](https://doi.org/10.1016/j.bbi.2024.02.028)

Abstract

Objective: Maternal history of inflammatory conditions has been linked to offspring developmental and behavioural outcomes. This phenomenon may be explained by the maternal immune activation (MIA) hypothesis, which posits that dysregulation of the gestational immune environment affects foetal neurodevelopment. The timing of inflammation is critical. We aimed to understand maternal asthma symptoms during pregnancy, in contrast with paternal asthma symptoms during the same period, on child behaviour problems and executive function in a population-based cohort.

Methods: Data were obtained from 844 families from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort. Parent asthma symptoms during the prenatal period were reported. Asthma symptoms in children were reported longitudinally from two to five years old, while behavioural problems and executive functioning were obtained at seven years old. Parent and child measures were compared between mothers with and without prenatal asthma symptoms. Generalized linear and Bayesian phenomics models were used to determine the relation between parent or child asthma symptoms and child outcomes.

Results: Children of mothers with prenatal asthma symptoms had greater behavioural and executive problems than controls (Cohen's d : 0.43-0.75; all $p < 0.05$). This association remained after adjustments for emerging asthma symptoms during the preschool years and fathers' asthma symptoms during the prenatal period. After adjusting for dependence between child outcomes, the Bayesian phenomics model showed that maternal prenatal asthma symptoms were associated with child internalising symptoms and higher-order executive function, while child asthma symptoms were associated with executive function

skills. Paternal asthma symptoms during the prenatal period were not associated with child outcomes.

Conclusions: Associations between child outcomes and maternal but not paternal asthma symptoms during the prenatal period suggests a role for MIA. These findings need to be validated in larger samples, and further research may identify behavioural and cognitive profiles of children with exposure to MIA.

Keywords: Asthma; Behavioural problems; Executive function; Maternal immune activation; Phenomics; Wheezing.

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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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Respirology

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. 2024 Feb 25.

doi: 10.1111/resp.14685. Online ahead of print.

[What makes asthma characterized by airway eosinophilia become severe?](#)

[Thomas Rothe](#)¹, [Niki Ubags](#)², [Christophe von Garnier](#)²

Affiliations expand

- PMID: 38403834
- DOI: [10.1111/resp.14685](https://doi.org/10.1111/resp.14685)

No abstract available

Keywords: eosinophilic asthma; nasal polyposis; steroid resistance.

- [13 references](#)

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Br J Clin Pharmacol

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. 2024 Feb 25.

doi: 10.1111/bcp.16025. Online ahead of print.

[Self-management support with the Respiratory Adherence Care Enhancer instrument in asthma and chronic obstructive pulmonary disease: An implementation trial](#)

[Claire D Visser¹](#), [Lisanne L M Antonisse¹](#), [Floor M Alleda¹](#), [Colin Bos²](#), [Privender Saini²](#), [Esther Kuipers³](#), [Henk-Jan Guchelaar¹](#), [Martina Teichert^{1,4,5}](#)

Affiliations expand

- PMID: 38403776
- DOI: [10.1111/bcp.16025](https://doi.org/10.1111/bcp.16025)

Abstract

Aim: Suboptimal self-management with controller inhalation therapy in asthma and COPD is frequently observed with poor treatment outcomes. The developed 'Respiratory Adherence Care Enhancer' (RACE) instrument identifies and addresses individual barriers to self-management with a theoretical underpinning. This study investigates the feasibility of pharmaceutical support with this instrument.

Methods: An implementation trial was conducted with asthma and COPD patients in 5 community pharmacies in the Netherlands. Patients were allocated to standard care or add-on support with the RACE instrument. Patients were invited to complete the RACE questionnaire at baseline, 5-week and 10-week follow-up. Barrier profiles were accessible for the intervention group with subsequent consultations at baseline and 5-weeks. Experiences were collected from patients and consultants with a questionnaire and reported findings. Primary endpoints focused on the acceptability, practicality and implementation process. Secondary endpoints included between-group differences in barrier and disease control outcomes from baseline at 10-weeks follow-up.

Results: In total, 84 patients were included; 48 were assigned to intervention and 36 to standard care. Patient satisfaction of support with the RACE instrument was high (71%). Patients felt motivated, reassured and more confident about their disease management. Consultants reported an increase in awareness of patient barriers. Patient recognition of barrier profiles was 83.9% ($\pm 12.9\%$). The barrier inhaler techniques decreased significantly for the intervention group at follow-up with odds ratio 0.30 (95% confidence interval, 0.10-0.91). No significant differences were observed for changes in number of barriers and disease control.

Conclusion: Self-management support with the RACE instrument is feasible and appreciated, facilitating behaviour change with patient-centred pharmaceutical care in asthma and COPD.

Keywords: asthma; chronic obstructive pulmonary disease; implementation; patient-centred care; self-management (self-care); tailored care.

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- [44 references](#)

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1
Osteoporos Int

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. 2024 Mar 2.

doi: 10.1007/s00198-024-07037-0. Online ahead of print.

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

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

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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2

Allergy



. 2024 Mar 2.

doi: 10.1111/all.16052. Online ahead of print.

[House dust mite SCIT reduces asthma risk and significantly improves long-term rhinitis and asthma control-A RWE study](#)

[Marek Jutel](#)^{1,2}, [Ludger Klimek](#)³, [Hartmut Richter](#)⁴, [Bernd Brüggenjürgen](#)⁵, [Christian Vogelberg](#)⁶

Affiliations [expand](#)

- PMID: 38429981
- DOI: [10.1111/all.16052](https://doi.org/10.1111/all.16052)

Abstract

Background: The German Therapy Allergen Ordinance (TAO) triggered an ongoing upheaval in the market for house dust mite (HDM) allergen immunotherapy (AIT) products. Three HDM subcutaneous AIT (SCIT) products hold approval in Germany and therefore will be available after the scheduled completion of the TAO procedure in 2026. In general, data from clinical trials on the long-term effectiveness of HDM AIT are rare. We evaluated real-world data (RWD) in a retrospective, observational cohort study based on a longitudinal claims database including 60% of all German statutory healthcare prescriptions to show the long-term effectiveness of one of these products in daily life. Aim of this analysis was

to provide a per product analysis on effectiveness of mite AIT as it is demanded by international guidelines on AIT.

Methods: Subjects between 5 and 70 years receiving their first (index) prescription of SCIT with a native HDM product (SCIT group) between 2009 and 2013 were included. The exactly 3:1 matched control group received prescriptions for only symptomatic AR medication (non-AIT group); the evaluation period for up to 6 years of follow-up ended in February 2017. Study endpoints were the progression of allergic rhinitis (AR) and asthma, asthma occurrence and time to the onset of asthma after at least 2 treatment years.

Results: In total, 892 subjects (608 adults and 284 children/adolescents) were included in the SCIT group and 2676 subjects (1824 adults and 852 children/adolescents) in the non-AIT group. During the follow-up period after at least 2 years of SCIT, the number of prescriptions in the SCIT group was reduced by 62.8% ($p < .0001$) for AR medication and by 42.4% for asthma medication ($p = .0003$). New-onset asthma risk was significantly reduced in the SCIT vs non-AIT group by 27.0% ($p = .0212$). The asthma-preventive effect of SCIT occurred 15 months after start of the treatment. In the SCIT group, the time to onset of asthma was prolonged compared to the non-AIT group ($p = .0010$).

Conclusion: In this first product based RWD analysis on SCIT with a native HDM product, patients aged 5 to 70 years benefited from AIT in the long term in terms of reduced progression of AR and asthma after at least 2 years of treatment. The effects seemed to last for up to 6 years after treatment termination. A significantly reduced risk of asthma onset was observed, starting after 15 months of treatment.

Keywords: allergen immunotherapy; house dust mite; long-term effect; real-world evidence; subcutaneous immunotherapy.

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3

Review

Clin Transl Allergy

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. 2024 Mar;14(3):e12344.

doi: 10.1002/ctt2.12344.

Non-pharmacological interventions for asthma prevention and management across the life course: Umbrella review

[Xunliang Tong](#)¹, [Xinyue Zhang](#)², [Mengyuan Wang](#)³, [Zijun Wang](#)⁴, [Fawu Dong](#)², [Enying Gong](#)^{5,6}, [Torsten Zuberbier](#)⁷, [Yanming Li](#)¹

Affiliations expand

- PMID: 38423800
- PMCID: [PMC10904350](#)
- DOI: [10.1002/ctt2.12344](#)

Abstract

Background: The impact of non-pharmacological interventions (NPIs) on asthma prevention and management is insufficiently examined. We aim to comprehensively evaluate and synthesize existing evidence regarding the effectiveness of various NPIs throughout the life course.

Methods: We conducted a systematic search and screening of reviews that examined the effectiveness of various NPIs on asthma prevention and control in the Cochrane Library, PubMed, Embase, and Ovid databases. Data extraction was performed by considering the type of NPIs and the life course stages of the target population. Recommendations were

provided by considering the quality of review assessed using the AMSTAR2 tool and the consistency of findings across reviews.

Results: We identified 145 reviews and mapped the evidence on the impact of 25 subtypes of NPIs on asthma prevention and control based on five stages of life course. Reviews indicated a shift of focus and various impacts of major NPIs on asthma prevention and control across life courses, while a few types of NPIs, such as physical exercise, appeared to be beneficial in children, adolescents and adults. Consistent and high-level evidence was observed only for psychological intervention on asthma control and quality of life among adults and older adults. Potential benefit with high-level evidence was reported on certain NPIs, such as vitamin D in reducing risk of developing asthma in offsprings in the prenatal stage, digital health interventions in improving asthma control from childhood to older adulthood, and breathing exercise in improving quality of life, asthma-related symptoms and lung function in adulthood and older adulthood.

Conclusion: This study emphasizes the significance of delivering NPIs to improve asthma prevention and management and highlights the heterogeneity regarding the impact of NPIs across life courses. High-quality research is urgently needed to further strengthen the evidence base of NPIs and tailored interventions should be considered in guideline development.

Keywords: asthma; life course; non-pharmacological interventions; umbrella review.

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Conflict of interest statement

The authors have none to declare.

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

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Case Reports

Respirol Case Rep

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. 2024 Feb 27;12(3):e01311.

doi: 10.1002/rcr2.1311. eCollection 2024 Mar.

[Efficacy of tezepelumab against uncontrolled severe non-type 2 asthma refractory to bronchial thermoplasty, benralizumab, dupilumab and mepolizumab](#)

[Yoshiro Kai](#)¹, [Kentaro Suzuki](#)¹, [Ryosuke Kataoka](#)¹, [Ichiro Sato](#)², [Shinji Tamaki](#)³, [Shigeo Muro](#)²

Affiliations expand

- PMID: 38420113
- PMCID: [PMC10898956](#)
- DOI: [10.1002/rcr2.1311](#)

Free PMC article

Abstract

Severe asthma affects approximately 5%-10% of patients with asthma. Herein, we describe a case of non-type 2 asthma that progressively worsened over the years. An 80-year-old woman was diagnosed with asthma 11 years back. She experienced repeated exacerbations requiring treatment with systemic corticosteroid despite therapy with

medications including high-dose inhaled corticosteroids/long-acting beta-agonists plus long-acting muscarinic antagonist. The patient presented with non-eosinophilic asthma. Therefore, the patient was initially treated with bronchial thermoplasty, which was effective for 1 year only. Treatment with bronchial thermoplasty, benralizumab, dupilumab, and mepolizumab was ineffective. The fourth treatment, which included tezepelumab, was initiated. The patient's symptoms and quality of life improved significantly. This is the first case of a patient who did not respond to sequential bronchial thermoplasty, benralizumab, dupilumab, and mepolizumab but who presented with good clinical response to tezepelumab. Therefore, tezepelumab may be useful for patients with non-type 2 asthma.

Keywords: benralizumab; bronchial thermoplasty; dupilumab; mepolizumab; tezepelumab.

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Conflict of interest statement

None declared.

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

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[Practice Guideline](#)

Otolaryngol Head Neck Surg

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. 2024 Mar;170 Suppl 1:S1-S42.

doi: 10.1002/ohn.648.

Clinical Practice Guideline: Immunotherapy for Inhalant Allergy

[Richard K Gurgel](#)¹, [Fuad M Baroody](#)², [Cecelia C Damask](#)³, [James Whit Mims](#)⁴, [Stacey L Ishman](#)⁵, [Dole P Baker Jr](#)⁶, [Kevin J Contrera](#)⁷, [Fariha S Farid](#)⁸, [John A Fornadley](#)⁹, [Donna D Gardner](#)¹⁰, [LaKeisha R Henry](#)¹¹, [Jean Kim](#)¹², [Joshua M Levy](#)¹³, [Christine M Reger](#)¹⁴, [Howard J Ritz](#)¹⁵, [Robert J Stachler](#)¹⁶, [Tulio A Valdez](#)¹⁷, [Joe Reyes](#)¹⁸, [Nui Dhepyasuwan](#)¹⁸

Affiliations expand

- PMID: 38408152
- DOI: [10.1002/ohn.648](https://doi.org/10.1002/ohn.648)

Abstract

Objective: Allergen immunotherapy (AIT) is the therapeutic exposure to an allergen or allergens selected by clinical assessment and allergy testing to decrease allergic symptoms and induce immunologic tolerance. Inhalant AIT is administered to millions of patients for allergic rhinitis (AR) and allergic asthma (AA) and is most commonly delivered as subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Despite its widespread use, there is variability in the initiation and delivery of safe and effective immunotherapy, and there are opportunities for evidence-based recommendations for improved patient care.

Purpose: The purpose of this clinical practice guideline (CPG) is to identify quality improvement opportunities and provide clinicians trustworthy, evidence-based recommendations regarding the management of inhaled allergies with immunotherapy. Specific goals of the guideline are to optimize patient care, promote safe and effective therapy, reduce unjustified variations in care, and reduce the risk of harm. The target patients for the guideline are any individuals aged 5 years and older with AR, with or without AA, who are either candidates for immunotherapy or treated with immunotherapy for their inhalant allergies. The target audience is all clinicians involved in the administration of immunotherapy. This guideline is intended to focus on evidence-based quality improvement opportunities judged most important by the guideline development group (GDG). It is not intended to be a comprehensive, general guide regarding the management of inhaled allergies with immunotherapy. The statements in this guideline are

not intended to limit or restrict care provided by clinicians based on their experience and assessment of individual patients.

Action statements: The GDG made a strong recommendation that (Key Action Statement [KAS] 10) the clinician performing allergy skin testing or administering AIT must be able to diagnose and manage anaphylaxis. The GDG made recommendations for the following KASs: (KAS 1) Clinicians should offer or refer to a clinician who can offer immunotherapy for patients with AR with or without AA if their patients' symptoms are inadequately controlled with medical therapy, allergen avoidance, or both, or have a preference for immunomodulation. (KAS 2A) Clinicians should not initiate AIT for patients who are pregnant, have uncontrolled asthma, or are unable to tolerate injectable epinephrine. (KAS 3) Clinicians should evaluate the patient or refer the patient to a clinician who can evaluate for signs and symptoms of asthma before initiating AIT and for signs and symptoms of uncontrolled asthma before administering subsequent AIT. (KAS 4) Clinicians should educate patients who are immunotherapy candidates regarding the differences between SCIT and SLIT (aqueous and tablet) including risks, benefits, convenience, and costs. (KAS 5) Clinicians should educate patients about the potential benefits of AIT in (1) preventing new allergen sensitizations, (2) reducing the risk of developing AA, and (3) altering the natural history of the disease with continued benefit after discontinuation of therapy. (KAS 6) Clinicians who administer SLIT to patients with seasonal AR should offer pre- and co-seasonal immunotherapy. (KAS 7) Clinicians prescribing AIT should limit treatment to only those clinically relevant allergens that correlate with the patient's history and are confirmed by testing. (KAS 9) Clinicians administering AIT should continue escalation or maintenance dosing when patients have local reactions (LRs) to AIT. (KAS 11) Clinicians should avoid repeat allergy testing as an assessment of the efficacy of ongoing AIT unless there is a change in environmental exposures or a loss of control of symptoms. (KAS 12) For patients who are experiencing symptomatic control from AIT, clinicians should treat for a minimum duration of 3 years, with ongoing treatment duration based on patient response to treatment. The GDG offered the following KASs as options: (KAS 2B) Clinicians may choose not to initiate AIT for patients who use concomitant beta-blockers, have a history of anaphylaxis, have systemic immunosuppression, or have eosinophilic esophagitis (SLIT only). (KAS 8) Clinicians may treat polysensitized patients with a limited number of allergens.

Keywords: allergen immunotherapy; allergic asthma; allergic rhinitis; anaphylaxis; inhalant allergy; subcutaneous immunotherapy; sublingual immunotherapy.

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EClinicalMedicine

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. 2024 Feb 17:69:102500.

doi: 10.1016/j.eclinm.2024.102500. eCollection 2024 Mar.

[Long-term risks of respiratory diseases in patients infected with SARS-CoV-2: a longitudinal, population-based cohort study](#)

[Meijun Meng](#)^{1,2,3}, [Rui Wei](#)², [Yanjun Wu](#)^{2,3}, [Ruijie Zeng](#)^{2,4}, [Dongling Luo](#)¹, [Yuying Ma](#)^{2,3}, [Lijun Zhang](#)^{2,5}, [Wentao Huang](#)^{2,3}, [Hanshi Zeng](#)⁶, [Felix W Leung](#)^{7,8}, [Xinqi Qiu](#)⁹, [Weihong Sha](#)^{1,2,3,4,5}, [Hao Chen](#)^{1,2,3,4,5}

Affiliations expand

- PMID: 38389713
- PMCID: [PMC10882104](#)
- DOI: [10.1016/j.eclinm.2024.102500](#)

Free PMC article

Abstract

Background: In the post-pandemic era, growing apprehension exists regarding the potential sequelae of COVID-19. However, the risks of respiratory diseases following SARS-CoV-2 infection have not been comprehensively understood. This study aimed to investigate whether COVID-19 increases the long-term risk of respiratory illness in patients with COVID-19.

Methods: In this longitudinal, population-based cohort study, we built three distinct cohorts age 37-73 years using the UK Biobank database; a COVID-19 group diagnosed in medical records between January 30th, 2020 and October 30th, 2022, and two control groups, a contemporary control group and a historical control group, with cutoff dates of October 30th, 2022 and October 30th, 2019, respectively. The follow-up period of all three groups was 2.7 years (the median (IQR) follow-up time was 0.8 years). Respiratory outcomes diagnosed in medical records included common chronic pulmonary diseases (asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), pulmonary vascular disease (PVD), and lung cancer. For the data analysis, we calculated hazard ratios (HRs) along with their 95% CIs using Cox regression models, following the application of inverse probability weights (IPTW).

Findings: A total of 3 cohorts were included in this study; 112,311 individuals in the COVID-19 group with a mean age (\pm SDs) of 56.2 (8.1) years, 359,671 in the contemporary control group, and 370,979 in the historical control group. Compared with the contemporary control group, those infected with SARS-CoV-2 exhibited elevated risks for developing respiratory diseases. This includes asthma, with a HR of 1.49 and a 95% CI 1.28-1.74; bronchiectasis (1.30; 1.06-1.61); COPD (1.59; 1.41-1.81); ILD (1.81; 1.38-2.21); PVD (1.59; 1.39-1.82); and lung cancer (1.39; 1.13-1.71). With the severity of the acute phase of COVID-19, the risk of pre-described respiratory outcomes increases progressively. Besides, during the 24-months follow-up, we observed an increasing trend in the risks of asthma and bronchiectasis over time. Additionally, the HR of lung cancer for 0-6 month follow-up was 3.07 (CI 1.73-5.44), and the association of lung cancer with COVID-19 disease disappeared at 6-12 month follow-up (1.06; 0.43-2.64) and at 12-24 months (1.02; 0.45-2.34). Compared to those with one SARS-CoV-2 infection, reinfected patients were at a higher risk of asthma (3.0; 1.32-6.84), COPD (3.07; 1.42-6.65), ILD (3.61; 1.11-11.8), and lung cancer (3.20; 1.59-6.45). Similar findings were noted when comparing with a historical cohort serving as a control group, including asthma (1.31; 1.13-1.52); bronchiectasis (1.53; 1.23-1.89); COPD (1.41; 1.24-1.59); ILD (2.53; 2.05-3.13); PVD (2.30; 1.98-2.66); and lung cancer (2.23; 1.78-2.79).

Interpretation: Our research suggests that patients with COVID-19 may have an increased risk of developing respiratory diseases, and the risk increases with the severity of infection and reinfection. Even during the 24-month follow-up, the risk of asthma and bronchiectasis continued to increase. Hence, implementing appropriate follow-up strategies for these individuals is crucial to monitor and manage potential long-term respiratory health issues.

Additionally, the increased risk in lung cancer in the COVID-19 individuals was probably due to the diagnostic tests conducted and incidental diagnoses.

Funding: The National Natural Science Foundation of China of China Regional Innovation and Development Joint Foundation; National Natural Science Foundation of China; Program for High-level Foreign Expert Introduction of China; Natural Science Foundation for Distinguished Young Scholars of Guangdong Province; Guangdong Basic and Applied Basic Research Foundation; Climbing Program of Introduced Talents and High-level Hospital Construction Project of Guangdong Provincial People's Hospital; VA Clinical Merit and ASGE clinical research funds.

Keywords: COVID-19 (coronavirus disease 2019); Epidemiological study; Respiratory diseases; SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).

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Conflict of interest statement

All authors declare no competing interests.

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

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World Allergy Organ J

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. 2024 Feb 15;17(3):100879.

doi: 10.1016/j.waojou.2024.100879. eCollection 2024 Mar.

Diagnostic biomarkers for chronic rhinosinusitis in adult asthmatics in real-world practice

[Jae-Hyuk Jang](#)¹, [Eun-Mi Yang](#)¹, [Youngsoo Lee](#)¹, [Yoo Seob Shin](#)¹, [Young-Min Ye](#)¹, [Hae-Sim Park](#)¹

Affiliations [expand](#)

- PMID: 38380106
- PMCID: [PMC10877182](#)
- DOI: [10.1016/j.waojou.2024.100879](#)

Free PMC article

Abstract

Background: Chronic rhinosinusitis (CRS) is a common comorbid condition of asthma that affects the long-term outcome of asthmatic patients. CRS is a heterogeneous disease requiring multiple biomarkers to explain its pathogenesis. This study aimed to develop potential biomarkers for predicting CRS in adult asthmatic patients in a real-world clinical setting.

Methods: This study enrolled 108 adult asthmatic patients who had maintained anti-asthmatic medications, including medium-to-high doses of inhaled corticosteroid plus long-acting β 2-agonists, and compared clinical characteristics between patients with CRS (CRS group) and those without CRS (non-CRS group). CRS was diagnosed based on the results of paranasal sinus X-ray and/or osteomeatal-unit CT as well as clinical symptoms. Type-2 parameters, including blood eosinophil count, serum levels of periostin/dipeptidyl peptidase 10 (DPP10) and clinical parameters, such as FEV1% and fractional exhaled nitric oxide (FeNO), were analyzed. All biomarkers were evaluated by logistic regression and classification/regression tree (CRT) analyses.

Results: The CRS group had higher blood eosinophil counts/FeNO levels and prevalence of aspirin-exacerbated respiratory disease (AERD) than the non-CRS group (n = 57, 52.8% vs. n = 75, 47.2%; $P < 0.05$), but no differences in sex/smoking status or asthma control status were noted. The CRS group had higher serum periostin/DPP10 levels than the non-CRS group. Moreover, logistic regression demonstrated that serum periostin/DPP10 and the AERD phenotype were significant factors for predicting CRS in

asthmatic patients (adjusted odds ratio, 2.14/1.94/12.39). A diagnostic algorithm and the optimal cutoff values determined by CRT analysis were able to predict CRS with 86.27% sensitivity (a 0.17 negative likelihood ratio).

Conclusion: Serum periostin, DPP10 and the phenotype of AERD are valuable biomarkers for predicting CRS in adult asthmatic patients in clinical practice.

Keywords: Asthma; Biomarkers; Dipeptidyl-peptidases and tripeptidyl-peptidases; Eosinophils; Fractional exhaled nitric oxide testing; Periostin; Rhinitis; Sinusitis.

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Conflict of interest statement

None.

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

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Randomized Controlled Trial

Respir Med

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. 2024 Mar;223:107539.

doi: 10.1016/j.rmed.2024.107539. Epub 2024 Feb 5.

Improving asthma control and quality of life via a smartphone self-management app: A randomized controlled trial

[Mehrdad Farzandipour¹](#), [Marzieh Heidarzadeh Arani²](#), [Reihane Sharif³](#), [Ehsan Nabovati¹](#), [Hossein Akbari⁴](#), [Shima Anvari¹](#)

Affiliations expand

- PMID: 38325663
- DOI: [10.1016/j.rmed.2024.107539](https://doi.org/10.1016/j.rmed.2024.107539)

Abstract

Background: Mobile phone applications (apps) show promise for enhancing asthma self-management, but their effectiveness varies. This study examined the effect of a smartphone asthma app on asthma control and quality of life.

Methods: Using block randomization, 60 patients with asthma were allocated to an intervention group (n = 30) or control group (n = 30) for this single-blind randomized controlled trial. At baseline, both groups completed the Asthma Control Test (ACT) and Asthma Quality of Life Questionnaire-Marks (AQLQ-M). The intervention group used a smartphone-based asthma self-management app plus their regular treatment, while the control group received only usual care. Follow-up ACT and AQLQ-M assessments occurred at 3 and 6 months. SPSS version 26 was used for analysis, including descriptive statistics, non-parametric tests (Wilcoxon and Mann-Whitney U), and analysis of variance with repeated measurements.

Results: Both groups showed improved asthma control and quality of life at 3 and 6 months compared to baseline. However, after 6 months the intervention group had significantly greater improvement than controls ($p < 0.05$). Repeated measures ANOVA revealed divergent changes in ACT and AQLQ-M scores over time, with the intervention group demonstrating greater enhancement of asthma control and quality of life ($p < 0.001$).

Conclusion: This study demonstrated that use of a smartphone-based asthma self-management app improved asthma control and quality of life after 6 months compared to

usual care alone. These findings indicate that guideline-based asthma apps can positively impact outcomes.

Keywords: Asthma; Asthma control; Mobile applications; Quality of life; mHealth.

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Conflict of interest statement

Declaration of competing interest There is no conflict of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

Adv Ther

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. 2024 Mar;41(3):1262-1283.

doi: 10.1007/s12325-023-02746-0. Epub 2024 Feb 4.

[The Association Between Short-Acting \$\beta_2\$ -Agonist Over-Prescription, and Patient-Reported Acquisition and Use](#)

on Asthma Control and Exacerbations: Data from Australia

[David Price](#)^{1,2,3,4}, [Christine Jenkins](#)⁵, [Kerry Hancock](#)^{6,7}, [Rebecca Vella](#)⁸, [Florian Heraud](#)⁹, [Porsche Le Cheng](#)⁸, [Ruth Murray](#)¹⁰, [Maarten Beekman](#)¹¹, [Sinthia Bosnic-Anticevich](#)^{12,13}, [Fabio Botini](#)⁸, [Victoria Carter](#)¹⁰, [Angelina Catanzariti](#)¹⁴, [Joe Doan](#)¹⁵, [Kirsty Fletton](#)¹⁰, [Ata Kichkin](#)¹⁶, [Thao Le](#)¹⁷, [Chantal Le Lievre](#)⁸, [Chi Ming Lau](#)¹⁸, [Dominique Novic](#)¹⁹, [John Pakos](#)²⁰, [Kanchanamala Ranasinghe](#)^{21,22}, [Alexander Roussos](#)⁸, [Josephine Samuel-King](#)²³, [Anita Sharma](#)²⁴, [Deb Stewart](#)²⁵, [Bruce Willet](#)²⁶, [Eric Bateman](#)²⁷; [OPCA Improving Asthma Outcomes in Australia Research Group](#)

Collaborators, Affiliations expand

- PMID: 38310584
- PMCID: [PMC10879376](#)
- DOI: [10.1007/s12325-023-02746-0](#)

Free PMC article

Abstract

Introduction: In Australia, short-acting β_2 -agonists (SABA) are available both over the counter (OTC) and on prescription. This ease of access may impact SABA use in the Australian population. Our aim was to assess patterns and outcome associations of prescribed, acquired OTC and reported use of SABA by Australians with asthma.

Methods: This was a cross-sectional study, using data derived from primary care electronic medical records (EMRs) and patient completed questionnaires within Optimum Patient Care Research Database Australia (OPCRDA). A total of 720 individuals aged ≥ 12 years with an asthma diagnosis in their EMRs and receiving asthma therapy were included. The annual number of SABA inhalers authorised on prescription, acquired OTC and reported, and the association with self-reported exacerbations and asthma control were investigated.

Results: 92.9% (n = 380/409) of individuals issued with SABA prescription were authorised ≥ 3 inhalers annually, although this differed from self-reported usage. Of individuals reporting SABA use (n = 546) in the last 12 months, 37.0% reported using ≥ 3 inhalers. These patients who reported SABA overuse experienced 2.52 (95% confidence interval [CI] 1.73-3.70) times more severe exacerbations and were 4.51 times (95% CI 3.13-6.55) more likely to have poor asthma control than those who reported using 1-2 SABA inhalers. Patients who did not receive SABA on prescription (43.2%; n = 311/720) also experienced

2.71 (95% CI 1.07-7.26) times more severe exacerbations than those prescribed 1-2 inhalers. Of these patients, 38.9% reported using OTC SABA and other prescription medications, 26.4% reported using SABA OTC as their only asthma medication, 13.2% were prescribed other therapies but not SABA OTC and 14.5% were not using any medication.

Conclusion: Both self-reported SABA overuse and zero SABA prescriptions were associated with poor asthma outcomes. The disconnect between prescribing authorisation, OTC availability and actual use, make it difficult for clinicians to quantify SABA use.

Keywords: Asthma management; Asthma outcomes; Over-the-counter medication; Prescription patterns; Short-acting β 2-agonists.

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Conflict of interest statement

Kerry L. Hancock has received speakers' fees, consulting honoraria and/or travel grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Menarini Australia, Mylan and Novartis. Sinthia Bosnic-Anticevich has received honorarium for participation in expert advisory boards and given lectures for Teva Pharmaceuticals, AstraZeneca, GSK, Meda, Mundipharma, Sanofi, Mylan and received unrestricted research grants from Mylan, AstraZeneca, Teva and Mundipharma International. Angelina Catanzariti is an employee of AstraZeneca. Christine Jenkins, Joe Doan, Ata Kichkin, Chi Ming Lau, Dominique Novic, John Pakos, Kanchanamala Ranasinghe, Josephine Samuel-King, Bruce Willet, and Thao Le declares no conflict of interest. Anita Sharma is a practising Primary Care Physician and Senior Lecturer, School of Clinical Medicine-Primary Care Clinical Unit, University of Queensland. She supervises clinical training of primary care doctors and serves on advisory boards for Diabetes, Heart Failure and Osteoporosis for Novartis, Merck Sharp & Dohme and Boehringer Ingelheim, Eli Lilly and Amgen. Eric Bateman has received honorarium for participation in advisory boards from ALK, AstraZeneca, Novartis, Regeneron and Sanofi Aventis, and for giving lectures for AstraZeneca, Chiesi, Menarini, Novartis, Orion, Regeneron and Sanofi Aventis. He is a member of the Board and Science Committee of GINA. Maarten JHI Beekman was an employee of AstraZeneca at time of study conduct. Rebecca Vella, Florian Heraud, Porsche Le Cheng, Fabio Botini, Thao Le, Chantal Le Lievre, Alex Roussos are employees of Optimum Patient Care Australia. Ruth Murray is a consultant for the Observational and Pragmatic Research Institute. Victoria Carter is an employee of Optimum Patient Care Global and has 5% shareholding of Optimum Patient Care Australia. Kirsty Fletton is an employee of Optimum Patient Care United Kingdom. David Price has advisory board membership with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatrix, Teva Pharmaceuticals; consultancy agreements with AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Viatrix, Teva Pharmaceuticals; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Chiesi, Viatrix, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, and UK

National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Inside Practice, GlaxoSmithKline, Medscape, Viatrix, Novartis, Regeneron Pharmaceuticals and Sanofi Genzyme, Teva Pharmaceuticals; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Novartis, Medscape, Teva Pharmaceuticals.; stock/stock options from AKL Research and Development Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); 5% shareholding in Timestamp which develops adherence monitoring technology; is peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation programme, and Health Technology Assessment; and was an expert witness for GlaxoSmithKline.

- [32 references](#)
- [5 figures](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Randomized Controlled Trial

Adv Ther

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. 2024 Mar;41(3):1201-1225.

doi: 10.1007/s12325-023-02774-w. Epub 2024 Feb 1.

Effect of Individual Patient Characteristics and Treatment Choices on Reliever Medication Use in Moderate–Severe Asthma: A Poisson Analysis of Randomised Clinical Trials

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Affiliations expand

- PMID: 38296921
- PMCID: [PMC10879282](#)
- DOI: [10.1007/s12325-023-02774-w](#)

Free PMC article

Abstract

Introduction: Even though increased use of reliever medication, including short-acting beta agonists (SABA), provides an indirect measure of symptom worsening, there have been limited efforts to assess how different patterns of reliever use correlate with symptom control and future risk of exacerbations. Here, we evaluate the effect of individual baseline characteristics on reliever use in patients with moderate-severe asthma on regular maintenance therapy with fluticasone propionate (FP) or combination therapy with fluticasone propionate/salmeterol (FP/SAL) or budesonide/formoterol (BUD/FOR).

Methods: A drug-disease model describing the number of 24-h puffs and overnight occasions was developed with data from five clinical studies (N = 6212). The model was implemented using a nonlinear mixed effects approach and a Poisson function, considering clinical and demographic baseline characteristics. Goodness of fit and model predictive performance were assessed. Heatmaps were created to summarise the effect of concurrent baseline factors on reliever utilisation.

Results: The final model accurately described individual patterns of reliever use, which is significantly increased with time since diagnosis, smoking, higher Asthma Control

Questionnaire (ACQ-5) score and higher body mass index (BMI) at baseline. Whilst the number of puffs decreases slowly after an initial drop relative to the start of treatment, exacerbating patients utilise significantly more reliever than those who do not exacerbate. The mean effect of FP/SAL (median dose: 250/50 µg BID) on reliever use was slightly higher than that of BUD/FOR (median dose: 160/4.5 µg BID), i.e. a 75.3% vs 69.3% reduction in reliever use, respectively.

Conclusions: The availability of individual-level patient data in conjunction with a parametric approach enabled the characterisation of interindividual differences in the patterns of reliever use in patients with moderate-severe asthma. Taken together, individual demographic and clinical characteristics, as well as exacerbation history, can be considered an indicator of the degree of asthma control. High SABA reliever use suggests suboptimal clinical management of patients on maintenance therapy.

Keywords: Asthma symptom control; Drug-disease modelling; Exacerbation; ICS/LABA combination therapy; Inhaled corticosteroids; Reliever medication; Rescue medication; SABA; Short-acting beta agonists.

Plain language summary

In this study, we tried to understand how patients with moderate to severe asthma use their quick-relief inhalers (like albuterol), how it relates to their symptoms and the risk of having asthma attacks. To evaluate whether differences in reliever inhaler use between patients are associated with factors like smoking or their asthma symptoms at the beginning of treatment, we gathered data from five clinical studies (n = 6212 patients). These data allowed us to create a model that predicts how often patients use their reliever inhalers (expressed as number of puffs in 24 h) during maintenance therapy with inhaled corticosteroids alone or in combination with long-acting beta agonists. The final model showed that reliever inhaler use is higher in patients who have been diagnosed with asthma for > 10 years, are smokers, have higher asthma symptom scores, and are obese or extremely obese. Patients who had asthma attacks also used their reliever inhalers more often. In addition, to understand how relief inhalers are used in real-life situations, we also created heatmaps that include a wide range of patient characteristics. By using individual patient data together with this model, we have learned that smoking, asthma control, BMI, long history of asthma and previous asthma attacks significantly influence reliever use. This information can help physicians and healthcare professionals understand how well someone's asthma is managed. A patient who uses their reliever inhaler often is likely not to have their asthma well controlled by their regular medications.

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Conflict of interest statement

Ian Pavord has received honoraria for speaking at sponsored meetings from AstraZeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK, and payments for organising educational events from AstraZeneca, GSK, Sanofi/Regeneron and Teva; he has received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi and Knopp and payments to support FDA approval meetings from GSK; he has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, AstraZeneca, Teva and Chiesi; he has received a grant from Chiesi to support a Phase 2 clinical trial in Oxford; he is co-patent holder of the rights to the Leicester Cough Questionnaire and has received payments for its use in clinical trials from Merck, Bayer and Insmad; and in 2014–2015 he was an expert witness for a patent dispute involving AstraZeneca and Teva; Guy Brusselle has acted as a speaker/consultant for AstraZeneca, Boehringer-Ingelheim, Chiesi, GSK, Novartis, Sanofi and Teva; Arzu Yorgancıoğlu has received research grants from Novartis, MSD, AstraZeneca and Sanofi, and has acted as a speaker/consultant for AstraZeneca, Abdi İbrahim, GSK, Novartis, Chiesi and Bilim; Paulo Pitrez has acted as a speaker/consultant for AstraZeneca, GSK, Novartis, Boehringer Ingelheim and Sanofi; Sven van Dijkman, Sean Oosterholt, Sourabh Fulmali, Anurita Majumdar and Oscar Della Pasqua are GSK employees and hold stocks/shares in GSK.

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

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Am J Physiol Lung Cell Mol Physiol

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. 2024 Mar 1;326(3):L280-L291.

Early-life pulmonary viral infection leads to long-term functional and lower airway structural changes in the lungs

[Carrie-Anne Malinczak](#)¹, [Wendy Fonseca](#)¹, [Steven M Hrycaj](#)², [Susan B Morris](#)¹, [Andrew J Rasky](#)¹, [Kazuma Yagi](#)¹, [Deneen M Wellik](#)³, [Steven F Ziegler](#)⁴, [Rachel L Zemans](#)², [Nicholas W Lukacs](#)^{1,5}

Affiliations expand

- PMID: 38290164
- DOI: [10.1152/ajplung.00300.2023](https://doi.org/10.1152/ajplung.00300.2023)

Abstract

Early-life respiratory virus infections have been correlated with enhanced development of childhood asthma. In particular, significant numbers of respiratory syncytial virus (RSV)-hospitalized infants go on to develop lung disease. It has been suggested that early-life viral infections may lead to altered lung development or repair that negatively impacts lung function later in life. Our data demonstrate that early-life RSV infection modifies lung structure, leading to decreased lung function. At 5 wk postneonatal RSV infection, significant defects are observed in baseline pulmonary function test (PFT) parameters consistent with decreased lung function as well as enlarged alveolar spaces. Lung function changes in the early-life RSV-infected group continue at 3 mo of age. The altered PFT and structural changes induced by early-life RSV were mitigated in *TSLPR*^{-/-} mice that have previously been shown to have reduced immune cell accumulation associated with a persistent Th2 environment. Importantly, long-term effects were demonstrated using a secondary RSV infection 3 mo following the initial early-life RSV infection and led to significant additional defects in lung function, with severe mucus deposition within the airways, and consolidation of the alveolar spaces. These studies suggest that early-life respiratory viral infection leads to alterations in lung structure/repair that predispose to diminished lung function later in life. **NEW & NOTEWORTHY** These studies outline a novel finding that early-life respiratory virus infection can alter lung structure and function long-term. Importantly, the data also indicate that there are critical links between inflammatory responses and subsequent events that produce a more severe pathogenic response later in

life. The findings provide additional data to support that early-life infections during lung development can alter the trajectory of airway function.

Keywords: RSV; lung function.

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Respir Med



. 2024 Mar;223:107543.

doi: 10.1016/j.rmed.2024.107543. Epub 2024 Jan 28.

[The diagnostic value of bronchial provocation testing combined with fractional exhaled nitric oxide \(FeNO\) in children with chest tightness - variant asthma \(CTVA\)](#)

[Tengteng Zhang](#)¹, [Lijuan Xu](#)², [Yingqian Zhang](#)¹, [Lina Zhen](#)³

Affiliations expand

- PMID: 38286340

- DOI: [10.1016/j.rmed.2024.107543](https://doi.org/10.1016/j.rmed.2024.107543)

Abstract

Background: Chest tightness-variant asthma (CTVA) is a novel atypical asthma characterized by chest tightness as the sole or primary symptom.

Objectives: To investigate the value of bronchial provocation testing combined with fractional exhaled nitric oxide (FeNO) in the diagnosis of CTVA in children.

Methods: This study included 95 children aged 6-14 years with chest tightness as the sole symptom, with a duration of symptoms exceeding 4 weeks. All subjects underwent FeNO measurement, pulmonary function testing, and bronchial provocation testing using the Astograph method. Subjects with positive bronchial provocation testing were classified as the CTVA group, while those with negative results served as the non-CTVA control group.

Results: The lung function of children in both groups was normal. The FeNO level in the CTVA group was (22.35 ± 9.91) ppb, significantly higher than the control group (14.85 ± 5.63) ppb, with a statistically significant difference ($P < 0.05$). The value of FeNO in diagnosing CTVA was analyzed using an ROC curve, with an area under the curve of 0.073 ($P < 0.05$). The optimal cutoff point for diagnosing CTVA using FeNO was determined to be 18.5 ppb, with a sensitivity of 60.3 % and specificity of 77.8 %. There was a negative correlation between FeNO and Dmin as well as PD15 ($P = 0.006$).

Conclusion: FeNO can serve as an adjunctive diagnostic tool for CTVA, with the optimal cutoff point for diagnosing CTVA being 18.5 ppb. However, FeNO is not a specific diagnostic marker for CTVA and should be used in conjunction with bronchial provocation testing to enhance its diagnostic value.

Keywords: Bronchial provocation testing; CTVA; Chest tightness-variant asthma; Fractional exhaled nitric oxide.

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Conflict of interest statement

Declaration of competing interest None.

SUPPLEMENTARY INFO

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Meta-Analysis

Allergy



. 2024 Mar;79(3):643-655.

doi: 10.1111/all.16000. Epub 2024 Jan 23.

Plasma protein signatures of adult asthma

[Gordon J Smilnak¹](#), [Yura Lee²](#), [Abhijnan Chattopadhyay¹](#), [Annah B Wyss¹](#), [Julie D White^{1,3}](#), [Sinjini Sikdar^{1,4}](#), [Jianping Jin⁵](#), [Andrew J Grant⁶](#), [Alison A Motsinger-Reif⁷](#), [Jian-Liang Li⁸](#), [Mikyeong Lee¹](#), [Bing Yu²](#), [Stephanie J London¹](#)

Affiliations expand

- PMID: 38263798
- DOI: [10.1111/all.16000](https://doi.org/10.1111/all.16000)

Abstract

Background: Adult asthma is complex and incompletely understood. Plasma proteomics is an evolving technique that can both generate biomarkers and provide insights into disease mechanisms. We aimed to identify plasma proteomic signatures of adult asthma.

Methods: Protein abundance in plasma was measured in individuals from the Agricultural Lung Health Study (ALHS) (761 asthma, 1095 non-case) and the Atherosclerosis Risk in Communities study (470 asthma, 10,669 non-case) using the SOMAScan 5K array. Associations with asthma were estimated using covariate adjusted logistic regression and

meta-analyzed using inverse-variance weighting. Additionally, in ALHS, we examined phenotypes based on both asthma and seroatopy (asthma with atopy (n = 207), asthma without atopy (n = 554), atopy without asthma (n = 147), compared to neither (n = 948)).

Results: Meta-analysis of 4860 proteins identified 115 significantly (FDR<0.05) associated with asthma. Multiple signaling pathways related to airway inflammation and pulmonary injury were enriched (FDR<0.05) among these proteins. A proteomic score generated using machine learning provided predictive value for asthma (AUC = 0.77, 95% CI = 0.75-0.79 in training set; AUC = 0.72, 95% CI = 0.69-0.75 in validation set). Twenty proteins are targeted by approved or investigational drugs for asthma or other conditions, suggesting potential drug repurposing. The combined asthma-atopy phenotype showed significant associations with 20 proteins, including five not identified in the overall asthma analysis.

Conclusion: This first large-scale proteomics study identified over 100 plasma proteins associated with current asthma in adults. In addition to validating previous associations, we identified many novel proteins that could inform development of diagnostic biomarkers and therapeutic targets in asthma management.

Keywords: allergy; area under curve; biomarkers; precision medicine; proteomics.

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- [73 references](#)

SUPPLEMENTARY INFO

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

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[Review](#)

Acta Physiol (Oxf)



. 2024 Mar;240(3):e14092.

doi: 10.1111/apha.14092. Epub 2024 Jan 22.

The gut–lung axis and asthma susceptibility in early life

[Fariz G Kahhaleh](#)¹, [Gabriela Barrientos](#)^{2,3}, [Melanie L Conrad](#)¹

Affiliations expand

- PMID: 38251788
- DOI: [10.1111/apha.14092](https://doi.org/10.1111/apha.14092)

Abstract

Asthma is the most common chronic disease among children, with more than 300 million cases worldwide. Over the past several decades, asthma incidence has grown, and epidemiological studies identify the modernized lifestyle as playing a strong contributing role in this phenomenon. In particular, lifestyle factors that modify the maternal gut microbiome during pregnancy, or the infant microbiome in early life, can act as developmental programming events which determine health or disease susceptibility later in life. Microbial colonization of the gut begins at birth, and factors such as delivery mode, breastfeeding, diet, antibiotic use, and exposure to environmental bacteria influence the development of the infant microbiome. Colonization of the gut microbiome is crucial for proper immune system development and disruptions to this process can predispose a child to asthma development. Here, we describe the importance of early-life events for shaping immune responses along the gut-lung axis and why they may provide a window of opportunity for asthma prevention.

Keywords: DOHaD; antibiotic; asthma; early life; gut-lung axis; hygiene hypothesis; microbiome.

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- [142 references](#)

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Publication types, MeSH terms, Grants and fundingexpand

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Pediatr Infect Dis J



. 2024 Mar 1;43(3):234-241.

doi: 10.1097/INF.0000000000004193. Epub 2024 Jan 18.

[Risk Factors for Severe and Critical Coronavirus Disease 2019 in Children](#)

[Kyung-Shin Lee](#)¹, [Ye Kyung Kim](#)², [Youn Young Choi](#)^{1,3}, [Young June Choe](#)⁴, [Myoung-Hee Kim](#)⁵, [Hyunju Lee](#)^{6,7}

Affiliations expand

- PMID: 38241652
- DOI: [10.1097/INF.0000000000004193](https://doi.org/10.1097/INF.0000000000004193)

Abstract

Background: Coronavirus disease 2019 (COVID-19) is generally mild in children; however, severe or critical cases may occur. In this nationwide study, we analyzed clinical manifestations in children diagnosed with severe acute respiratory syndrome coronavirus 2

to identify high-risk groups for severe or critical disease and compared the clinical features between the Delta- and Omicron-dominant periods.

Methods: Data were retrieved from the National Health Insurance Service (NHIS) database and merged with the Korea Disease Control and Prevention Agency-COVID-19-NHIS cohort, which includes information on COVID-19 cases and vaccination records. We included individuals <20 years old diagnosed with COVID-19 during both periods (Delta: July 25, 2021-January 15, 2022; Omicron: January 16, 2022-March 31, 2022).

Results: Proportion of severe or critical cases was higher during the Delta period than during the Omicron period. The Omicron period saw increased hospitalization for pneumonia and croup and increased likelihood of hospitalization for neurological manifestations. The risk of severe COVID-19 depended on age group (Delta: highest for 12-19 years; Omicron: 0-4 years). This risk was high in children with multiple complex chronic conditions during both periods and with obesity or asthma during the Delta but not during the Omicron period. Two-dose COVID-19 vaccination provided strong protection against severe disease in the Delta period (adjusted odds ratio: 0.20), with reduced effectiveness in the Omicron period (adjusted odds ratio: 0.91). However, it significantly reduced the risk of critical illness (adjusted odds ratio: 0.14).

Conclusions: These findings can facilitate identification of children at high risk of severe or critical COVID-19, who may require intensive medical support, and development of vaccination policies.

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Conflict of interest statement

The authors have no funding or conflicts of interest to disclose.

- [37 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Clinical Trial

Respir Investig

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. 2024 Mar;62(2):216-222.

doi: 10.1016/j.resinv.2023.12.009. Epub 2024 Jan 10.

Safety and efficacy of sirolimus in hospitalised patients with COVID-19 pneumonia

[Abhishek Singla](#)¹, [Nusrat Harun](#)², [Daniel F Dilling](#)³, [Karim Merchant](#)⁴, [Susan McMahan](#)¹, [Rebecca Ingledue](#)¹, [Alexandria French](#)¹, [Josefina A Corral](#)⁵, [Leslie Korbee](#)⁶, [Elizabeth J Kopras](#)¹, [Nishant Gupta](#)⁷

Affiliations expand

- PMID: 38211546
- DOI: [10.1016/j.resinv.2023.12.009](https://doi.org/10.1016/j.resinv.2023.12.009)

Abstract

Background: There is a critical need to develop novel therapies for COVID-19.

Methods: We conducted a phase 2, multicentre, placebo-controlled, double-blind, randomised trial; hospitalised patients with hypoxemic respiratory failure due to COVID-19 and at least one poor prognostic biomarker, were given sirolimus (6 mg on Day 1 followed by 2 mg daily for 14 days or hospital discharge, whichever happens first) or placebo, in a 2:1 randomization scheme favouring sirolimus. Primary outcome was the proportion of patients alive and free from advanced respiratory support measures at Day 28.

Results: Between April 2020 and April 2021, 32 patients underwent randomization and 28 received either sirolimus (n = 18) or placebo (n = 10). Mean age was 57 years and 75 % of

the subjects were men. Twenty-two subjects had at least one co-existing condition (Diabetes, hypertension, obesity, CHF, or asthma/COPD) associated with worse prognosis. Mean FiO₂ requirement was 0.35. There was no difference in the proportion of patients who were alive and free from advanced respiratory support measures in the sirolimus group (n = 15, 83 %) compared with the placebo group (n = 8, 80 %). Although patients in the sirolimus group demonstrated faster improvement in oxygenation and spent less time in the hospital, these differences were not statistically significant. There was no between-group difference in the rate of change in serum biomarkers such as LDH, ferritin, d-dimer or lymphocyte count. There was a decreased risk of thromboembolic complications in patients on sirolimus compared with placebo.

Conclusions: Larger studies are warranted to evaluate the role sirolimus in COVID-19 infection.

Keywords: Clinical trial; Rapamycin; SARS-CoV-2; SCOPE; mTOR.

Published by Elsevier B.V.

Conflict of interest statement

Declaration of competing interest The authors report no conflict of interest.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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[Review](#)

Respir Investig

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. 2024 Mar;62(2):206-215.

doi: 10.1016/j.resinv.2023.12.015. Epub 2024 Jan 10.

Efficacy and safety of macrolide therapy for adult asthma: A systematic review and meta-analysis

[Yosuke Fukuda](#)¹, [Nobuyuki Horita](#)², [Masaharu Aga](#)³, [Fumihiro Kashizaki](#)⁴, [Yu Hara](#)⁵, [Yasushi Obase](#)⁶, [Akio Niimi](#)⁷, [Takeshi Kaneko](#)⁵, [Hiroshi Mukae](#)⁶, [Hironori Sagara](#)⁸

Affiliations expand

- PMID: 38211545
- DOI: [10.1016/j.resinv.2023.12.015](https://doi.org/10.1016/j.resinv.2023.12.015)

Free article

Abstract

Background: The evidence for macrolide therapy in adult asthma is not properly established and remains controversial. We conducted a systematic review and meta-analysis to examine the efficacy and safety of macrolide therapy for adult asthma.

Methods: We searched randomized controlled trials from MEDLINE via the PubMed, CENTRAL, and Ichushi Web databases. The primary outcome was asthma exacerbation. The secondary outcomes were serious adverse events (including mortality), asthma-related quality of life (symptom scales, Asthma Control Questionnaire, and Asthma Quality of Life Questionnaire), rescue medication (puffs/day), respiratory function (morning peak expiratory flow, evening peak flow, and forced expiratory volume in 1 s), bronchial hyperresponsiveness, and minimum oral corticosteroid dose. Of the 805 studies, we selected seven studies for the meta-analysis, which was conducted using a random-effects model.

Systematic review registration: University Hospital Medical Information Network Clinical Trials Registry (UMIN000050824).

Results: No significant difference between macrolide and placebo for asthma exacerbations was observed (risk ratio 0.71, 95 % confidence interval [CI] 0.46-1.09; $p = 0.12$). Macrolide therapy for adult asthma showed a significant improvement in rescue medication with short-acting beta-agonists (mean difference -0.41, 95 % CI -0.78 to -0.04;

$p = 0.03$). Macrolide therapy did not show more serious adverse events (odds ratio 0.61, 95% CI 0.34-1.10; $p = 0.10$) than those with placebo. The other secondary outcomes were not significantly different between the macrolide and placebo groups.

Conclusions: Macrolide therapy for adult asthma may be more effective than placebo and could be a treatment option.

Keywords: Adult; Asthma; Azithromycin; Clarithromycin; Exacerbation; Macrolide.

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Conflict of interest statement

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

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Am J Physiol Lung Cell Mol Physiol

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. 2024 Mar 1;326(3):L266-L279.

doi: 10.1152/ajplung.00419.2022. Epub 2023 Dec 27.

[Small airway fibroblasts from patients with chronic obstructive pulmonary disease exhibit cellular senescence](#)

[Catherine L Wrench](#)^{1,2}, [Jonathan R Baker](#)¹, [Sue Monkley](#)³, [Peter S Fenwick](#)¹, [Lynne Murray](#)², [Louise E Donnelly](#)¹, [Peter J Barnes](#)¹

Affiliations expand

- PMID: 38150543
- DOI: [10.1152/ajplung.00419.2022](https://doi.org/10.1152/ajplung.00419.2022)

Free article

Abstract

Small airway disease (SAD) is a key early-stage pathology of chronic obstructive pulmonary disease (COPD). COPD is associated with cellular senescence whereby cells undergo growth arrest and express the senescence-associated secretory phenotype (SASP) leading to chronic inflammation and tissue remodeling. Parenchymal-derived fibroblasts have been shown to display senescent properties in COPD, however small airway fibroblasts (SAFs) have not been investigated. Therefore, this study investigated the role of these cells in COPD and their potential contribution to SAD. To investigate the senescent and fibrotic phenotype of SAF in COPD, SAFs were isolated from nonsmoker, smoker, and COPD lung resection tissue ($n = 9-17$ donors). Senescence and fibrotic marker expressions were determined using iCELLigence (proliferation), qPCR, Seahorse assay, and ELISAs. COPD SAFs were further enriched for senescent cells using FACS Aria Fusion based on cell size and autofluorescence (10% largest/autofluorescent vs. 10% smallest/nonautofluorescent). The phenotype of the senescence-enriched population was investigated using RNA sequencing and pathway analysis. Markers of senescence were observed in COPD SAFs, including senescence-associated β -galactosidase, SASP release, and reduced proliferation. Because the pathways driving this phenotype were unclear, we used cell sorting to enrich senescent COPD SAFs. This population displayed increased p21^{CIP1} and p16^{INK4a} expression and mitochondrial dysfunction. RNA sequencing suggested these senescent cells express genes involved in oxidative stress response, fibrosis, and mitochondrial dysfunction pathways. These data suggest COPD SAFs are senescent and may be associated with fibrotic properties and mitochondrial dysfunction. Further understanding of cellular senescence in SAFs may lead to potential therapies to limit SAD progression. **NEW & NOTEWORTHY** Fibroblasts and senescence are thought to play key roles in the pathogenesis of small airway disease and COPD; however, the characteristics of small airway-derived fibroblasts are not well explored. In this study we isolate and enrich the senescent small airway-derived fibroblast (SAF) population from COPD lungs and explore the pathways driving this phenotype using bulk RNA-seq.

Keywords: COPD; fibroblast; senescence; small airway disease.

- [Cited by 1 article](#)

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MeSH terms, Supplementary concepts, Grants and fundingexpand

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Pediatr Pulmonol

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. 2024 Mar;59(3):798-800.

doi: 10.1002/ppul.26825. Epub 2023 Dec 27.

[Asthma care: The need for evidence-based, equitable, and affordable approaches](#)

[Kavita Jyoti Prakash](#)¹, [Anand Gourishankar](#)²

Affiliations expand

- PMID: 38149486
- DOI: [10.1002/ppul.26825](https://doi.org/10.1002/ppul.26825)

No abstract available

Keywords: asthma and early wheeze; asthma care; equity; social dimensions of pulmonary medicine.

- [11 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and fundingexpand

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Meta-Analysis

Arch Gerontol Geriatr

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. 2024 Mar;118:105310.

doi: 10.1016/j.archger.2023.105310. Epub 2023 Dec 12.

[Causal relationship between frailty and chronic obstructive pulmonary disease or asthma: A two sample bidirectional Mendelian randomization study](#)

[Jingge Qu](#)¹, [Ying Liang](#)¹, [Yafei Rao](#)¹, [Yuqiang Pei](#)¹, [Danyang Li](#)¹, [Yue Zhang](#)¹, [Yahong Chen](#)¹, [Yongchang Sun](#)²

Affiliations expand

- PMID: 38128266
- DOI: [10.1016/j.archger.2023.105310](https://doi.org/10.1016/j.archger.2023.105310)

Abstract

Background: Observational studies have established a strong association between frailty and obstructive lung diseases. However, the causal nature of this association remains unclear. To address this gap, we conducted a bidirectional Mendelian randomization (MR) study to investigate the causal relationship between frailty, as measured by the frailty index (FI), and chronic obstructive pulmonary disease (COPD) or asthma.

Methods: The latest meta-analysis of genome-wide association studies for FI, which included individuals of European ancestry from UK Biobank and TwinGene (N = 175,226), yielded the genetic instruments for frailty and outcome summary statistics. The genetic instrument for COPD and asthma, as well as the outcome summary data, were derived from the GWAS conducted on individuals of European ancestry from the FinnGen, with a sample size of 16,410 cases and 283,589 controls for COPD, and 37,253 cases and 187,112 controls for asthma. The analysis of MR was conducted employing the inverse-variance weighted (IVW) method, complemented by the weighted median method, MR-Egger regression, and MR pleiotropy residual sum and outlier (MR-PRESSO) test.

Results: Our results showed that genetically predicted higher FI was significantly associated with increased risk of COPD (odds ratio [OR] 1.75, 95 % confidence interval [CI] 1.29-2.36) and asthma (OR 2.10, 95 % CI 1.44-3.16). In the reverse direction analysis, genetic liability to both COPD (beta 0.06, 95 % CI 0.01-0.10) and asthma (beta 0.08, 95 % CI 0.06-0.11) showed significant associations with a higher FI.

Conclusions: Our research has reinforced the existing evidence supporting a reciprocal causal relationship between frailty and obstructive lung diseases. A deeper comprehension of this interconnection is imperative for the prevention and treatment of obstructive lung diseases.

Keywords: Asthma; Chronic obstructive pulmonary disease; Frailty; Mendelian randomization study.

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Conflict of interest statement

Declaration of Competing Interest The authors have declared no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Observational Study

Pediatr Pulmonol

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. 2024 Mar;59(3):743-749.

doi: 10.1002/ppul.26824. Epub 2023 Dec 20.

[Palivizumab prophylaxis in preterm infants and subsequent wheezing/asthma: 10-year follow-up study](#)

[Masahiko Kato](#)^{1,2}, [Hiroyuki Mochizuki](#)^{1,2}, [Yuichi Kama](#)¹, [Satoshi Kusuda](#)³, [Kenji Okada](#)⁴, [Shigemi Yoshihara](#)⁵, [Hiroyuki Furuya](#)⁶, [Eric A F Simões](#)⁷; [Scientific Committee for Elucidation of Infantile Asthma \(SCELIA\)](#)

Affiliations [expand](#)

- PMID: 38116923
- DOI: [10.1002/ppul.26824](https://doi.org/10.1002/ppul.26824)

Abstract

Background: Respiratory syncytial virus (RSV) causes not only infantile recurrent wheezing but also the development of asthma. To investigate whether palivizumab, an anti-RSV

monoclonal antibody, prophylaxis given to preterm infants during the first RSV season reduces the incidence of subsequent recurrent wheezing and/or development of asthma, at 10 years of age.

Methods: We conducted an observational prospective multicenter (52 registered hospitals in Japan) case-control study in preterm infants with a gestational age between 33 and 35 weeks followed for 6 years. During the 2007-2008 RSV season, the decision to administer palivizumab was made based on standard medical practice (SCELIA study). Here, we followed these subjects until 10 years of age. Parents of study subjects reported the patients' physician's assessment of recurrent wheezing/asthma, using a report card and a novel mobile phone-based reporting system using the internet. The relationship between RSV infection and asthma development, as well as the relationship between other factors and asthma development, were investigated.

Results: Of 154 preterm infants enrolled, 113 received palivizumab during the first year of life. At 10 years, although both recurrent wheezing and development of asthma were not significantly different between the treated and untreated groups, maternal smoking with aeroallergen sensitization of the patients was significantly correlated with physician-diagnosed asthma.

Conclusions: In contrast to the prior study results at 6 years, by 10 years palivizumab prophylaxis had no impact on recurrent wheezing or asthma, but there was a significant correlation between maternal passive smoking with aeroallergen sensitization and development of asthma by 10 years of age.

Keywords: aeroallergen sensitization; asthma development; palivizumab; passive smoking; respiratory syncytial virus.

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- [33 references](#)

SUPPLEMENTARY INFO

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. 2024 Mar;20(3):335-344.

doi: 10.1016/j.sapharm.2023.12.002. Epub 2023 Dec 10.

The association of depressive symptoms and medication adherence in asthma patients: The mediation effect of medication beliefs

[Ruiying Dong](#)¹, [Shanwen Sun](#)¹, [Yajun Sun](#)¹, [Yali Wang](#)¹, [Xiaochun Zhang](#)²

Affiliations expand

- PMID: 38110324
- DOI: [10.1016/j.sapharm.2023.12.002](https://doi.org/10.1016/j.sapharm.2023.12.002)

Free article

Abstract

Background: The significant role of depression in influencing medication beliefs, which are pivotal cognitive factors that strongly influence medication adherence, has been established. Poor adherence to asthma-controlled medication poses an significant barrier to achieving optimal asthma management.

Objective: To explore the potential mediating effects of medication beliefs on the relationship between depressive symptoms and medication adherence in patients with asthma.

Methods: Demographic and clinical characteristics, depressive symptoms, medication adherence, and medication beliefs were collected using questionnaires. Structural equation modeling, was utilized to model medication beliefs as mediators in the relationship between depressive symptoms and medication adherence. Bootstrapping was performed

to analyze the mediation- and contrast-specific indirect effects of the two medication beliefs.

Results: Among the patients who participated in the study, 29.6 % with depressive symptoms were more prone to poor adherence and exhibited skepticism toward asthma medications. Depression had a direct effect (direct effect = -0.275, 95%CI: -0.369 to -0.190) and an indirect effect on adherence mediated by medication beliefs (indirect effect = -0.168, 95%CI: -0.224 to -0.121). The specific mediation effect of concern belief was stronger than that of necessity belief (difference = -0.076, 95%CI: -0.132 to -0.029).

Conclusion: Depressive symptoms have a direct impact on medication adherence as well as an indirect effect mediated by beliefs about medication, particularly concerns belief.

Keywords: Adherence; Asthma; Depressive symptoms; Medication beliefs.

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MeSH termsexpand

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23

Randomized Controlled Trial

J Pediatr

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. 2024 Mar;266:113867.

doi: 10.1016/j.jpeds.2023.113867. Epub 2023 Dec 6.

Effect of the Telemedicine Enhanced Asthma Management Through the Emergency Department (TEAM-ED) Program on Asthma Morbidity: A Randomized Controlled Trial

[Jill S Halterman](#)¹, [Maria Fagnano](#)², [Paul Tremblay](#)², [Arlene Butz](#)³, [Tamara T Perry](#)⁴, [Hongyue Wang](#)⁵

Affiliations expand

- PMID: 38065280
- DOI: [10.1016/j.jpeds.2023.113867](https://doi.org/10.1016/j.jpeds.2023.113867)

Abstract

Objective: To test the effectiveness of a telemedicine-based program in reducing asthma morbidity among children who present to the emergency department (ED) for asthma, by facilitating primary care follow-up and promoting delivery of guideline-based care.

Study design: We included children (3-12 years of age) with persistent asthma who presented to the ED for asthma, who were then randomly assigned to Telemedicine Enhanced Asthma Management through the Emergency Department (TEAM-ED) or enhanced usual care. TEAM-ED included (1) school-based telemedicine follow-ups, completed by a primary care provider, (2) point-of-care prompting to promote guideline-based care, and 3) an opportunity for 2 additional telemedicine follow-ups. The primary outcome was the mean number of symptom-free days (SFDs) over 2 weeks at 3, 6, 9, and 12 months.

Results: We included 373 children from 2016 through 2021 (participation rate 68%; 54% Black, 32% Hispanic, 77% public insurance; mean age, 6.4 years). Demographic characteristics and asthma severity were similar between groups at baseline. Most (91%) TEAM-ED children had ≥ 1 telemedicine visit and 41% completed 3 visits. At 3 months, caregivers of children in TEAM-ED reported more follow-up visits (66% vs 48%; aOR, 2.07; 95% CI, 1.28-3.33), preventive asthma medication actions (90% vs 79%; aOR, 3.28; 95% CI, 1.56-6.89), and use of a preventive medication (82% vs 69%; aOR, 2.716; 95% CI, 1.45-5.08), compared with enhanced usual care. There was no difference between groups in medication adherence or asthma morbidity. When only prepandemic data were included,

there was greater improvement in SFDs over time for children in TEAM-ED vs enhanced usual care.

Conclusions: TEAM-ED significantly improved follow-up and preventive care after an ED visit for asthma. We also saw improved SFDs with prepandemic data. The lack of overall improvement in morbidity and adherence indicates the need for additional ongoing management support.

Trial registration: [NCT02752165](https://www.clinicaltrials.gov/ct2/show/study/NCT02752165).

Keywords: asthma; child; emergency department; prevention; telemedicine.

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Conflict of interest statement

Declaration of Competing Interest The authors declare no conflicts of interest. Funded by a grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health (R01HL091835). The funder had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Associated data, Grants and fundingexpand

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24

Case Reports

J Diabetes Investig

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. 2024 Mar;15(3):388-390.

A case of type 2 diabetes mellitus with weight gain and worsening of glycemic management after tezepelumab administration for severe bronchial asthma

[Kotaro Umamoto](#)¹, [Ryotaro Bouchi](#)^{1,2}, [Noriko Ihana-Sugiyama](#)^{1,2}, [Noriko Kodani](#)¹, [Mitsuru Ohsugi](#)^{1,2}, [Masayuki Hojo](#)³, [Kohjiro Ueki](#)^{1,4}, [Hiroshi Kajio](#)¹

Affiliations expand

- PMID: 38064175
- PMCID: [PMC10906019](#)
- DOI: [10.1111/jdi.14127](#)

Free PMC article

Abstract

Some cases of bronchial asthma are refractory to conventional therapies. As the pathogenesis of bronchial asthma has been clarified, new treatments, such as bronchial thermoplasty and biological drugs, have been developed. Tezepelumab, an anti-thymic stromal lymphopoietin antibody, has been reported to inhibit the exacerbation of severe asthma; however, its adverse effects on glucose metabolism have not yet been reported. We encountered a case of weight gain and worsening glycemic management in a patient with type 2 diabetes and refractory bronchial asthma after the initiation of tezepelumab treatment. It has been reported that the overexpression of thymic stromal lymphopoietin in mice resulted in an enhanced release of free fatty acids from adipose tissues and the liver; thus, the administration of anti-thymic stromal lymphopoietin antibodies in the present case might have caused obesity, fatty liver and lower glucose tolerance.

Keywords: Asthma; Obesity; Tezepelumab.

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

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Pulm Ther

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. 2024 Mar;10(1):53-67.

doi: 10.1007/s41030-023-00245-9. Epub 2023 Dec 8.

[Effect of Tezepelumab on the Humoral Immune Response to Seasonal Quadrivalent Influenza Vaccination in Patients with Moderate to Severe Asthma: The Phase 3b VECTOR Study](#)

[Jeremy Cole](#)¹, [Iwona Capała-Szczurko](#)², [Stephanie Roseti](#)³, [Claudia Chen](#)⁴, [Scott Caveney](#)⁵, [Anastasia A Aksyuk](#)⁶, [Katie Streicher](#)⁶, [Sandhia Ponnarambil](#)^{7,8}, [Gene Colice](#)³

Affiliations [expand](#)

- PMID: 38064153

- PMID: [PMC10881940](#)
- DOI: [10.1007/s41030-023-00245-9](#)

Free PMC article

Abstract

Introduction: Annual influenza vaccinations are recommended for adolescents and adults with moderate to severe asthma. This study investigated the effect of tezepelumab, a human monoclonal antibody that blocks the activity of thymic stromal lymphopoietin, on the humoral immune response to the quadrivalent seasonal influenza vaccine in patients with moderate to severe asthma.

Methods: VECTOR was a phase 3b, randomized, multicenter, double-blind, parallel-group, placebo-controlled study. Adolescents (aged 12-17 years) and young adults (aged 18-21 years) with moderate to severe asthma were enrolled across 15 centers in the USA. Patients received tezepelumab 210 mg or placebo subcutaneously at weeks 0, 4, 8, and 12, and a single dose of inactivated quadrivalent seasonal influenza vaccine at week 12 before receiving study treatment. Immediately before vaccination and at 4 weeks postvaccination (week 16), strain-specific antibody responses were assessed for four influenza antigens by hemagglutination inhibition (HAI) and microneutralization (MN) assays. Safety was assessed.

Results: Seventy patients were randomized to tezepelumab (n = 35) or placebo (n = 35). There were no meaningful differences in HAI or MN antibody responses between treatment groups at week 16. HAI assay geometric mean fold rises (GMFRs) for influenza strains were 1.76-7.34 for tezepelumab and 1.46-4.75 for placebo. MN assay GMFRs were 4.00-14.56 for tezepelumab and 3.56-10.62 for placebo. In the HAI assay, a fourfold or larger rise in antibody titer from weeks 12 to 16 occurred in 15.2-78.8% and 15.2-51.5% of tezepelumab and placebo recipients, respectively, and 97.0-100% of patients in both treatment groups achieved an antibody titer of at least 40 at week 16. No unexpected safety findings occurred.

Conclusion: There was no observed suppression of the humoral immune response after influenza vaccination in adolescents and young adults with moderate to severe asthma treated with tezepelumab. Therefore, the influenza vaccine can be administered to this patient population during tezepelumab treatment.

Gov identifier: [NCT05062759](#).

Keywords: Airway obstruction; Hemagglutinin; Inflammatory disorders; Microneutralization; Thymic stromal lymphopoietin.

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Conflict of interest statement

Jeremy Cole has nothing to declare. Iwona Cąpała-Szczurko, Stephanie Roseti, Claudia Chen, Anastasia A Aksyuk, Katie Streicher, and Sandhia Ponnarambil are employees of AstraZeneca and may own stock or stock options in AstraZeneca. Scott Caveney is an employee of Amgen and owns stock in Amgen. Gene Colice was an employee of AstraZeneca at the time of the study.

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

SUPPLEMENTARY INFO

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J Infect Dis

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. 2024 Mar 1;229(Supplement_1):S70-S77.

doi: 10.1093/infdis/jiad510.

Respiratory Syncytial Virus–Associated Hospitalization in Adults With

Comorbidities in 2 European Countries: A Modeling Study

[Richard Osei-Yeboah](#)¹, [Caroline Klint Johannesen](#)², [Amanda Marie Egeskov-Cavling](#)³, [Junru Chen](#)⁴, [Toni Lehtonen](#)⁵, [Arantxa Urchueguía Fornes](#)⁶, [John Paget](#)⁷, [Thea K Fischer](#)², [Xin Wang](#)^{1,4}, [Harish Nair](#)¹, [Harry Campbell](#)¹

Affiliations expand

- PMID: 37970679
- DOI: [10.1093/infdis/jiad510](https://doi.org/10.1093/infdis/jiad510)

Abstract

Background: Individuals with comorbidities are at increased risk of severe respiratory syncytial virus (RSV) infection. We estimated RSV-associated respiratory hospitalization among adults aged ≥ 45 years with comorbidities in Denmark and Scotland.

Methods: By analyzing national hospital and virologic data, we estimated annual RSV-associated hospitalizations by 7 selected comorbidities and ages between 2010 and 2018. We estimated rate ratios of RSV-associated hospitalization for adults with comorbidity than the overall population.

Results: In Denmark, annual RSV-associated hospitalization rates per 1000 adults ranged from 3.1 for asthma to 19.4 for chronic kidney disease (CKD). In Scotland, rates ranged from 2.4 for chronic liver disease to 9.0 for chronic obstructive pulmonary disease (COPD). In both countries, we found a 2- to 4-fold increased risk of RSV hospitalization for adults with COPD, ischemic heart disease, stroke, and diabetes; a 1.5- to 3-fold increased risk for asthma; and a 3- to 7-fold increased risk for CKD. RSV hospitalization rates among adults aged 45 to 64 years with COPD, asthma, ischemic heart disease, or CKD were higher than the overall population.

Conclusions: This study provides important evidence for identifying risk groups and assisting health authorities in RSV vaccination policy making.

Keywords: adults; comorbidity; hospitalization; respiratory syncytial virus.

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Conflict of interest statement

Potential conflicts of interest. H. C. reports grants, personal fees, and nonfinancial support from the World Health Organization; grants and personal fees from Sanofi Pasteur; and grants from the Bill and Melinda Gates Foundation, outside this submitted work. H. C. is a shareholder in the Journal of Global Health Ltd. H. N. reports grants from Pfizer and Icosavax and consulting fees from the World Health Organization, Pfizer, Bill and Melinda Gates Foundation, Abbvie, and Sanofi, outside the submitted work. H. N. reports participation on a data safety monitoring board or advisory board for GSK, Sanofi, Merck, the World Health Organization, Janssen, Novavax, Resvinct, Icosavax, and Pfizer. X. W. reports grants from GlaxoSmithKline and consultancy fees from Pfizer, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

SUPPLEMENTARY INFO

Grants and funding [expand](#)

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Review

Br J Pharmacol

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. 2024 Mar;181(5):610-639.

doi: 10.1111/bph.16272. Epub 2023 Dec 20.

[Use of human airway smooth muscle in vitro and ex vivo to investigate drugs](#)

for the treatment of chronic obstructive respiratory disorders

[Luigino Calzetta](#)¹, [Clive Page](#)², [Maria Gabriella Matera](#)³, [Mario Cazzola](#)⁴, [Paola Rogliani](#)⁴

Affiliations expand

- PMID: 37859567
- DOI: [10.1111/bph.16272](https://doi.org/10.1111/bph.16272)

Abstract

Isolated airway smooth muscle has been extensively investigated since 1840 to understand the pharmacology of airway diseases. There has often been poor predictability from murine experiments to drugs evaluated in patients with asthma or chronic obstructive pulmonary disease (COPD). However, the use of isolated human airways represents a sensible strategy to optimise the development of innovative molecules for the treatment of respiratory diseases. This review aims to provide updated evidence on the current uses of isolated human airways in validated in vitro methods to investigate drugs in development for the treatment of chronic obstructive respiratory disorders. This review also provides historical notes on the pioneering pharmacological research on isolated human airway tissues, the key differences between human and animal airways, as well as the pivotal differences between human medium bronchi and small airways. Experiments carried out with isolated human bronchial tissues in vitro and ex vivo replicate many of the main anatomical, pathophysiological, mechanical and immunological characteristics of patients with asthma or COPD. In vitro models of asthma and COPD using isolated human airways can provide information that is directly translatable into humans with obstructive lung diseases. Regardless of the technique used to investigate drugs for the treatment of chronic obstructive respiratory disorders (i.e., isolated organ bath systems, videomicroscopy and wire myography), the most limiting factors to produce high-quality and repeatable data remain closely tied to the manual skills of the researcher conducting experiments and the availability of suitable tissue.

Keywords: COPD; airway smooth muscle; asthma; epithelium damage; in vitro models; isolated human airways.

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SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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J Asthma

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. 2024 Mar;61(3):194-202.

doi: 10.1080/02770903.2023.2260868. Epub 2024 Feb 8.

[The relationships between Physical activity and asthma control and Body Mass Index \(BMI\) in patients with asthma](#)

[Bonny Rockette-Wagner](#)¹, [Juan P Wisnivesky](#)², [Fernando Holguin](#)³, [Jyoti Ankam](#)², [Arushi Arora](#)², [Emily Federmann](#)², [Vongphone Smith](#)³, [Alex D Federman](#)², [Molly B Conroy](#)⁴

Affiliations expand

- PMID: 37847059
- DOI: [10.1080/02770903.2023.2260868](https://doi.org/10.1080/02770903.2023.2260868)

Abstract

Objective: Asthma is one of the most common chronic conditions in developed countries. We examined whether physical activity (PA) is related to asthma control and body mass index (BMI) in asthma patients.

Methods: Cross-sectional data collected on PA (ActiGraph GT3X-BT), asthma control (the Asthma Control Questionnaire; ACQ), and BMI were examined in 206 adults (mean[*sd*] age 47.2[13.8] years; 49.5% had an obese BMI) with clinically diagnosed asthma. Relationships between PA and continuous BMI and asthma control were assessed using linear regression. Differences in PA across obesity (non-obese: <30 Kg/m²/obese: ≥30 Kg/m²) and asthma control categories (controlled: ≤0.75/uncontrolled: >0.75 ACQ score) were also examined.

Results: Median (*p*₂₅, *p*₇₅) steps counts and peak cadence were 6035 (4248, 8461) steps/day and 123 (115, 133) steps in a minute, respectively. There were nearly 2000 fewer steps/day among those with uncontrolled asthma versus controlled and among those with obese BMI versus nonobese, respectively (both *p* < 0.05). In regression models adjusted for relevant covariates each 1-unit increase in ACQ score was associated with -686 [95%CI -997, -13] (*p* ≤ 0.05) average steps/day. The statistical significance of these findings was attenuated (*p* ≥ 0.05) when BMI was added to the model. However, the point estimate was not reduced (-766 [95%CI -1060, 34]).

Conclusions: Overall step counts were low in this population despite peak cadence values suggesting that most participants could perform moderate intensity activity. Increasing step counts should be considered an important lifestyle intervention goal in obese and non-obese asthma patients with low PA levels.

Keywords: Overweight; accelerometry; cadence; obesity; steps.

SUPPLEMENTARY INFO

MeSH termsexpand

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Allergy

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. 2024 Mar;79(3):656-666.

doi: 10.1111/all.15918. Epub 2023 Oct 17.

Tezepelumab decreases airway epithelial IL-33 and T2-inflammation in response to viral stimulation in patients with asthma

[A Sverrild](#)¹, [S Cerps](#)², [J J Nieto-Fontarigo](#)^{2,3,4}, [S Ramu](#)², [M Hvidtfeldt](#)¹, [M Menzel](#)², [J Kearley](#)⁵, [J M Griffiths](#)⁶, [J R Parnes](#)⁷, [C Porsbjerg](#)¹, [L Uller](#)²

Affiliations expand

- PMID: 37846599
- DOI: [10.1111/all.15918](https://doi.org/10.1111/all.15918)

Abstract

Background: Respiratory virus infections are main triggers of asthma exacerbations. Tezepelumab, an anti-TSLP mAb, reduces exacerbations in patients with asthma, but the effect of blocking TSLP on host epithelial resistance and tolerance to virus infection is not known.

Aim: To examine effects of blocking TSLP in patients with asthma on host resistance (IFN β , IFN λ , and viral load) and on the airway epithelial inflammatory response to viral challenge.

Methods: Bronchoalveolar lavage fluid (BALF, n = 39) and bronchial epithelial cells (BECs) were obtained from patients with uncontrolled asthma before and after 12 weeks of tezepelumab treatment (n = 13) or placebo (n = 13). BECs were cultured in vitro and exposed to the viral infection mimic poly(I:C) or infected by rhinovirus (RV). Alarmins, T2- and pro-inflammatory cytokines, IFN β IFN λ , and viral load were analyzed by RT-qPCR and multiplex ELISA before and after stimulation.

Results: IL-33 expression in unstimulated BECs and IL-33 protein levels in BALF were reduced after 12 weeks of tezepelumab. Further, IL-33 gene and protein levels decreased in BECs challenged with poly(I:C) after tezepelumab whereas TSLP gene expression remained unaffected. Poly(I:C)-induced IL-4, IL-13, and IL-17A release from BECs was also

reduced with tezepelumab whereas IFN β and IFN λ expression and viral load were unchanged.

Conclusion: Blocking TSLP with tezepelumab in vivo in asthma reduced the airway epithelial inflammatory response including IL-33 and T2 cytokines to viral challenge without affecting anti-viral host resistance. Our results suggest that blocking TSLP stabilizes the bronchial epithelial immune response to respiratory viruses.

Keywords: airway epithelium; asthma; tezepelumab; virus.

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- [33 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grants and fundingexpand

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Multicenter Study

J Asthma

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. 2024 Mar;61(3):232-237.

doi: 10.1080/02770903.2023.2263078. Epub 2024 Feb 8.

[Safety and efficacy of benralizumab in elderly subjects with severe asthma](#)

[Marcela Valverde-Monge](#)^{1,2}, [Remedios Cárdenas](#)³, [Ismael García-Moguel](#)^{4,5}, [Ana Rosado](#)⁶, [Mar Gandolfo-Cano](#)^{7,8}, [Teresa Robledo Echarren](#)^{9,10}, [María Del Mar Moro-Moro](#)¹¹, [María Del Mar Reaño Martos](#)¹², [Rafael Pineda-Pineda](#)¹³, [Cristina Martín-Arriscado Arroba](#)¹⁴, [Javier Domínguez-Ortega](#)¹⁵, [AIRE Group](#)

Affiliations expand

- PMID: 37737844
- DOI: [10.1080/02770903.2023.2263078](https://doi.org/10.1080/02770903.2023.2263078)

Abstract

Introduction: The prevalence of asthma in adults >65 years old is approximately 12-14%, and 10% have severe asthma. A higher mortality rate is observed in subjects with asthma >65 years old and especially >80 years old.

Objective: To analyze the effectiveness and safety of at least three doses of benralizumab in a subgroup of elderly subjects (>65 years old) with uncontrolled severe eosinophilic asthma in real-life conditions.

Methods: This was a retrospective multicenter study (AUTOBENRA study) conducted in 9 hospitals that included 72 patients aged >18 years old with uncontrolled severe asthma based on the Spanish Asthma Guidelines who were treated with at least three doses of benralizumab, self-administered at home since before April 30, 2021. The recruitment period ended on October 1, 2021. Written consent was obtained before the study commencement. In this subanalysis, we compared the results between patients >65 years old and patients <65 years old.

Results: A total of 72 subjects with severe asthma were screened, and 54 were included (*MD*: 57.3 ± 10 years old). There were 12 subjects aged >65 years old [*MD*: 69.8 ± 4.3 years old (minimum: 65 years old; maximum: 83 years old)]. Subjects >65 years old experienced statistically significant improvement in lung function, ACT and mini-AQLQ with benralizumab. Additionally, 9 patients (75%) experienced no asthma exacerbation ($p = 0.0047$), half (3/6) were able to stop OCS ($p = 0.08$), and no adverse effects with benralizumab were reported during the 20 months of follow-up.

Conclusions: In patients aged >65 years old, benralizumab was an effective and safe therapy for severe eosinophilic asthma in our study, with no significant differences from the younger subgroup. This is especially important since they are a group with numerous comorbidities, medications and worse quality of life.

Keywords: >65 years old; Benralizumab; elderly; safety; self-administration; severe eosinophilic asthma.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances expand

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Cite

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31

J Asthma

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. 2024 Mar;61(3):238-248.

doi: 10.1080/02770903.2023.2263090. Epub 2024 Feb 8.

[Adherence to the asthma pathway, including pre-triage bronchodilator history, reduces hospitalizations](#)

[Suttipong Ittiporn](#)^{1,2}, [Kanlaya Prajongdee](#)³

Affiliations expand

- PMID: 37737546
- DOI: [10.1080/02770903.2023.2263090](https://doi.org/10.1080/02770903.2023.2263090)

Abstract

Objective: To determine if adherence to an asthma treatment pathway is associated with a decrease in hospitalizations. **Methods:** A prospective cohort design was conducted of Thai children aged 2-15 years who visited the emergency department with severe asthma

exacerbations, defined as a Buddhasothorn Asthma Severity Score ≥ 8 . Patients who received systemic corticosteroids and nebulized short-acting beta-2 agonists combined with ipratropium bromides were classified as the adherence group. The timing of steroid and bronchodilator administration, length of hospital stay, and hospitalization rate were examined in relation to adherence to the asthma pathway. Multivariable logistic regression models and adjusted odds ratios were used to assess associations. **Results:** A total of 118 episodes of asthma exacerbations (EAEs) from 59 participants were included. Patients who adhered to the pathway had a significantly higher rate of systemic corticosteroid administration within 1 h of arrival at triage (88.6% vs. 41.9%, adjusted Odds Ratio: aOR 10.21; 95%CI 3.52-29.62). A higher proportion of the patients who adhered to the pathway also received inhaled ipratropium bromide ≥ 2 doses within 1 h of arrival at triage (72.7% vs. 12.2%, aOR 23.51; 95%CI 7.73-71.54) and it was administered significantly faster by 31 min (5 min vs. 36 min, $p < 0.001$) compared to non-adherence group. The hospitalization rate was significantly lower by almost half of EAEs for adherence group (36.4% vs. 63.5%, aOR 0.41; 95%CI 0.18-0.93). **Conclusions:** Accurate assessment of severity and adherence to the clinical pathway can reduce hospitalization in pediatric patients with severe asthma exacerbations.

Keywords: Asthma; clinical pathway; emergency department; hospital admissions; pediatrics.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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J Asthma

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. 2024 Mar;61(3):203-211.

doi: 10.1080/02770903.2023.2260881. Epub 2024 Feb 8.

Predicting pediatric severe asthma exacerbations: an administrative claims-based predictive model

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Affiliations expand

- PMID: 37725084
- DOI: [10.1080/02770903.2023.2260881](https://doi.org/10.1080/02770903.2023.2260881)

Abstract

Objective: Previous machine learning approaches fail to consider race and ethnicity and social determinants of health (SDOH) to predict childhood asthma exacerbations. A predictive model for asthma exacerbations in children is developed to explore the importance of race and ethnicity, rural-urban commuting area (RUCA) codes, the Child Opportunity Index (COI), and other ICD-10 SDOH in predicting asthma outcomes.

Methods: Insurance and coverage claims data from the Arkansas All-Payer Claims Database were used to capture risk factors. We identified a cohort of 22,631 children with asthma aged 5-18 years with 2 years of continuous Medicaid enrollment and at least one asthma diagnosis in 2018. The goal was to predict asthma-related hospitalizations and asthma-related emergency department (ED) visits in 2019. The analytic sample was 59% age 5-11 years, 39% White, 33% Black, and 6% Hispanic. Conditional random forest models were used to train the model.

Results: The model yielded an area under the curve (AUC) of 72%, sensitivity of 55% and specificity of 78% in the OOB samples and AUC of 73%, sensitivity of 58% and specificity of 77% in the training samples. Consistent with previous literature, asthma-related hospitalization or ED visits in the previous year (2018) were the two most important variables in predicting hospital or ED use in the following year (2019), followed by the total number of reliever and controller medications.

Conclusions: Predictive models for asthma-related exacerbation achieved moderate accuracy, but race and ethnicity, ICD-10 SDOH, RUCA codes, and COI measures were not important in improving model accuracy.

Keywords: Random forest; claims data; conditional random forest; machine learning; variable importance.

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

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Cite

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33

Review

J Asthma

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. 2024 Mar;61(3):260-264.

doi: 10.1080/02770903.2023.2260884. Epub 2023 Sep 16.

[Dual biologics therapy in a patient with severe asthma and chronic urticaria: a case report and review of the literature](#)

[Ozge Can Bostan](#)¹, [Gul Karakaya](#)¹, [Ali Fuat Kalyoncu](#)¹, [Ebru Damadoglu](#)¹

Affiliations expand

- PMID: 37715663
- DOI: [10.1080/02770903.2023.2260884](https://doi.org/10.1080/02770903.2023.2260884)

Abstract

Introduction: The data on the use of dual biologics are scant, but a topic of current interest.

Case study: In this report, the treatment regimen of a patient with two T helper 2 pathway-related comorbidities, severe asthma, and chronic spontaneous urticaria, was presented.

Results: Both urticaria and asthma symptoms of the patient could not be controlled entirely with monotherapy while both diseases could be controlled after omalizumab-mepolizumab dual treatment. No adverse events were observed after 6 months of dual biologics use.

Conclusion: This report supports other publications in the literature involving the use of dual biologics and provides a summary of the literature.

Keywords: Severe asthma; chronic spontaneous urticarial; dual biologics; mepolizumab; omalizumab.

- [Cited by 1 article](#)

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Publication types, MeSH terms, Substancesexpand

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Cite

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J Asthma

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. 2024 Mar;61(3):177-183.

doi: 10.1080/02770903.2023.2255277. Epub 2023 Sep 14.

Breathing pattern disorder in chronic rhinosinusitis with severe asthma: nasal obstruction and polyps do not increase prevalence

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Affiliations expand

- PMID: 37668326
- DOI: [10.1080/02770903.2023.2255277](https://doi.org/10.1080/02770903.2023.2255277)

Abstract

Objectives: Chronic rhinosinusitis (CRS) with severe asthma are associated with breathing pattern disorder (BPD). Mouth breathing is a sign of breathing pattern disorder, and nose breathing a fundamental part of breathing pattern retraining for BPD. The prevalence of BPD in relation to CRS subtypes and the relationship of nasal obstruction to BPD in CRS and associated severe asthma is unknown. The breathing pattern assessment tool (BPAT) can identify BPD. Our objective was to thus investigate the prevalence of BPD, nasal airflow obstruction and measures of airway disease severity in CRS with (CRSwNP) and without nasal polyps (CRSsNP) in severe asthma.

Methods: We determined whether CRS status, peak nasal inspiratory flow (PNIF) or polyp disease increased BPD prevalence. Demographic factors, measures of airway function and breathlessness in relation to BPD status and CRS subtypes were also evaluated.

Results: 130 Patients were evaluated ($n = 69$ had BPD). The prevalence of BPD in CRS with severe asthma was 53.1%. There was no difference between BPD occurrence between CRSwNP and CRSsNP. The mean polyp grade and PNIF were not statistically different between the BPD and non-BPD group. The presence of nasal polyps did not increase breathlessness.

Conclusions: BPD and CRS are commonly co-associated. CRS status and nasal obstruction per se does not increase BPD prevalence.

Keywords: Chronic rhinosinusitis; breathing pattern disorder; nasal obstruction; severe asthma.

SUPPLEMENTARY INFO

MeSH termsexpand

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Review

Laryngoscope

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. 2024 Mar;134(3):1005-1013.

doi: 10.1002/lary.30992. Epub 2023 Aug 24.

[Non-Type 2 and Mixed Inflammation in Chronic Rhinosinusitis and Lower Airway Disease](#)

[Austin Heffernan](#)¹, [Amir Shafiee](#)¹, [Teffran Chan](#)¹, [Sydney Sparanese](#)¹, [Andrew Thamboo](#)¹

Affiliations expand

- PMID: 37615304
- DOI: [10.1002/lary.30992](https://doi.org/10.1002/lary.30992)

Abstract

Objective: The aim was to discuss the role of non-type 2 inflammation in patients diagnosed with chronic rhinosinusitis (CRS) and comorbid lower airway disease.

Data sources: Medline, Embase, National Institute for Health and Care Excellence, TRIP Database, ProQuest, Clinicaltrials.gov, Cochrane Central Registry of Controlled Trials, Web of Science, government and health organizations, and graduate-level theses.

Review methods: This scoping review followed PRISMA-ScR guidelines. Search strategy was peer-reviewed by medical librarians. Studies were included if they utilized airway sampling, non-type 2 cytokines, and patients with CRS and lower airway disease.

Results: Twenty-seven from 7060 articles were included. In patients with CRS and comorbid asthma, aspirin-exacerbated respiratory disease (AERD), and chronic obstructive pulmonary disease (COPD)/bronchiectasis, 60% (n = 12), 33% (n = 2), and 100% (n = 1), respectively, demonstrated mixed or non-type 2 endotypes. Comorbid CRS and asthma produced type 1 (n = 1.5), type 2 (n = 8), type 3 (n = 1), mixed type 1/2 (n = 1), and mixed type 1/2/3 (n = 8.5) endotype shifts. AERD demonstrated type 2 (n = 4), mixed type 2/3 (n = 1), and mixed type 1/2/3 (n = 1) endotype shifts. CRS with COPD or bronchiectasis demonstrated a mixed 1/2 (n = 1) endotype shift.

Conclusion: Type 2 disease has been extensively reviewed due to advent biologics targeting type 2 inflammation, but outcomes may be suboptimal due to the presence of non-type 2 inflammation. A proportion of patients with CRS and comorbid lower airway disease demonstrated mixed and non-type 2 endotype shifts. This emphasizes that patients with unified airway disease may have forms of inflammation beyond classical type 2 disease which could inform biologic development. *Laryngoscope*, 134:1005-1013, 2024.

Keywords: chronic rhinosinusitis; endotypes; mixed inflammation; non-type 2 inflammation; unified airway disease.

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Allergy

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. 2024 Feb 29.

doi: 10.1111/all.16082. Online ahead of print.

Immunoglobulin free light chains in severe asthma patient: Could they be a new biomarker?

[C Caruso](#)¹, [G Ciasca](#)², [I Baglivo](#)³, [R Di Santo](#)², [A Gasbarrini](#)³, [D Firinu](#)⁴, [D Bagnasco](#)⁵, [G Passalacqua](#)⁵, [M Schiappoli](#)⁶, [M Caminati](#)⁷, [G W Canonica](#)^{8,9}, [E Heffler](#)^{8,9}, [C Crimi](#)¹⁰, [R Intravaia](#)¹¹, [V Basile](#)¹², [M Marino](#)¹³, [S Colantuono](#)¹, [S Del Giacco](#)⁴

Affiliations expand

- PMID: 38425088
- DOI: [10.1111/all.16082](https://doi.org/10.1111/all.16082)

Abstract

Background: Increasing evidence is available about the presence of increased serum concentration of immunoglobulin (Ig) free light chains (FLCs) in both atopic and non-atopic inflammatory diseases, including severe asthma, providing a possible new biomarker of disease.

Methods: We analyzed clinical and laboratory data, including FLCs, obtained from a cohort of 79 asthmatic subjects, clinically classified into different GINA steps. A control group of 40 age-matched healthy donors (HD) was considered. Particularly, HD have been selected according to the absence of monoclonal components (in order to exclude paraproteinemias), were tested for total IgE (that were in the normal ranges) and were negative for aeroallergens specific IgE. Moreover, no abnormality of common inflammatory markers (i.e., erythrocyte sedimentation rate and C-reactive protein) was detectable.

Results: FLC- κ levels were significantly increased in the asthmatic population, compared to the control group. Despite the absence of statistically significant differences in FLC- λ levels, the FLC- κ /FLC- λ ratio displayed remarkable differences between the two groups. A positive correlation between FLC- κ and FLC- λ levels was found. FLC- λ level displayed a significant negative correlation with the FEV1 value. Moreover, the FLC- κ /FLC- λ ratio was negatively correlated with the SNOT-22 score and a positive correlation was observed between FLCs and Staphylococcus Aureus IgE enterotoxins sensitization.

Conclusions: Our findings confirmed the role of FLCs in asthma as a potential biomarker in an inflammatory disease characterized by different endotypes and phenotypes. In particular, FLC- κ and FLC- κ /FLC- λ ratio could be a qualitative indicator for asthma, while FLC- λ levels could be a quantitative indicator for clinical severity parameters.

Keywords: biomarker; free light chains; severe asthma; type 2 inflammation.

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Allergy

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. 2024 Feb 29.

doi: 10.1111/all.16093. Online ahead of print.

[Blood basophils and asthma among participants from CONSTANCES, the French population-based cohort](#)

[Rachel Nadif](#)¹, [Joseph Henny](#)², [Tajidine Tsiavia](#)¹, [Céline Ribet](#)², [Marcel Goldberg](#)², [Marie Zins](#)^{2,3}, [Laurent Orsi](#)¹, [Nicolas Roche](#)^{1,4}

Affiliations expand

- PMID: 38425050
- DOI: [10.1111/all.16093](https://doi.org/10.1111/all.16093)

No abstract available

- [6 references](#)

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Publication types, Grants and funding expand

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Curr Opin Pulm Med

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. 2024 Feb 29.

doi: 10.1097/MCP.0000000000001062. Online ahead of print.

[Recent developments in occupational asthma](#)

[Claudia Blouin](#)^{1,2}, [Catherine Lemièr](#)^{1,2}

Affiliations expand

- PMID: 38415698
- DOI: [10.1097/MCP.0000000000001062](https://doi.org/10.1097/MCP.0000000000001062)

Abstract

Purpose of this review: Occupational asthma (OA) is a complex condition that can be difficult to diagnose. The purpose of this review is to describe some recent findings regarding the epidemiology of OA, the occupational sensitizing agents, the prognosis of OA, and its primary prevention.

Recent findings: The risk of developing OA varies according to the geographic localization of the worker, the type of industry and the type of sensitizing agents. New findings have been reported for several known sensitizing agents, such as isocyanates, seafood & cleaning agents, and their related industries, such as hairdressing salons and schools. Moreover, a few new sensitizing agents, such as cannabis, have been identified in the past few years. The prognosis of OA seems worse than that of nonwork-related asthma. It is mainly determined by the duration and the level of exposure. Primary prevention is crucial to reduce the number of new cases of OA. Complete avoidance of exposure to the causal agent remains the optimal treatment of sensitizer-induced OA.

Summary: Improving our knowledge regarding OA and its causative agents is key to enable an early recognition of this condition and improve its prognosis. Further research is still needed to improve primary prevention.

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- [40 references](#)

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[Review](#)

FASEB J



. 2024 Feb 29;38(4):e23485.

doi: 10.1096/fj.202302584RR.

Th2 cells in rapid immune responses and protective avoidance reactions

[Edward J Goetzl](#)¹

Affiliations expand

- PMID: 38372961
- DOI: [10.1096/fj.202302584RR](https://doi.org/10.1096/fj.202302584RR)

Abstract

Type 2 helper cells (Th2 cells) differentiate from CD4 helper T cells under the influence of IL-4 and conventional or monocyte-derived CD11b⁺ dendritic cells. Th2 cells are capable of generating IL-4, IL-5, and IL-13, as well as evoking immunoglobulin class-switch to IgE. Three types of rapid immune responses are Th2 cell-dependent: (1) mast cell-IgE mediated allergic reactions, (2) Th2 cell-derived cytokine-mediated reactions that complement allergic reactions and protect the host from toxins, xenobiotics, environmental irritants, and helminthic parasites, and (3) IgE-stimulated mast cell-derived cysteinyl-leukotriene mediated avoidance of toxins. The contributions of Th2 cell-derived cytokines to eosinophilia (IL-5), IgE class-switch, and epithelial barrier activation, mucous secretion, and metaplasia (IL-4 and IL-13) in asthma, allergic rhinitis with polyps and atopic dermatitis have led to anti-cytokine monoclonal antibody treatments. Anti-IL-5 neutralizing monoclonal antibody in asthma and anti-IL-4/IL-13 receptor neutralizing monoclonal antibody in asthma and atopic dermatitis are proven successful therapies in appropriately selected patients who are not sufficiently improved by conventional treatments.

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- [17 references](#)

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Review

Life Sci

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. 2024 Feb 28:122538.

doi: 10.1016/j.lfs.2024.122538. Online ahead of print.

Targeting type I PRMTs as promising targets for the treatment of pulmonary disorders: Asthma, COPD, lung cancer, PF, and PH

[Shuyan Zhou](#)¹, [Qiangsheng Zhang](#)¹, [Honglin Yang](#)¹, [Yongxia Zhu](#)², [Xiang Hu](#)¹, [Guoquan Wan](#)¹, [Luoting Yu](#)³

Affiliations expand

- PMID: 38428571
- DOI: [10.1016/j.lfs.2024.122538](https://doi.org/10.1016/j.lfs.2024.122538)

Abstract

Pulmonary disorders, including asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis (PF), pulmonary hypertension (PH), and lung cancer, seriously impair the quality of lives of patients. A deeper understanding of the occurrence and development of the above diseases may inspire new strategies to remedy the scarcity of treatments. Type I protein arginine methyltransferases (PRMTs) can affect processes of inflammation, airway remodeling, fibroblast proliferation, mitochondrial mass, and epithelial dysfunction through substrate methylation and non-enzymatic activity, thus affecting the occurrence and development of asthma, COPD, lung cancer, PF, and PH. As potential therapeutic targets, inhibitors of type I PRMTs are developed, moreover, representative compounds such as GSK3368715 and MS023 have also been used for early research. Here, we collated structures of type I PRMTs inhibitors and compared their activity. Finally, we highlighted the physiological and pathological associations of type I PRMTs with asthma, COPD, lung cancer, PF, and PH. The developing of type I PRMTs modulators will be beneficial for the treatment of these diseases.

Keywords: Asthma; COPD; Epigenetics; Lung cancer; Pulmonary fibrosis; Pulmonary hypertension; Type I PRMTs.

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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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Practice Guideline



The 1st EoETALY Consensus on the Diagnosis and Management of Eosinophilic Esophagitis - Definition, Clinical Presentation and Diagnosis

[Nicola de Bortoli](#)¹, [Pierfrancesco Visaggi](#)¹, [Roberto Penagini](#)², [Bruno Annibale](#)³, [Federica Baiano Svizzero](#)¹, [Giovanni Barbara](#)⁴, [Ottavia Bartolo](#)⁵, [Edda Battaglia](#)⁶, [Antonio Di Sabatino](#)⁷, [Paola De Angelis](#)⁸, [Ludovico Docimo](#)⁹, [Marzio Frazzoni](#)¹⁰, [Manuele Furnari](#)¹¹, [Andrea Iori](#)¹², [Paola Iovino](#)¹³, [Marco Vincenzo Lenti](#)¹⁴, [Elisa Marabotto](#)¹¹, [Giovanni Marasco](#)⁴, [Aurelio Mauro](#)¹⁵, [Salvatore Oliva](#)¹⁶, [Gaia Pellegatta](#)¹⁷, [Marcella Pesce](#)¹⁸, [Antonino Carlo Privitera](#)¹⁹, [Ilaria Puxeddu](#)²⁰, [Francesca Racca](#)²¹, [Mentore Ribolsi](#)²², [Erminia Ridolo](#)²³, [Salvatore Russo](#)²⁴, [Giovanni Sarnelli](#)¹⁸, [Salvatore Tolone](#)²⁵, [Patrizia Zentilin](#)²⁶, [Fabiana Zingone](#)²⁷, [Brigida Barberio](#)²⁷, [Matteo Ghisa](#)²⁷, [Edoardo Vincenzo Savarino](#)²⁸

Affiliations expand

- PMID: 38423918
- DOI: [10.1016/j.dld.2024.02.005](https://doi.org/10.1016/j.dld.2024.02.005)

Abstract

Eosinophilic esophagitis (EoE) is a chronic type 2-mediated inflammatory disease of the esophagus that represents the most common eosinophilic gastrointestinal disease. Experts in the field of EoE across Italy (i.e., EoETALY Consensus Group) including gastroenterologists, endoscopists, allergologists/immunologists, and paediatricians conducted a Delphi process to develop updated consensus statements for the management of patients with EoE and update the previous position paper of the Italian Society of Gastroenterology (SIGE) in light of recent evidence. Grading of the strength and quality of the evidence of the recommendations was performed using accepted GRADE criteria. The guideline is divided in two documents: Part 1 includes three chapters, namely 1) definition, epidemiology, and pathogenesis; 2) clinical presentation and natural history, and 3) diagnosis, while Part 2 includes two chapters: 4) treatment and 5) monitoring and

follow-up. This document has received the endorsement of three Italian national societies including the SIGE, the Italian Society of Neurogastroenterology and Motility (SINGEM), and the Italian Society of Allergology, Asthma, and Clinical Immunology (SIAAIC). With regards to patients' involvement, these guidelines involved the contribution of members of ESEO Italia, the Italian Association of Families Against EoE.

Keywords: EoE; EoETALY; Eosinophilic esophagitis; Guidelines.

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Conflict of interest statement

Declaration of competing interest Nicola de Bortoli: Advisory board member for: AlfaSigma, Sanofi Genzyme, Dr Falk; Lecture grants from Reckitt-Benckiser, Malesci, Dr. Flak, Sofar, Alfa-Sigma, Pharma-Line. Pierfrancesco Visaggi: Has served as speaker for Dr Falk, JB Pharmaceuticals, Malesci. Roberto Penagini: Has served as speaker for Dr Falk, Sanofi. Edda Battaglia: has served as consultant for NZP, GUNA Gaia Pellegatta has served as speaker for Dr Falk, Sanofi Genzyme, Malesci. Paola Iovino: Has served as consultant for Dr Falk Giovanni Marasco: Served as an advisory board member for AlfaSigma, EG Pharma, MontereSearch srl, Recordati, Cineca. Received lecture grants from Agave, AlfaSigma, Bromatech, Clorofilla, Echosens, Ferring, Mayoly Spindler, Menarini and Schwabe Pharma. Salvatore Oliva: Has served as speaker for Sanofi, Medtronic; Has served as consultant for: Sanofi, Medtronic, Bristol; Has received research support from Alfa Sigma, Medtronic. Francesca Racca: has served as speaker for Sanofi; has served as consultant for Dr Falk, Sanofi, GSK Erminia Ridolo: has served as consultant for Dr Falk Edoardo Vincenzo Savarino: has served as speaker for Abbvie, Agave, AGPharma, Alfasigma, Aurora Pharma, CaDiGroup, Celltrion, Dr Falk, EG Stada Group, Fenix Pharma, Fresenius Kabi, Galapagos, Janssen, JB Pharmaceuticals, Innovamedica/Adacyte, Malesci, Mayoly Biohealth, Omega Pharma, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda, Tillots, Unifarco; has served as consultant for Abbvie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, Diadema Farmaceutici, Dr. Falk, Fenix Pharma, Fresenius Kabi, Janssen, JB Pharmaceuticals, Merck & Co, Nestlè, Reckitt Benckiser, Regeneron, Sanofi, SILA, Sofar, Synformulas GmbH, Tssakeda, Unifarco; he received research support from Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, Zeta Farmaceutici. Bruno Annibale, Federica Baiano Svizzero, Giovanni Barbara, Brigida Barberio, Ottavia Bartolo, Antonio Di Sabatino, Ludovico Docimo, Marzio Frazzoni, Manuele Furnari, Matteo Ghisa, Andrea Iori, Marco Vincenzo Lenti, Elisa Marabotto, Aurelio Mauro, Marcella Pesce, Antonino Carlo Privitera, Ilaria Puxeddu, Mentore Ribolsi, Salvatore Russo, Giovanni Sarnelli, Salvatore Tolone, Patrizia Zentilin, Fabiana Zingone: None.

SUPPLEMENTARY INFO

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Respir Res



. 2024 Feb 28;25(1):104.

doi: 10.1186/s12931-024-02710-8.

[The effect of combining an inhaled corticosteroid and a long-acting muscarinic antagonist on human airway epithelial cells in vitro](#)

[Maria Gabriella Matera](#)¹, [Barbara Rinaldi](#)², [Cecilia Calabrese](#)³, [Carmela Belardo](#)², [Luigino Calzetta](#)⁴, [Mario Cazzola](#)⁵, [Clive Page](#)⁶

Affiliations expand

- PMID: 38419021
- PMCID: [PMC10902985](#)
- DOI: [10.1186/s12931-024-02710-8](#)

Free PMC article

Abstract

Background: Airway epithelial cells (AECs) are a major component of local airway immune responses. Direct effects of type 2 cytokines on AECs are implicated in type 2 asthma, which is driven by epithelial-derived cytokines and leads to airway obstruction. However, evidence suggests that restoring epithelial health may attenuate asthmatic features.

Methods: We investigated the effects of passive sensitisation on IL-5, NF- κ B, HDAC-2, ACh, and ChAT in human bronchial epithelial cells (HBEpCs) and the effects of fluticasone furoate (FF) and umeclidinium (UME) alone and in combination on these responses.

Results: IL-5 and NF- κ B levels were increased, and that of HDAC-2 reduced in sensitised HBEpCs. Pretreatment with FF reversed the effects of passive sensitisation by concentration-dependent reduction of IL-5, resulting in decreased NF- κ B levels and restored HDAC-2 activity. Addition of UME enhanced these effects. Sensitized HBEpCs also exhibited higher ACh and ChAT levels. Pretreatment with UME significantly reduced ACh levels, and addition of FF caused a further small reduction.

Conclusion: This study confirmed that passive sensitisation of AECs results in an inflammatory response with increased levels of IL-5 and NF- κ B, reduced levels of HDAC-2, and higher levels of ACh and ChAT compared to normal cells. Combining FF and UME was found to be more effective in reducing IL-5, NF- κ B, and ACh and restoring HDAC-2 compared to the individual components. This finding supports adding a LAMA to established ICS/LABA treatment in asthma and suggests the possibility of using an ICS/LAMA combination when needed.

Keywords: Airway epithelial cells; Asthma; Inflammation; Inhaled corticosteroid; Long-acting muscarinic antagonists.

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Conflict of interest statement

MGM participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of ABC Farmaceutici, Almirall, AstraZeneca, Chiesi Farmaceutici, GlaxoSmithKline and Novartis, was a consultant to Chiesi Farmaceutici and GSK, and her department was funded by GSK and Novartis. CC received honoraria for lectures from AstraZeneca, GSK, Sanofi and Novartis, and support for attending meetings and/or travel received from AstraZeneca, GSK, Sanofi and Novartis. LC has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis, received nonfinancial support from AstraZeneca, received a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; has been a consultant to ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon. MC participated as a faculty member and advisor in scientific meetings and courses under the sponsorship of Abdi Ibrahim, Alkem, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, Cipla, Eurodrug, GSK, Glenmark, Lallemand, Mankind

Pharma, Menarini Group, Mundipharma, Novartis, Pfizer, Recipharm, Sanofi, Teva, Verona Pharma and Zambon, and is or was a consultant to ABC Farmaceutici, AstraZeneca, Chiesi Farmaceutici, GSK, Lallemand, Novartis, Ockham Biotech, Recipharm, Verona Pharma and Zambon. CP has acted as a consultant to Eurodrug, Recipharm, Glycosynnovation and PrEP Biopharma, and also holds equity in Verona Pharma. BR and CB declare no conflict of interest.

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

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Occup Environ Med

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. 2024 Feb 28:oemed-2023-109100.

doi: 10.1136/oemed-2023-109100. Online ahead of print.

[Chronic occupational exposures to irritants and asthma in the CONSTANCES cohort](#)

[Guillaume Sit](#)¹, [Laurent Orsi](#)¹, [Yuriko Iwatsubo](#)², [Brigitte Dananché](#)¹, [Florence Orsi](#)¹, [Marcel Goldberg](#)^{3,4}, [Benedicte Leynaert](#)¹, [Rachel Nadif](#)¹, [Céline Ribet](#)^{3,4}, [Nicolas Roche](#)⁵, [Yves Roquelaure](#)⁶, [Raphäelle Varraso](#)¹, [Marie Zins](#)^{3,4}, [Corinne Pilorget](#)², [Nicole Le Moual](#)¹, [Orianne Dumas](#)⁷

Affiliations expand

- PMID: 38418224
- DOI: [10.1136/oemed-2023-109100](https://doi.org/10.1136/oemed-2023-109100)

Abstract

Objectives: The impact of chronic occupational exposures to irritants on asthma remains discussed. We studied the associations between occupational exposures and asthma, with specific interest for chronic exposure to irritants, including disinfectants and cleaning products (DCPs) and solvents.

Methods: Cross-sectional analyses included 115 540 adults (55% women, mean age 43 years, 10% current asthma) working at inclusion in the French population-based CONSTANCES cohort (2012-2020). Current asthma was defined by ever asthma with symptoms, medication or asthma attacks (past 12 months), and the asthma symptom score by the sum of 5 respiratory symptoms (past 12 months). Both lifetime and current occupational exposures were assessed by the Occupational Asthma-specific Job-Exposure Matrix. Associations were evaluated by gender using logistic and binomial negative regressions adjusted for age, smoking status and body mass index.

Results: In women, associations were observed between current asthma and lifetime exposure to irritants (OR 1.05, 95% CI 1.00 to 1.11), DCPs (1.06, 95% CI 1.00 to 1.12) and solvents (1.06, 95% CI 0.98 to 1.14). In men, only lifetime exposure to DCPs (1.10, 95% CI 1.01 to 1.20) was associated with current asthma. Lifetime exposure to irritants was associated with higher asthma symptom score both in women (mean score ratio: 1.08, 95% CI 1.05 to 1.11) and men (1.11, 95% CI 1.07 to 1.15), especially for DCPs (women: 1.09, 95% CI 1.06 to 1.13, men: 1.21, 95% CI 1.15 to 1.27) and solvents (women 1.14, 95% CI 1.10 to 1.19, men: 1.10, 95% CI 1.05 to 1.15). For current exposures, no consistent associations were observed with current asthma and asthma symptom score.

Conclusions: Lifetime occupational exposures to irritants were associated with current asthma and higher asthma symptom score. These exposures should be carefully considered in asthma management.

Keywords: Asthma; Cross-Sectional Studies; Epidemiology; Occupational Health; Solvents.

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Conflict of interest statement

Competing interests: None declared.

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Review

Eur Respir Rev

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. 2024 Feb 28;33(171):230174.

doi: 10.1183/16000617.0174-2023. Print 2024 Jan 31.

[Preclinical models of maternal asthma and progeny outcomes: a scoping review](#)

[Joshua L Robinson](#)^{1,2,3}, [Kathryn L Gatford](#)^{1,4}, [Danielle N Bailey](#)¹, [Andrea J Roff](#)^{1,4}, [Vicki L Clifton](#)⁵, [Janna L Morrison](#)³, [Michael J Stark](#)^{6,2,7}

Affiliations expand

- PMID: 38417970
- PMCID: [PMC10900068](#)
- DOI: [10.1183/16000617.0174-2023](#)

Abstract

There is an increased risk of adverse perinatal outcomes in the ~17% of women with asthma during pregnancy. The mechanisms linking maternal asthma and adverse outcomes are largely unknown, but reflect joint effects of genetics and prenatal exposure to maternal asthma. Animal models are essential to understand the underlying mechanisms independent of genetics and comorbidities, and enable safe testing of interventions. This scoping review aimed to explore the methodology, phenotype, characteristics, outcomes and quality of published studies using preclinical maternal asthma models. MEDLINE (PubMed), Embase (Elsevier) and Web of Science were systematically searched using previously validated search strings for maternal asthma and for animal models. Two reviewers independently screened titles and abstracts, full texts, and then extracted and assessed the quality of each study using the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) 2.0 guidelines. Out of 3618 studies identified, 39 were eligible for extraction. Most studies were in rodents (86%) and all were models of allergic asthma. Maternal and progeny outcomes included airway hyperresponsiveness, airway resistance, inflammation, lung immune cells, lung structure and serum immunoglobulins and cytokines. Experimental design (100%), procedural details (97%) and rationale (100%) were most often reported. Conversely, data exclusion (21%), blinding (18%) and adverse events (8%) were reported in a minority of studies. Species differences in physiology and timing of development, the use of allergens not relevant to humans and a lack of comparable outcome measures may impede clinical translation. Future studies exploring models of maternal asthma should adhere to the minimum core outcomes set presented in this review.

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Conflict of interest statement

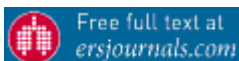
Conflict of interest: The authors declare no conflicts of interest.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Respiration



. 2024 Feb 28.

doi: 10.1159/000537918. Online ahead of print.

[Associations of depressive and anxiety disorders with pulmonary disorders in the community – the PneumoLaus and PsyCoLaus studies](#)

[Brice Touilloux](#), [Alessio Casutt](#), [Marie-Pierre F Strippoli](#), [Alexandra Lenoir](#), [Simone Janett](#), [Peter Vollenweider](#), [Julien Vaucher](#), [Laurent Nicod](#), [Martin Preisig](#), [Christophe Von Garnier](#)

- PMID: 38417406
- DOI: [10.1159/000537918](https://doi.org/10.1159/000537918)

Abstract

Introduction: Mental health disorders figure among the many comorbidities of obstructive respiratory diseases. The multisystemic characteristics of chronic respiratory disease and its impact on quality of life could affect depressive and/or anxiety disorders. We aimed to evaluate the association of spirometric indices, ventilatory disorders and self-reported respiratory diseases with psychiatric disorders considering potential confounders.

Methods: We analysed data from CoLaus|PsyCoLaus, a Swiss population-based cohort study, consisting of 2'774 participants (56% women; mean age: 62.3 (SD=±9.9) years) who performed spirometry and completed semi-structured psychiatric interviews. We defined

ventilatory disorders using GLI-2012 references. Major depressive episode (MDE) and anxiety disorders were defined using the DSM-IV (Diagnostic and Statistical Manual).

Results: 630 subjects (22.7%) presented a recent MDE. Reversible obstructive ventilatory disorders were associated with recent MDE (OR=1.94, 95% CI 1.10-3.43) and recent anxiety disorders (2.21 [1.16-4.22]) only in unadjusted model. Self-reported COPD and asthma were associated with MDE with ORs of 2.49 (95%CI, 1.19-5.27) and 1.56 (95% CI, 1.04-2.35) after adjustment, respectively. Possible restrictive ventilatory impairment was positively associated with recent anxiety disorders (OR=2.46, 1.10-5.51). Z-scores of FEV₁, FVC and maximum mid expiratory flow (MMEF) were not associated with psychiatric disorders. There was no association between ventilatory disorders and MDE in adjusted models.

Conclusions: In this cross-sectional population-based study, the association between respiratory disorders and depressive disorders was observed for self-reported COPD and asthma, but not with objective diagnoses based on spirometry. Lung volumes are not associated with psychiatric disorders. Further prospective studies will be necessary to understand the significance of the association.

The Author(s). Published by S. Karger AG, Basel.

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[Review](#)

J Asthma

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. 2024 Feb 28:1-14.

doi: 10.1080/02770903.2024.2324862. Online ahead of print.

[A Comprehensive Review of the Intersection Between Asthma and Depression](#)

[Tahoorah Abdul Nasir Surve](#)¹, [Dhruvi Kumari D Sharma](#)², [Kiyan Ghani Khan](#)³, [Neisha Ghanie](#)⁴, [Riley Charanrak](#)⁵, [Mouhammad Sharifa](#)⁶, [Samreen Begum](#)⁷, [Maria Jose Auz](#)⁸, [Nozima Akbarova](#)⁹, [Maneeth Mylavarapu](#)¹⁰

Affiliations expand

- PMID: 38415695
- DOI: [10.1080/02770903.2024.2324862](https://doi.org/10.1080/02770903.2024.2324862)

Abstract

Objective To emphasize the necessity for increased research in this field, incorporating depression into the preventative, diagnostic, and therapeutic considerations for asthma. Additionally, we seek to highlight upcoming advancements that can be applied to simultaneously address these comorbidities, ultimately improving the overall well-being and quality of life for individuals coping with these conditions. **Methods** A rigorous search in PubMed using the MeSH terms "asthma" and "depression" was performed, and papers were screened by the authors in view of their eligibility to contribute to the study. **Results** There exists a correlation between these two conditions, with specific biological mechanisms and genetic factors playing a crucial role in their concurrent occurrence. In this review, we present preclinical and clinical research data, shed light on the possible mechanisms contributing to the co-occurrence of symptoms associated with both asthma and depression, and explore the intricate relationship between both conditions. **Conclusion** The evidence presented here supports the existence of a correlation between asthma and depression. By acknowledging these shared biological mechanisms, genetic factors, and epidemiological trends, we can formulate more efficacious strategies for addressing the dual impact of asthma and depression.

Keywords: Health Related Quality of Life (HRQoL); Hospital Anxiety and Depression Scale (HADS) Scores; Major Depressive Disorder (MDD); NF- κ B; oxidative stress.

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Randomized Controlled Trial

Respir Care

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. 2024 Feb 28;69(3):345-348.

doi: 10.4187/respcare.10980.

[Randomized Controlled Trial Assessing a Vibrating Mesh Nebulizer Compared to a Jet Nebulizer in Severe Asthma Exacerbations](#)

[Haval Chweich](#)¹, [Najia Idrees](#)¹, [Jesse Rideout](#)¹, [Brien Barnewolt](#)¹, [Lauren Rice](#)¹, [Nicholas S Hill](#)²

Affiliations expand

- PMID: 37816543
- DOI: [10.4187/respcare.10980](https://doi.org/10.4187/respcare.10980)

No abstract available

Keywords: asthma; emergency department; exacerbation; nebulizer; vibrating mesh.

Conflict of interest statement

The authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Allergy Clin Immunol Pract

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. 2024 Feb 27:S2213-2198(24)00203-4.

doi: 10.1016/j.jaip.2024.02.029. Online ahead of print.

[Comparative Impact of Asthma Biologics - A Nationwide US Claim-Based Analysis](#)

[Taha Al-Shaikhly](#)¹, [Matthew R Norris](#)², [Emily H Dennis](#)³, [Guodong Liu](#)³, [Timothy J Craig](#)²

Affiliations expand

- PMID: 38423294
- DOI: [10.1016/j.jaip.2024.02.029](https://doi.org/10.1016/j.jaip.2024.02.029)

Abstract

Background: Biologic modifiers targeting type-2 (T2) airway inflammation are effective in reducing asthma exacerbation, however real-world and comparative effectiveness studies remain limited.

Objective: to examine and compare the real-world impact of anti-T2 asthma biologics
METHODS: In this retrospective new user cohort study, we used the MarketScan, a Commercial Claims and Encounters Database, to identify adult patients with asthma who were started on an anti-T2 biologic agent (anti-IL-5s, dupilumab or omalizumab). We examined the influence of the biologic class on asthma exacerbation by comparing the average number of asthma exacerbation 1-year pre- and post-biologic initiation. We conducted multivariable regression analyses to compare the effectiveness of these asthma biologics on reducing the incidence of asthma exacerbations within 18-month of initial administration of biologics while controlling for demographic variables, comorbidities, and asthma severity.

Results: We identified 5,538 asthma patients who were initiated on an anti-T2 biologic [mean age (\pm SD); 45.6 (12.78) years; % females, 65.8%]. Asthma biologics reduced asthma exacerbation by 11-47%, particularly among patients with 2+ asthma exacerbations in the year preceding biologic initiation (31-65% reduction). Biologics were especially effective in reducing asthma-related hospitalizations (44.6-60%). After adjusting for baseline demographics, asthma medication, and co-morbidities, dupilumab was associated with a lower estimated mean number of asthma exacerbation per year and lower adjusted OR for developing asthma exacerbation relative to other biologics (50-80% less likely).

Conclusion: Anti-T2 asthma biologics reduced asthma exacerbation in real-world settings. Evidence supports growing literature that dupilumab might have a more favorable impact on asthma exacerbation relative to other asthma biologics.

Keywords: T2 high asthma; benralizumab; comparative efficacy; dupilumab; eosinophilic asthma; mepolizumab; omalizumab; reslizumab; severe asthma.

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BMJ Open Respir Res

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. 2024 Feb 27;11(1):e002127.

doi: 10.1136/bmjresp-2023-002127.

Real-world treatment trajectories of adults with newly diagnosed asthma or COPD

[Aniek F Markus](#)¹, [Peter R Rijnbeek](#)², [Jan A Kors](#)², [Edward Burn](#)^{3,4}, [Talita Duarte-Salles](#)^{2,3}, [Markus Haug](#)⁵, [Chungsoo Kim](#)⁶, [Raivo Kolde](#)⁵, [Youngsoo Lee](#)⁷, [Hae-Sim Park](#)⁷, [Rae Woong Park](#)⁶, [Daniel Prieto-Alhambra](#)^{2,4}, [Carlen Reyes](#)³, [Jerry A Krishnan](#)⁸, [Guy G Brusselle](#)^{#9,10}, [Katia Mc Verhamme](#)^{#2,11}

Affiliations expand

- PMID: 38413124
- PMCID: [PMC10900306](#)
- DOI: [10.1136/bmjresp-2023-002127](#)

Free PMC article

Abstract

Background: There is a lack of knowledge on how patients with asthma or chronic obstructive pulmonary disease (COPD) are globally treated in the real world, especially with regard to the initial pharmacological treatment of newly diagnosed patients and the different treatment trajectories. This knowledge is important to monitor and improve clinical practice.

Methods: This retrospective cohort study aims to characterise treatments using data from four claims (drug dispensing) and four electronic health record (EHR; drug prescriptions) databases across six countries and three continents, encompassing 1.3 million patients with asthma or COPD. We analysed treatment trajectories at drug class level from first diagnosis and visualised these in sunburst plots.

Results: In four countries (USA, UK, Spain and the Netherlands), most adults with asthma initiate treatment with short-acting β_2 agonists monotherapy (20.8%–47.4% of first-line treatments). For COPD, the most frequent first-line treatment varies by country. The largest percentages of untreated patients (for asthma and COPD) were found in claims databases

(14.5%-33.2% for asthma and 27.0%-52.2% for COPD) from the USA as compared with EHR databases (6.9%-15.2% for asthma and 4.4%-17.5% for COPD) from European countries. The treatment trajectories showed step-up as well as step-down in treatments.

Conclusion: Real-world data from claims and EHRs indicate that first-line treatments of asthma and COPD vary widely across countries. We found evidence of a stepwise approach in the pharmacological treatment of asthma and COPD, suggesting that treatments may be tailored to patients' needs.

Keywords: Asthma Pharmacology; COPD Pharmacology.

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Conflict of interest statement

Competing interests: AFM, PRR, JAK and KMV work for a department that receives/received unconditional research grants from Amgen, Chiesi, Johnson and Johnson, UCB Biopharma, the European Medicines Agency and the Innovative Medicines Initiative. DP-A's department has received grants from Amgen, Chiesi-Taylor, Lilly, Johnson and Johnson, Novartis, UCB Biopharma, the European Medicines Agency, and the Innovative Medicines Initiative. DP-A's research group has received consultancy fees from Astra Zeneca and UCB Biopharma. DP-A's department has organised training programmes funded or supported by Amgen, Astellas, Johnson and Johnson, Synapse Management Partners, and UCB Biopharma. JK's institute has received grants from the American Lung Association, COPD Foundation, National Heart Lung and Blood institute, PCORI, Regeneron, Sergey Brin Family Foundation and US National Institutes of Health. JK has received consultancy fees from AstraZeneca, BData and GlaxoSmithKline. JK has received honoraria from University of Chicago, University of Washington/VA Puget Sound and travel support from the Global Initiative for Asthma, American Thoracic Society. GBB's institute has received grants from Merck Sharp & Dohme. GBB has received honoraria from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Sanofi. All other authors declare no competing interests.

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

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MeSH terms, [Substancesexpand](#)

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BMJ Open Respir Res

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. 2024 Feb 27;11(1):e002006.

doi: 10.1136/bmjresp-2023-002006.

[Risk of exacerbation and mortality in asthma: a 10-year retrospective financial database analysis of the Hungarian Health Insurance Fund](#)

[Gábor Tomisa](#)¹, [Balázs Sánta](#)^{2,3}, [Alpár Horváth](#)^{3,4}, [László Németh](#)⁵, [Balázs Tamás](#)⁵, [Gabriella Gálffy](#)⁶, [Lilla Tamási](#)^{#7}, [Noémi Eszes](#)^{#1}

Affiliations expand

- PMID: 38413122
- PMCID: [PMC10900350](#)
- DOI: [10.1136/bmjresp-2023-002006](#)

Free PMC article

Abstract

Introduction: Asthma is the most prevalent obstructive pulmonary disease, with drastically improved treatment options over the past decades. However, there is still a proportion of patients with suboptimal level of asthma control, leading to multiple hospitalisation due to severe acute exacerbation (SAE) and earlier death. In our study, we aimed to assess the risk of SAEs and mortality in patients who suffered an SAE.

Methods: The database of the National Health Insurance Fund was used to retrospectively analyse the data of all asthmatic patients who had been hospitalised for an SAE between 2009 and 2019. We used a competing risk model to analyse the effect of each exacerbation on the risk of further SAEs with age, sex, Charlson index and the number of severe and moderate exacerbations included as covariates.

Result: Altogether, 9257 asthmatic patients suffered at least one exacerbation leading to hospitalisation during the study time. The majority (75.8%) were women, and the average age was 58.24 years. Most patients had at least one comorbidity. 3492 patients suffered at least one further exacerbation and 1193 patients died of any cause. In the competing risk model, each SAE increased the risk of further exacerbations (HR=2.078-7.026; $p < 0.0001$ for each case) but not death. The risk of SAEs was also increased by age (HR=1.008) female sex (HR=1.102) and with the number of days of the first SAE (HR=1.007).

Conclusions: Even though asthma is generally a well-manageable disease, there still are many patients who suffer SAEs that significantly increase the risk of further similar SAEs.

Keywords: asthma; asthma epidemiology; clinical epidemiology.

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Conflict of interest statement

Competing interests: The authors report that they have no conflicts of interest related to the submitted work. LT has received lecture or consultancy fees and/or support for conference attendance from Berlin-Chemie, Orion Corporation, Novartis, Chiesi, Teva Pharmaceutical and AstraZeneca. NE has received lecture or consultancy fees and/or support for conference attendance from Berlin-Chemie, Orion Corporation, Novartis, Chiesi, Teva Pharmaceutical and AstraZeneca. GG has accepted reports personal fees from Astra-Zeneca, Chiesi, BMS, MSD, Berlin Chemie, Boehringer Ingelheim, Roche, Novartis, Pfizer, Ipsen, Mylen, Orion outside the submitted work. Santa, G. Tomisa and A. Horváth are all employees of Chiesi Hungary.

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

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Inflamm Bowel Dis



. 2024 Feb 27:izae027.

doi: 10.1093/ibd/izae027. Online ahead of print.

[Comorbidity Between Inflammatory Bowel Disease and Asthma and Allergic Diseases: A Genetically Informed Study](#)

[Tong Gong](#)¹, [Bronwyn K Brew](#)^{1,2}, [Cecilia Lundholm](#)¹, [Awad I Smew](#)¹, [Arvid Harder](#)¹, [Ralf Kuja-Halkola](#)¹, [Jonas F Ludvigsson](#)^{1,3}, [Yi Lu](#)¹, [Catarina Almqvist](#)^{1,4}

Affiliations expand

- PMID: 38412344
- DOI: [10.1093/ibd/izae027](https://doi.org/10.1093/ibd/izae027)

Abstract

Background: Little is known about shared origins between inflammatory bowel disease (IBD) and allergic diseases (asthma, allergic rhinitis, and eczema). We aimed to expand current knowledge on the etiological sources of comorbidities between these disorders using a range of genetically informed methods.

Methods: Within-individual and familial co-aggregation analysis was applied to 2 873 445 individuals born in Sweden from 1987 to 2014 and their first- and second-degree relatives. Quantitative genetic modeling was applied to 38 723 twin pairs to decompose the genetic and environmental sources for comorbidity. Polygenic risk score analysis between IBD and

allergic diseases was conducted in 48 186 genotyped twins, and linkage disequilibrium score regression was applied using publicly available data to explore the genetic overlap.

Results: IBD was associated with asthma (adjusted odds ratio [aOR], 1.35; 95% confidence interval [CI], 1.30 to 1.40), allergic rhinitis (aOR, 1.27; 95% CI, 1.20 to 1.34), and eczema (aOR, 1.47; 95% CI, 1.38 to 1.56), with similar estimates for ulcerative colitis or Crohn's disease. The ORs for familial co-aggregation decreased with decreasing genetic relatedness. Quantitative genetic modeling revealed little evidence of common genetic factors between IBD and allergic diseases (eg, IBD and allergic rhinitis; genetic correlation $r_g = 0.06$; 95% CI, -0.03 to 0.15) but did reveal some evidence of unique environmental factors between IBD and eczema ($r_e = 0.16$; 95% CI, 0.00 to 0.32). Molecular genetic analyses were similarly null for IBD and allergic diseases, except for a slight association between Crohn's disease polygenic risk score and eczema (OR, 1.09; 95% CI, 1.06 to 1.12).

Conclusions: We found little evidence to support a shared origin between IBD and any allergic disease but weak evidence for shared genetic and unique environmental components for IBD and eczema.

Keywords: Crohn's disease; allergic rhinitis; asthma; eczema; familial co-aggregation; genetic correlation; ulcerative colitis.

Plain language summary

Comorbidities between inflammatory bowel disease (IBD) with asthma and allergic diseases have been documented, but shared origin remains unknown. Using multiple genetically informed approaches, we found little evidence of a shared origin explaining the comorbidities of IBD with asthma and allergic rhinitis but weak evidence for IBD and eczema.

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Curr Opin Pulm Med



. 2024 Feb 27.

doi: 10.1097/MCP.0000000000001065. Online ahead of print.

[Examining the impact of air pollution, climate change, and social determinants of health on asthma and environmental justice](#)

[Felicia T Canaday](#)¹, [Steve N Georas](#), [Daniel P Croft](#)

Affiliations expand

- PMID: 38411188
- DOI: [10.1097/MCP.0000000000001065](https://doi.org/10.1097/MCP.0000000000001065)

Abstract

Purpose of review: In this review, we discuss the current literature examining the impact air pollution and climate change has on asthma onset, control, and exacerbation. This review also addresses the risk of exposure to specific disproportionately affected communities, highlighting health disparities in exposure and asthma outcomes.

Recent findings: Recent studies have shifted from highlighting the associations between asthma exacerbations and indoor and outdoor air pollution. Studies are now focused on confirming the association of asthma incidence from these same exposures. Many studies have linked particulate matter to adverse asthma outcomes, however, the pollutant exposures that pose the greatest risk and the effect of natural disasters fueled by climate change are under current study. Some studies have observed that the true burden that pollutant exposures have on asthma outcomes occurs at the intersection of exposure and vulnerability. Future studies in this area will address social determinants of health, societal factors such as redlining and other systemic racism practices.

Summary: Although decades of research support the causal link between gaseous and particulate air pollution and the exacerbation of preexisting asthma, recent studies suggest air pollution can cause incident (new onset) asthma. Studies have started to focus on the underlying drivers of poor outcomes in asthma. Many of the structural impediments to high quality asthma care at the society level (e.g. poverty, redlining, systemic racism) also are risk factors for worsened climate events and air pollution exposure. The individuals in these disproportionately affected groups are doubly affected by worsened exposure and worsened access to care for the resultant asthma exacerbations or incident asthma. More research is needed to understand the specific climate and air pollution mitigation efforts where disproportionately affected communities would derive the most benefit.

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Curr Opin Pulm Med

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. 2024 Feb 27.

doi: 10.1097/MCP.0000000000001061. Online ahead of print.

[Viral infections causing asthma exacerbations in the age of biologics and the COVID-19 pandemic](#)

[Pedro A Lamothe](#)¹, [Violeta Capric](#), [F Eun-Hyung Lee](#)

Affiliations expand

- PMID: 38411178
- DOI: [10.1097/MCP.0000000000001061](https://doi.org/10.1097/MCP.0000000000001061)

Abstract

Purpose of review: Asthma exacerbations are associated with substantial symptom burden and healthcare costs. Viral infections are the most common identified cause of asthma exacerbations. The epidemiology of viral respiratory infections has undergone a significant evolution during the COVID-19 pandemic. The relationship between viruses and asthmatic hosts has long been recognized but it is still incompletely understood. The use of newly approved asthma biologics has helped us understand this interaction better.

Recent findings: We review recent updates on the interaction between asthma and respiratory viruses, and we address how biologics and immunotherapies could affect this relationship by altering the respiratory mucosa cytokine milieu. By exploring the evolving epidemiological landscape of viral infections during the different phases of the COVID-19 pandemic, we emphasize the early post-pandemic stage, where a resurgence of pre-pandemic viruses with atypical seasonality patterns occurred. Finally, we discuss the newly developed RSV and SARS-CoV-2 vaccines and how they reduce respiratory infections.

Summary: Characterizing how respiratory viruses interact with asthmatic hosts will allow us to identify tailored therapies to reduce the burden of asthma exacerbations. New vaccination strategies are likely to shape the future viral asthma exacerbation landscape.

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. 2024 Feb 26:107581.

doi: 10.1016/j.rmed.2024.107581. Online ahead of print.

No remission in 60% of those with childhood-onset asthma - A population-based cohort followed from 8 to 28 years of age

[Linnéa Almqvist](#)¹, [Martin Andersson](#)², [Helena Backman](#)², [Eva Rönmark](#)², [Linnéa Hedman](#)²

Affiliations expand

- PMID: 38417585
- DOI: [10.1016/j.rmed.2024.107581](https://doi.org/10.1016/j.rmed.2024.107581)

Abstract

Background: Although remission occur, childhood-onset asthma may persist until adulthood. Since few longitudinal population-based studies have followed a cohort from childhood until adulthood, the knowledge on predictors of persistence of asthma is sparse.

Aim: To estimate persistence of asthma from 8 to 28 years and its associated factors.

Methods: Within the OLIN (Obstructive Lung Disease in Northern Sweden) studies, a cohort was recruited in 1996 (age 8y, n = 3430) and followed annually with questionnaires about asthma and risk factors until 19y. Clinical examinations included skin prick tests (at 8, 12 and 19y) and lung function tests (17 and 19y) whereof a subsample performed bronchial hyperreactivity test. We identified n = 248 with asthma at 8y whereof 170 (69%) participated in a follow-up at 28y (73% of possible to invite).

Results: Of the 170 participants at 28y, 105 (61.8%) had persistent asthma (women: 49/76, 64.5%; men: 56/94, 59.6%, p = 0.513). Factors collected at recruitment: allergic sensitization (OR7.8, 95%CI 3.0-20.2), severe respiratory infection (OR2.6, 95%CI 1.1-6.3) and higher

asthma severity score (OR1.6, 95%CI 1.1-2.4) were associated with asthma at 28y after adjustment for sex, family history of asthma, breastfeeding <3 months and eczema. Replacing allergic sensitization with rhinoconjunctivitis in the model yielded OR3.4 (95%CI 1.5-8.0). Bronchial hyperreactivity at age 17y associated with asthma at 28y (OR9.0, 95%CI 1.7-47.0).

Conclusions: Among children with asthma onset by 8y, 62% still had asthma at age 28 years. Persistent asthma was associated with allergic sensitization, rhinoconjunctivitis, severe respiratory infection, a more severe asthma and bronchial hyperreactivity.

Keywords: Asthma; Epidemiology; Longitudinal; Relapse; Remission; Risk factors.

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Conflict of interest statement

Declaration of competing interest HB: Personal fees for presentation at scientific meeting outside the submitted work from AstraZeneca, Boehringer Ingelheim and GlaxoSmithKline. None of the other authors have any conflicts of interest.

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Curr Opin Pediatr

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. 2024 Feb 26.

doi: 10.1097/MOP.0000000000001343. Online ahead of print.

Precision care in the treatment of pediatric asthma

[Lina Mahmood](#)¹, [Sevdenuur Keskin](#), [Akilah A Jefferson](#)

Affiliations expand

- PMID: 38411592
- 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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- [59 references](#)

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ERJ Open Res



. 2024 Feb 26;10(1):00853-2023.

doi: 10.1183/23120541.00853-2023. eCollection 2024 Jan.

[ERS International Congress 2023: highlights from the Paediatrics Assembly](#)

[Susanne J H Vijverberg](#)^{1,2}, [Asterios Kampouras](#)³, [Halime Nayir Büyüksahin](#)⁴, [Heidi Makrinioti](#)⁵, [Laura Petrarca](#)^{6,7}, [Mehtap Schmidt](#)⁸, [Leonie D Schreck](#)^{9,10}, [Ruth M Urbantat](#)^{11,12,13}, [Nicole Beydon](#)^{14,15}, [Myrofora Goutaki](#)^{9,16}, [Anna Lavizzari](#)¹⁷, [Marijke Proesmans](#)¹⁸, [Dirk Schramm](#)¹⁹, [Mirjam Stahl](#)^{11,12,13}, [Angela Zacharasiewicz](#)⁸, [Alexander Moeller](#)²⁰, [Marielle W Pijnenburg](#)²¹

Affiliations expand

- PMID: 38410713
- PMCID: [PMC10895434](#)
- DOI: [10.1183/23120541.00853-2023](#)

Free PMC article

Abstract

Respiratory health in children is essential for general wellbeing and healthy development in the short and long term. It is well known that many respiratory diseases in adulthood have their origins in early life, and therefore research on prevention of respiratory diseases and management of children with respiratory diseases will benefit patients during the full life course. Scientific and clinical advances in the field of respiratory health are moving at a fast pace. This article summarises some of the highlights in paediatric respiratory medicine

presented at the hybrid European Respiratory Society (ERS) International Congress 2023 which took place in Milan (Italy). Selected sessions are summarised by Early Career Members of the Paediatrics Assembly (Assembly 7) under the supervision of senior ERS officers, and cover a wide range of research areas in children, including respiratory physiology and sleep, asthma and allergy, cystic fibrosis, respiratory infection and immunology, neonatology and intensive care, respiratory epidemiology and bronchology.

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Conflict of interest statement

Conflict of interest: S.J.H. Vijverberg received support from the ERS for attending meetings and is the Early Career Member Representative of the Paediatrics Assembly of the ERS. L. Petrarca received funding from Sanofi to attend the ERS Congress 2023. L.D. Schreck is supported by the Swiss National Science Foundation (320030B_192804/1). R.M. Urbantat received a travel grant from the Gesellschaft für Pädiatrische Pneumologie to attend the ERS Congress 2023. N. Beydon is chair of group 7.01 of the ERS and has received support from the ERS for attending meetings. M. Goutaki is chair of group 7.06 of the ERS and is supported by the Swiss National Science Foundation (PZ00P3_185923). A. Lavizzari is chair of group 7.05 and reports consulting fees from Chiesi SpA, Vyair medical and Getinge, and support from Accademia Techniche Nuove. M. Proesmans is chair of group 7.04 and has received support from the ERS for attending meetings. D. Schramm is past chair of group 7.07 of the ERS and has received support from the ERS for attending meetings. M. Stahl is secretary of group 7.03 and has been supported by the German Research Foundation (Deutsche Forschungsgemeinschaft); furthermore, she has received an independent RIA grant from Vertex Pharmaceuticals. A. Zacharasiewicz is chair of group 7.02, and has received payment for lectures and support to attend meetings from Vertex, AstraZeneca, Chiesi, Gilead and Novartis. A. Moeller is the current chair of the Paediatrics Assembly and reports to have received a research grant from Vertex Inc. and funding to attend the Vertex symposium at the annual conference of the Swiss Respiratory Society. M.W. Pijnenburg received support from the ERS for attending the ERS Congress and ERS meetings, and is the past chair of the Paediatrics Assembly. The other authors report no conflict of interests for this manuscript.

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

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ERJ Open Res



. 2024 Feb 26;10(1):00935-2023.

doi: 10.1183/23120541.00935-2023. eCollection 2024 Jan.

Articular manifestations related to anti-interleukin-5 therapies in severe asthma: a case series

[Clairelyne Dupin](#)^{1,2,3}, [Solène Valéry](#)^{1,3}, [Laurent Guilleminault](#)^{2,4,5}, [Gilles Devouassoux](#)^{2,6}, [Marine Merveilleau](#)⁶, [Maud Russier](#)⁷, [Gisèle Mourin](#)⁸, [Johana Pradelli](#)⁹, [Philippe Bonniaud](#)¹⁰, [Mathilde Le Brun](#)^{1,2}, [Esther Ebstein](#)¹¹, [Pierre-Antoine Juge](#)¹¹, [Agnès Lillo-Lelouet](#)¹², [Camille Taillé](#)^{1,2}

Affiliations expand

- PMID: 38410709
- PMCID: [PMC10895420](#)
- DOI: [10.1183/23120541.00935-2023](#)

Free PMC article

Abstract

Articular manifestations should be screened before and during anti-IL-5/5R biologic treatment in severe asthma. Rigorous multidisciplinary team discussion should be carried out to assess the risk-benefit balance of withholding effective treatment. <https://bit.ly/3vfPn4k>.

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Conflict of interest statement

Conflict of interest: C. Dupin reports consulting fees from AstraZeneca, Sanofi and GSK; lecture honoraria from AstraZeneca, GSK, Sanofi, Novartis, Chiesi, OPA Pratique, Pneumoscoop and La Lettre du Pneumologue; and travel support from AstraZeneca, Sanofi, Novartis, Chiesi and GSK; all outside the submitted work. Conflict of interest: L. Guilleminault reports grants from AstraZeneca; consulting fees from Bayer, MSD, AstraZeneca, GSK, Novartis, Sanofi and Chiesi; lecture honoraria from MSD, AstraZeneca, GSK, Novartis, Sanofi and Chiesi; payment for expert testimony from Bayer, MSD and Sanofi; and travel support from MSD, AstraZeneca, GSK, Novartis and Sanofi; all outside the submitted work. Conflict of interest: G. Devouassoux reports lecture or consulting fees from GSK, Menarini, ALK, AstraZeneca, Novartis, Chiesi and Sanofi; payment for expert testimony from GSK, AstraZeneca, Sanofi and Chiesi; and travel support from AstraZeneca, GSK, Sanofi, Novartis, Chiesi; all outside the submitted work. Conflict of interest: M. Le Brun reports grants from GSK, AstenSante and Novartis; lecture honoraria from GSK and La Revue du Praticien; and travel support from Asten Santé and Novartis; all outside the submitted work. Conflict of interest: G. Mourin reports lecture honoraria from AstraZeneca and GSK; and travel support from AstraZeneca, Sanofi, Menarini and GSK; all outside the submitted work. Conflict of interest: P. Bonniaud reports grants from AstraZeneca; lecture honoraria from Sanofi and AstraZeneca; travel support from AstraZeneca, Novartis and Sanofi; advisory board participation from AstraZeneca, Novartis, Sanofi and GSK; all outside the submitted work. Conflict of interest: E. Ebstein reports consulting fees from Abbvie, Novartis and BMS; lecture honoraria from UCB and Galapagos; and travel support from UCB and Novartis; all outside the submitted work. Conflict of interest: C. Taillé reports grants from GSK; consulting fees from AstraZeneca, GSK and Sanofi; lecture honoraria from AstraZeneca, GSK, Sanofi, Novartis, Stallergenes and Chiesi; and travel support from AstraZeneca and GSK; all outside the submitted work. Conflict of interest: S. Valéry, M. Merveilleau, M. Russier, J. Pradelli, P-A. Juge all have nothing to disclose.

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Int Forum Allergy Rhinol



. 2024 Feb 26.

doi: 10.1002/alr.23340. Online ahead of print.

Medication utilization for patients with chronic rhinosinusitis with nasal polyposis and asthma in 12 months pre- and post-dupilumab initiation

[Emily Garvey](#)¹, [Bita Naimi](#)¹, [Alexander Duffy](#)¹, [Chase Kahn](#)¹, [Douglas Farquhar](#)¹, [Marc Rosen](#)¹, [Mindy Rabinowitz](#)¹, [Damaris Pena Evertz](#)², [Jessica Most](#)², [Elina Toskala](#)¹, [Gurston G Nyquist](#)¹

Affiliations expand

- PMID: 38409897
- DOI: [10.1002/alr.23340](https://doi.org/10.1002/alr.23340)

Abstract

This study examines the impact of dupilumab on medication use for chronic rhinosinusitis with nasal polyposis (CRSwNP) and asthma patients. Patients on dupilumab had a reduction in oral/inhaled/topical steroids, antibiotics, and leukotriene receptor antagonists (LTRAs). The reduction in medication use had no impact on total polyp or SNOT-22 scores.

Keywords: asthma; chronic rhinosinusitis; quality of life; steroid therapy.

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- [6 references](#)

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Review

Int Arch Allergy Immunol

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. 2024 Feb 26:1-16.

doi: 10.1159/000536335. Online ahead of print.

[The Role of Regulatory T Cells in Allergic Diseases: Collegium Internationale Allergologicum \(CIA\) Update 2024](#)

[Leticia Martín-Cruz](#)^{1,2}, [Cristina Benito-Villalvilla](#)^{1,3}, [Sofía Sirvent](#)¹, [Alba Angelina](#)¹, [Oscar Palomares](#)¹

Affiliations expand

- PMID: 38408438
- DOI: [10.1159/000536335](https://doi.org/10.1159/000536335)

Abstract

Background: Allergy represents a major health problem of increasing prevalence worldwide with a high socioeconomic impact. Our knowledge on the molecular mechanisms underlying allergic diseases and their treatments has significantly improved over the last years. The generation of allergen-specific regulatory T cells (Tregs) is crucial in

the induction of healthy immune responses to allergens, preventing the development and worsening of allergic diseases.

Summary: In the last decades, intensive research has focused on the study of the molecular mechanisms involved in Treg development and Treg-mediated suppression. These mechanisms are essential for the induction of sustained tolerance by allergen-specific immunotherapy (AIT) after treatment discontinuation. Compelling experimental evidence demonstrated altered suppressive capacity of Tregs in patients suffering from allergic rhinitis, allergic asthma, food allergy, or atopic dermatitis, as well as the restoration of their numbers and functionality after successful AIT.

Key message: The better understanding of the molecular mechanisms involved in Treg generation during allergen tolerance induction might well contribute to the development of novel strategies for the prevention and treatment of allergic diseases.

Keywords: Allergen-specific immunotherapy; Allergic asthma; Allergic rhinitis; Atopic dermatitis; Food allergy; Regulatory T cells.

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Brain Behav Immun

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. 2024 Feb 25:S0889-1591(24)00272-1.

doi: 10.1016/j.bbi.2024.02.028. Online ahead of print.

Maternal asthma symptoms during pregnancy on child behaviour and executive function: A Bayesian phenomics approach

[Syeda Fabeha Husain¹](#), [Andrea Cremaschi²](#), [Noor Hidayatul Aini Suaini²](#), [Maria De Iorio³](#), [Evelyn X L Loo⁴](#), [Lynette P Shek⁵](#), [Anne E N Goh⁶](#), [Michael J Meaney⁷](#), [Elizabeth H Tham⁵](#), [Evelyn C Law⁸](#)

Affiliations expand

- PMID: 38412907
- DOI: [10.1016/j.bbi.2024.02.028](https://doi.org/10.1016/j.bbi.2024.02.028)

Abstract

Objective: Maternal history of inflammatory conditions has been linked to offspring developmental and behavioural outcomes. This phenomenon may be explained by the maternal immune activation (MIA) hypothesis, which posits that dysregulation of the gestational immune environment affects foetal neurodevelopment. The timing of inflammation is critical. We aimed to understand maternal asthma symptoms during pregnancy, in contrast with paternal asthma symptoms during the same period, on child behaviour problems and executive function in a population-based cohort.

Methods: Data were obtained from 844 families from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort. Parent asthma symptoms during the prenatal period were reported. Asthma symptoms in children were reported longitudinally from two to five years old, while behavioural problems and executive functioning were obtained at seven years old. Parent and child measures were compared between mothers with and without prenatal asthma symptoms. Generalized linear and Bayesian phenomics models were used to determine the relation between parent or child asthma symptoms and child outcomes.

Results: Children of mothers with prenatal asthma symptoms had greater behavioural and executive problems than controls (Cohen's d: 0.43-0.75; all $p < 0.05$). This association remained after adjustments for emerging asthma symptoms during the preschool years and fathers' asthma symptoms during the prenatal period. After adjusting for dependence between child outcomes, the Bayesian phenomics model showed that maternal prenatal asthma symptoms were associated with child internalising symptoms and higher-order executive function, while child asthma symptoms were associated with executive function

skills. Paternal asthma symptoms during the prenatal period were not associated with child outcomes.

Conclusions: Associations between child outcomes and maternal but not paternal asthma symptoms during the prenatal period suggests a role for MIA. These findings need to be validated in larger samples, and further research may identify behavioural and cognitive profiles of children with exposure to MIA.

Keywords: Asthma; Behavioural problems; Executive function; Maternal immune activation; Phenomics; Wheezing.

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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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Respirology

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. 2024 Feb 25.

doi: 10.1111/resp.14685. Online ahead of print.

[What makes asthma characterized by airway eosinophilia become severe?](#)

[Thomas Rothe](#)¹, [Niki Ubags](#)², [Christophe von Garnier](#)²

Affiliations expand

- PMID: 38403834
- DOI: [10.1111/resp.14685](https://doi.org/10.1111/resp.14685)

No abstract available

Keywords: eosinophilic asthma; nasal polyposis; steroid resistance.

- [13 references](#)

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Br J Clin Pharmacol

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. 2024 Feb 25.

doi: 10.1111/bcp.16025. Online ahead of print.

[Self-management support with the Respiratory Adherence Care Enhancer instrument in asthma and chronic obstructive pulmonary disease: An implementation trial](#)

[Claire D Visser](#)¹, [Lisanne L M Antonisse](#)¹, [Floor M Alleda](#)¹, [Colin Bos](#)², [Privender Saini](#)², [Esther Kuipers](#)³, [Henk-Jan Guchelaar](#)¹, [Martina Teichert](#)^{1,4,5}

Affiliations expand

- PMID: 38403776
- DOI: [10.1111/bcp.16025](https://doi.org/10.1111/bcp.16025)

Abstract

Aim: Suboptimal self-management with controller inhalation therapy in asthma and COPD is frequently observed with poor treatment outcomes. The developed 'Respiratory Adherence Care Enhancer' (RACE) instrument identifies and addresses individual barriers to self-management with a theoretical underpinning. This study investigates the feasibility of pharmaceutical support with this instrument.

Methods: An implementation trial was conducted with asthma and COPD patients in 5 community pharmacies in the Netherlands. Patients were allocated to standard care or add-on support with the RACE instrument. Patients were invited to complete the RACE questionnaire at baseline, 5-week and 10-week follow-up. Barrier profiles were accessible for the intervention group with subsequent consultations at baseline and 5-weeks. Experiences were collected from patients and consultants with a questionnaire and reported findings. Primary endpoints focused on the acceptability, practicality and implementation process. Secondary endpoints included between-group differences in barrier and disease control outcomes from baseline at 10-weeks follow-up.

Results: In total, 84 patients were included; 48 were assigned to intervention and 36 to standard care. Patient satisfaction of support with the RACE instrument was high (71%). Patients felt motivated, reassured and more confident about their disease management. Consultants reported an increase in awareness of patient barriers. Patient recognition of barrier profiles was 83.9% ($\pm 12.9\%$). The barrier inhaler techniques decreased significantly for the intervention group at follow-up with odds ratio 0.30 (95% confidence interval, 0.10-0.91). No significant differences were observed for changes in number of barriers and disease control.

Conclusion: Self-management support with the RACE instrument is feasible and appreciated, facilitating behaviour change with patient-centred pharmaceutical care in asthma and COPD.

Keywords: asthma; chronic obstructive pulmonary disease; implementation; patient-centred care; self-management (self-care); tailored care.

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

1

Allergy

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. 2024 Mar 2.

doi: 10.1111/all.16052. Online ahead of print.

[House dust mite SCIT reduces asthma risk and significantly improves long-term rhinitis and asthma control-A RWE study](#)

[Marek Jutel](#)^{1,2}, [Ludger Klimek](#)³, [Hartmut Richter](#)⁴, [Bernd Brüggjenjürgen](#)⁵, [Christian Vogelberg](#)⁶

Affiliations [expand](#)

- PMID: 38429981

- DOI: [10.1111/all.16052](https://doi.org/10.1111/all.16052)

Abstract

Background: The German Therapy Allergen Ordinance (TAO) triggered an ongoing upheaval in the market for house dust mite (HDM) allergen immunotherapy (AIT) products. Three HDM subcutaneous AIT (SCIT) products hold approval in Germany and therefore will be available after the scheduled completion of the TAO procedure in 2026. In general, data from clinical trials on the long-term effectiveness of HDM AIT are rare. We evaluated real-

world data (RWD) in a retrospective, observational cohort study based on a longitudinal claims database including 60% of all German statutory healthcare prescriptions to show the long-term effectiveness of one of these products in daily life. Aim of this analysis was to provide a per product analysis on effectiveness of mite AIT as it is demanded by international guidelines on AIT.

Methods: Subjects between 5 and 70 years receiving their first (index) prescription of SCIT with a native HDM product (SCIT group) between 2009 and 2013 were included. The exactly 3:1 matched control group received prescriptions for only symptomatic AR medication (non-AIT group); the evaluation period for up to 6 years of follow-up ended in February 2017. Study endpoints were the progression of allergic rhinitis (AR) and asthma, asthma occurrence and time to the onset of asthma after at least 2 treatment years.

Results: In total, 892 subjects (608 adults and 284 children/adolescents) were included in the SCIT group and 2676 subjects (1824 adults and 852 children/adolescents) in the non-AIT group. During the follow-up period after at least 2 years of SCIT, the number of prescriptions in the SCIT group was reduced by 62.8% ($p < .0001$) for AR medication and by 42.4% for asthma medication ($p = .0003$). New-onset asthma risk was significantly reduced in the SCIT vs non-AIT group by 27.0% ($p = .0212$). The asthma-preventive effect of SCIT occurred 15 months after start of the treatment. In the SCIT group, the time to onset of asthma was prolonged compared to the non-AIT group ($p = .0010$).

Conclusion: In this first product based RWD analysis on SCIT with a native HDM product, patients aged 5 to 70 years benefited from AIT in the long term in terms of reduced progression of AR and asthma after at least 2 years of treatment. The effects seemed to last for up to 6 years after treatment termination. A significantly reduced risk of asthma onset was observed, starting after 15 months of treatment.

Keywords: allergen immunotherapy; house dust mite; long-term effect; real-world evidence; subcutaneous immunotherapy.

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Otolaryngol Head Neck Surg



. 2024 Mar;170(3):668-674.

doi: 10.1002/ohn.649.

[Plain Language Summary: Immunotherapy for Inhalant Allergy](#)

[Richard K Gurgel](#)¹, [Fuad M Baroody](#)², [Cecelia C Damask](#)³, [James Whit Mims](#)⁴, [Donna D Gardner](#)⁵, [Christine M Reger](#)⁶, [Joe Reyes](#)⁷, [Nui Dhepyasuwan](#)⁷

Affiliations expand

- PMID: 38408155
- DOI: [10.1002/ohn.649](https://doi.org/10.1002/ohn.649)

Abstract

The plain language summary explains allergen immunotherapy to patients, families, and caregivers. The summary is for patients aged 5 years and older who are experiencing symptoms from inhalant allergies and are considering immunotherapy as a treatment option. It is based on the 2024 "Clinical Practice Guideline: Immunotherapy for Inhalant Allergy." This plain language summary is a companion publication to the full guideline, which provides greater detail for health care providers. Guidelines and their recommendations may not apply to every patient, but they can be used to find best practices and quality improvement opportunities.

Keywords: allergen immunotherapy; allergic asthma; allergic rhinitis; allergy; anaphylaxis; inhalant allergy; subcutaneous immunotherapy; sublingual immunotherapy.

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Otolaryngol Head Neck Surg

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. 2024 Mar;170(3):635-667.

doi: 10.1002/ohn.650.

[Executive Summary of Clinical Practice Guideline on Immunotherapy for Inhalant Allergy](#)

[Richard K Gurgel](#)¹, [Fuad M Baroody](#)², [Cecelia C Damask](#)³, [James Whit Mims](#)⁴, [Stacey L Ishman](#)⁵, [Dole P Baker](#)⁶, [Kevin J Contrera](#)⁷, [Fariha S Farid](#)⁸, [John A Fornadley](#)⁹, [Donna D Gardner](#)¹⁰, [LaKeisha R Henry](#)¹¹, [Jean Kim](#)¹², [Joshua M Levy](#)¹³, [Christine M Reger](#)¹⁴, [Howard J Ritz](#)¹⁵, [Robert J Stachler](#)¹⁶, [Tulio A Valdez](#)¹⁷, [Joe Reyes](#)¹⁸, [Nui Dhepyasuwan](#)¹⁸

Affiliations expand

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- DOI: [10.1002/ohn.650](https://doi.org/10.1002/ohn.650)

Abstract

Objective: Allergen immunotherapy (AIT) is the therapeutic exposure to an allergen or allergens selected by clinical assessment and allergy testing to decrease allergic symptoms and induce immunologic tolerance. Inhalant AIT is administered to millions of patients for allergic rhinitis (AR) and allergic asthma (AA) and is most commonly delivered as subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Despite its widespread use, there is variability in the initiation and delivery of safe and effective immunotherapy, and there are opportunities for evidence-based recommendations for improved patient care.

Purpose: The purpose of this clinical practice guideline is to identify quality improvement opportunities and provide clinicians trustworthy, evidence-based recommendations regarding the management of inhaled allergies with immunotherapy. Specific goals of the guideline are to optimize patient care, promote safe and effective therapy, reduce unjustified variations in care, and reduce risk of harm. The target patients for the guideline are any individuals aged 5 years and older with AR, with or without AA, who are either candidates for immunotherapy or treated with immunotherapy for their inhalant allergies. The target audience is all clinicians involved in the administration of immunotherapy. This guideline is intended to focus on evidence-based quality improvement opportunities judged most important by the guideline development group. It is not intended to be a comprehensive, general guide regarding the management of inhaled allergies with immunotherapy. The statements in this guideline are not intended to limit or restrict care provided by clinicians based on their experience and assessment of individual patients.

Action statements: The guideline development group made a strong recommendation that (Key Action Statement [KAS] 10) the clinician performing allergy skin testing or administering AIT must be able to diagnose and manage anaphylaxis. The guideline development group made recommendations for the following KASs: (KAS 1) Clinicians should offer or refer to a clinician who can offer immunotherapy for patients with AR with or without AA if their patients' symptoms are inadequately controlled with medical therapy, allergen avoidance, or both, or have a preference for immunomodulation. (KAS 2A) Clinicians should not initiate AIT for patients who are pregnant, have uncontrolled asthma, or are unable to tolerate injectable epinephrine. (KAS 3) Clinicians should evaluate the patient or refer the patient to a clinician who can evaluate for signs and symptoms of asthma before initiating AIT and for signs and symptoms of uncontrolled asthma before administering subsequent AIT. (KAS 4) Clinicians should educate patients who are immunotherapy candidates regarding the differences between SCIT and SLIT (aqueous and tablet) including risks, benefits, convenience, and costs. (KAS 5) Clinicians should educate patients about the potential benefits of AIT in (1) preventing new allergen sensitization, (2) reducing the risk of developing AA, and (3) altering the natural history of the disease with continued benefit after discontinuation of therapy. (KAS 6) Clinicians who administer SLIT to patients with seasonal AR should offer pre- and co-seasonal immunotherapy. (KAS 7) Clinicians prescribing AIT should limit treatment to only those clinically relevant allergens that correlate with the patient's history and are confirmed by testing. (KAS 9) Clinicians administering AIT should continue escalation or maintenance dosing when patients have local reactions to AIT. (KAS 11) Clinicians should avoid repeat allergy testing as an

assessment of the efficacy of ongoing AIT unless there is a change in environmental exposures or a loss of control of symptoms. (KAS 12) For patients who are experiencing symptomatic control from AIT, clinicians should treat for a minimum duration of 3 years, with ongoing treatment duration based on patient response to treatment. The guideline development group offered the following KASs as options: (KAS 2B) Clinicians may choose not to initiate AIT for patients who use concomitant beta-blockers, have a history of anaphylaxis, have systemic immunosuppression, or have eosinophilic esophagitis (SLIT only). (KAS 8) Clinicians may treat polysensitized patients with a limited number of allergens.

Keywords: allergen immunotherapy; allergic asthma; allergic rhinitis; anaphylaxis; inhalant allergy; subcutaneous immunotherapy; sublingual immunotherapy.

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[Practice Guideline](#)

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. 2024 Mar;170 Suppl 1:S1-S42.

doi: 10.1002/ohn.648.

Clinical Practice Guideline: Immunotherapy for Inhalant Allergy

[Richard K Gurgel¹](#), [Fuad M Baroody²](#), [Cecelia C Damask³](#), [James Whit Mims⁴](#), [Stacey L Ishman⁵](#), [Dole P Baker Jr⁶](#), [Kevin J Contrera⁷](#), [Fariha S Farid⁸](#), [John A Fornadley⁹](#), [Donna D Gardner¹⁰](#), [LaKeisha R Henry¹¹](#), [Jean Kim¹²](#), [Joshua M Levy¹³](#), [Christine M Reger¹⁴](#), [Howard J Ritz¹⁵](#), [Robert J Stachler¹⁶](#), [Tulio A Valdez¹⁷](#), [Joe Reyes¹⁸](#), [Nui Dhepyasuwan¹⁸](#)

Affiliations expand

- PMID: 38408152
- DOI: [10.1002/ohn.648](https://doi.org/10.1002/ohn.648)

Abstract

Objective: Allergen immunotherapy (AIT) is the therapeutic exposure to an allergen or allergens selected by clinical assessment and allergy testing to decrease allergic symptoms and induce immunologic tolerance. Inhalant AIT is administered to millions of patients for allergic rhinitis (AR) and allergic asthma (AA) and is most commonly delivered as subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Despite its widespread use, there is variability in the initiation and delivery of safe and effective immunotherapy, and there are opportunities for evidence-based recommendations for improved patient care.

Purpose: The purpose of this clinical practice guideline (CPG) is to identify quality improvement opportunities and provide clinicians trustworthy, evidence-based recommendations regarding the management of inhaled allergies with immunotherapy. Specific goals of the guideline are to optimize patient care, promote safe and effective therapy, reduce unjustified variations in care, and reduce the risk of harm. The target patients for the guideline are any individuals aged 5 years and older with AR, with or without AA, who are either candidates for immunotherapy or treated with immunotherapy for their inhalant allergies. The target audience is all clinicians involved in the administration of immunotherapy. This guideline is intended to focus on evidence-based quality improvement opportunities judged most important by the guideline development group (GDG). It is not intended to be a comprehensive, general guide regarding the management of inhaled allergies with immunotherapy. The statements in this guideline are not intended to limit or restrict care provided by clinicians based on their experience and assessment of individual patients.

Action statements: The GDG made a strong recommendation that (Key Action Statement [KAS] 10) the clinician performing allergy skin testing or administering AIT must be able to

diagnose and manage anaphylaxis. The GDG made recommendations for the following KASs: (KAS 1) Clinicians should offer or refer to a clinician who can offer immunotherapy for patients with AR with or without AA if their patients' symptoms are inadequately controlled with medical therapy, allergen avoidance, or both, or have a preference for immunomodulation. (KAS 2A) Clinicians should not initiate AIT for patients who are pregnant, have uncontrolled asthma, or are unable to tolerate injectable epinephrine. (KAS 3) Clinicians should evaluate the patient or refer the patient to a clinician who can evaluate for signs and symptoms of asthma before initiating AIT and for signs and symptoms of uncontrolled asthma before administering subsequent AIT. (KAS 4) Clinicians should educate patients who are immunotherapy candidates regarding the differences between SCIT and SLIT (aqueous and tablet) including risks, benefits, convenience, and costs. (KAS 5) Clinicians should educate patients about the potential benefits of AIT in (1) preventing new allergen sensitizations, (2) reducing the risk of developing AA, and (3) altering the natural history of the disease with continued benefit after discontinuation of therapy. (KAS 6) Clinicians who administer SLIT to patients with seasonal AR should offer pre- and co-seasonal immunotherapy. (KAS 7) Clinicians prescribing AIT should limit treatment to only those clinically relevant allergens that correlate with the patient's history and are confirmed by testing. (KAS 9) Clinicians administering AIT should continue escalation or maintenance dosing when patients have local reactions (LRs) to AIT. (KAS 11) Clinicians should avoid repeat allergy testing as an assessment of the efficacy of ongoing AIT unless there is a change in environmental exposures or a loss of control of symptoms. (KAS 12) For patients who are experiencing symptomatic control from AIT, clinicians should treat for a minimum duration of 3 years, with ongoing treatment duration based on patient response to treatment. The GDG offered the following KASs as options: (KAS 2B) Clinicians may choose not to initiate AIT for patients who use concomitant beta-blockers, have a history of anaphylaxis, have systemic immunosuppression, or have eosinophilic esophagitis (SLIT only). (KAS 8) Clinicians may treat polysensitized patients with a limited number of allergens.

Keywords: allergen immunotherapy; allergic asthma; allergic rhinitis; anaphylaxis; inhalant allergy; subcutaneous immunotherapy; sublingual immunotherapy.

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World Allergy Organ J



. 2024 Feb 15;17(3):100879.

doi: 10.1016/j.waojou.2024.100879. eCollection 2024 Mar.

[Diagnostic biomarkers for chronic rhinosinusitis in adult asthmatics in real-world practice](#)

[Jae-Hyuk Jang](#)¹, [Eun-Mi Yang](#)¹, [Youngsoo Lee](#)¹, [Yoo Seob Shin](#)¹, [Young-Min Ye](#)¹, [Hae-Sim Park](#)¹

Affiliations expand

- PMID: 38380106
- PMCID: [PMC10877182](#)
- DOI: [10.1016/j.waojou.2024.100879](#)

Free PMC article

Abstract

Background: Chronic rhinosinusitis (CRS) is a common comorbid condition of asthma that affects the long-term outcome of asthmatic patients. CRS is a heterogeneous disease requiring multiple biomarkers to explain its pathogenesis. This study aimed to develop potential biomarkers for predicting CRS in adult asthmatic patients in a real-world clinical setting.

Methods: This study enrolled 108 adult asthmatic patients who had maintained anti-asthmatic medications, including medium-to-high doses of inhaled corticosteroid plus

long-acting β 2-agonists, and compared clinical characteristics between patients with CRS (CRS group) and those without CRS (non-CRS group). CRS was diagnosed based on the results of paranasal sinus X-ray and/or osteomeatal-unit CT as well as clinical symptoms. Type-2 parameters, including blood eosinophil count, serum levels of periostin/dipeptidyl peptidase 10 (DPP10) and clinical parameters, such as FEV1% and fractional exhaled nitric oxide (FeNO), were analyzed. All biomarkers were evaluated by logistic regression and classification/regression tree (CRT) analyses.

Results: The CRS group had higher blood eosinophil counts/FeNO levels and prevalence of aspirin-exacerbated respiratory disease (AERD) than the non-CRS group (n = 57, 52.8% vs. n = 75, 47.2%; $P < 0.05$), but no differences in sex/smoking status or asthma control status were noted. The CRS group had higher serum periostin/DPP10 levels than the non-CRS group. Moreover, logistic regression demonstrated that serum periostin/DPP10 and the AERD phenotype were significant factors for predicting CRS in asthmatic patients (adjusted odds ratio, 2.14/1.94/12.39). A diagnostic algorithm and the optimal cutoff values determined by CRT analysis were able to predict CRS with 86.27% sensitivity (a 0.17 negative likelihood ratio).

Conclusion: Serum periostin, DPP10 and the phenotype of AERD are valuable biomarkers for predicting CRS in adult asthmatic patients in clinical practice.

Keywords: Asthma; Biomarkers; Dipeptidyl-peptidases and tripeptidyl-peptidases; Eosinophils; Fractional exhaled nitric oxide testing; Periostin; Rhinitis; Sinusitis.

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Conflict of interest statement

None.

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- [2 figures](#)

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. 2024 Feb 6:69:102467.

doi: 10.1016/j.eclinm.2024.102467. eCollection 2024 Mar.

[Efficacy and safety of stapokibart \(CM310\) in uncontrolled seasonal allergic rhinitis \(MERAK\): an investigator-initiated, placebo-controlled, randomised, double-blind, phase 2 trial](#)

[Yuan Zhang](#)^{1,2,3}, [Bing Yan](#)^{4,2,3}, [Zehua Zhu](#)^{1,4,2}, [Xueyan Wang](#)⁵, [Xicheng Song](#)^{6,7}, [Dongdong Zhu](#)^{8,9}, [Tingting Ma](#)⁵, [Yu Zhang](#)^{6,7}, [Cuida Meng](#)^{8,9}, [Guangke Wang](#)¹⁰, [Chengshuo Wang](#)^{4,2,3}, [Luo Zhang](#)^{1,4,2,3}

Affiliations [expand](#)

- PMID: 38356731
- PMCID: [PMC10864214](#)
- DOI: [10.1016/j.eclinm.2024.102467](#)

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Abstract

Background: There is no trial to assess the benefits of periodically using biologics during the pollen season in patients with uncontrolled seasonal allergic rhinitis (SAR), who have moderate-to-severe symptoms even after standard-of-care. This trial aimed to evaluate the efficacy and safety of the add-on administration of stapokibart, a humanised monoclonal antibody that targets interleukin-4 receptor alpha, in patients with uncontrolled SAR.

Methods: In this investigator-initiated, randomised, double-blind, placebo-controlled trial, eligible patients received either stapokibart 600-300 mg weekly (QW), every 2 weeks (Q2W), or placebo QW for 4 weeks. All patients were given mometasone furoate nasal spray and loratadine throughout the trial. The primary endpoint was the mean change from baseline in daily reflective total nasal symptom score (rTNSS) during 2-week treatment. Secondary efficacy outcomes included: the mean change from baseline in daily rTNSS during 4-week treatment; the mean changes and the mean percentage changes from baseline during 2-week and 4-week treatment in 1) daily rTNSS and reflective total ocular symptom score (rTOSS), 2) morning (AM)/evening (PM) rTNSS and rTOSS, 3) AM instantaneous total nasal symptom score (iTNSS) and instantaneous total ocular symptom score (iTOSS), 4) individual nasal and ocular symptoms; the change from baseline in Rhinoconjunctivitis Quality-of-Life Questionnaire score during 4-week treatment. Exploratory endpoints included the change of prespecified markers related to type 2 inflammation pre- and post-treatment. Safety, immunogenicity, and pharmacokinetics were also evaluated. This study is registered with www.clinicaltrials.gov ([NCT05470647](https://www.clinicaltrials.gov/ct2/show/study?term=NCT05470647)).

Findings: Between August 17, 2022, and December 28, 2022, 92 patients with uncontrolled SAR were enrolled from 4 centres in China and randomly assigned to receive stapokibart 600-300 mg QW (n = 31), stapokibart 600-300 mg Q2W (n = 30), or placebo QW (n = 31), of whom 86 (93%) completed the study. Both stapokibart Q2W and QW did not significantly improve mean change from baseline in daily rTNSS compared with placebo in 2 weeks. The least-squares (LS) mean differences (97.5% confidence interval [CI]) compared with placebo were -1.0 (-2.3, 0.2) in stapokibart Q2W group (p = 0.065) and -0.2 (-1.5, 1.0) in stapokibart QW group (p = 0.67). For the secondary outcomes, compared with placebo, stapokibart Q2W presented significant improvements in the mean percentage change from baseline in daily rTNSS in 2 weeks (LS mean difference -12.9%, 95% CI -25.3%, -0.4%, p = 0.043), as well as AM iTNSS over 2 weeks (LS mean difference -17.4%, 95% CI -31.0%, -3.8%, p = 0.013) and 4 weeks (LS mean difference -15.4%, 95% CI -29.0%, -1.9%, p = 0.026). Additionally, the nasal congestion score was significantly lower in stapokibart Q2W than placebo during 2-week (LS mean difference -0.4, 95% CI -0.7, -0.1, p = 0.014) and 4-week (LS mean difference -0.4, 95% CI -0.7, -0.04, p = 0.028) treatment. Treatment-emergent adverse events (TEAEs) occurred in 48% (15/31), 33% (10/30), and 61% (19/31) of patients receiving stapokibart QW, Q2W, and placebo, respectively. Most reported TEAEs were sinus bradycardia, hyperlipidaemia, and blood uric acid increased.

Interpretation: In this phase 2 trial, both stapokibart regimens had an acceptable safety and tolerability profile but did not significantly improve daily rTNSS in patients with uncontrolled SAR. The efficacy of stapokibart in patients with uncontrolled SAR is being further investigated in ongoing phase 3 trials (clinicaltrials.gov, [NCT05908032](https://www.clinicaltrials.gov/ct2/show/study?term=NCT05908032)).

Funding: Ministry of Science and Technology of the People's Republic of China; Ministry of Education of the People's Republic of China; National Natural Science Foundation of China; Chinese Academy of Medical Sciences.

Keywords: Co-seasonal application; Interleukin-4 receptor alpha; Monoclonal antibody; Seasonal allergic rhinitis; Uncontrolled.

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Conflict of interest statement

LZ was supported by grants from the Ministry of Science and Technology of the People's Republic of China; the Ministry of Education of the People's Republic of China and the Chinese Academy of Medical Sciences; CW declares support from the National Natural Science Foundation of China.

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. 2024 Mar;170(3):708-723.

doi: 10.1002/ohn.612. Epub 2023 Dec 18.

Evaluating the Association of Obesity and Chronic Rhinosinusitis: A Systematic Review and Meta-analysis

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Affiliations expand

- PMID: 38108590
- DOI: [10.1002/ohn.612](https://doi.org/10.1002/ohn.612)

Abstract

Objective: The aim of this Meta-analysis and systematic review was to perform a comprehensive assessment of the association of chronic rhinosinusitis (CRS) with overweight/obesity, leptin hormone, and its associated metabolic dysregulation.

Data sources: Ovid MEDLINE, Embase, Web of Science, and Cochrane Central Register of Controlled Trials, were searched for studies from 1946 to October 2022, using predefined syntax.

Review methods: Outcome data for the meta-analysis were extracted on odds ratios (OR) of CRS prevalence based on the presence of overweight/obesity and mean serum leptin levels. A Meta-analysis was performed using the DerSimonian-Laird estimator to pool extracted data by the generalized inverse variance approach. Random effect models were utilized due to the small sample size. A qualitative synthesis was performed on articles that did not meet the inclusion criteria for the Meta-analysis.

Results: Thirty-six studies met the systematic review inclusion criteria out of 1113 articles screened. A total of 6 studies were included in the pooled Meta-analysis of the various outcome variables. Our pooled meta-analysis observed a positive association between overweight/obesity and the prevalence of CRS (OR = 1.33, 95% confidence interval [CI]: 1.17-1.51). The pooled ratio of the means analysis of the mean serum leptin levels between CRS with nasal polyposis and control patients was 2.21 (95% CI: 1.45; 3.36).

Conclusion: Our pooled Meta-analysis indicates a positive association between overweight/obesity and CRS. Future prospective studies are needed to explore the association between CRS and obesity with an understanding of potential confounding

comorbidities, including studies focused on assessing the underlying immunologic mechanism of this association.

Keywords: childhood obesity; chronic rhinosinusitis; dyslipidemia; leptin; metabolic syndrome; obesity; overweight.

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Otolaryngol Head Neck Surg

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. 2024 Mar;170(3):919-927.

doi: 10.1002/ohn.614. Epub 2023 Dec 17.

Long-Term Efficacy and Safety of Subcutaneous Immunotherapy in Monosensitized and Polysensitized Children With Allergic Rhinitis

[Xuan Yuan](#)^{1,2,3,4}, [Shaobing Xie](#)^{1,2,3,4}, [Hua Zhang](#)^{1,2,3,4}, [Junyi Zhang](#)^{1,2,3,4}, [Ruohao Fan](#)^{1,2,3,4}, [Weihong Jiang](#)^{1,2,3,4}, [Zhihai Xie](#)^{1,2,3,4}

Affiliations expand

- PMID: 38104318
- DOI: [10.1002/ohn.614](https://doi.org/10.1002/ohn.614)

Abstract

Objective: To evaluate the efficacy and safety of dust mite subcutaneous immunotherapy (SCIT) in monosensitized and polysensitized children with allergic rhinitis (AR).

Study design: Prospective cohort study.

Setting: Tertiary referral center.

Methods: One hundred thirty children were enrolled and categorized into 2 groups: monosensitized to only dust mites and polysensitized to at least 1 additional allergen beyond dust mites. All patients received SCIT targeting dust mites for 3 years, followed by a 5-year monitoring period. The Total Nasal Symptom Score (TNSS), Symptom and Medication Score (SMS), Visual Analogue Scale (VAS), and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) were assessed before SCIT (T0); at 1 (T1) and 2 (T2) years of SCIT; immediately after SCIT (T3); and 2 years post-SCIT (T5). Safety was assessed based on adverse events (AEs).

Results: Fifty-one monosensitized and 50 polysensitized children completed the study. At T3, 47 monosensitized and 46 polysensitized children were effectively treated, with no significant between-group difference in efficacy ($P > .05$). The TNSS, SMS, VAS scores, and RQLQ score were significantly lower at T1, T2, T3, and T5 than at T0 in both groups ($P < .05$). The differences in the TNSS, SMS, VAS score, and RQLQ score between the 2 groups were nonsignificant at T0, T1, T2, and T3 ($P > .05$), but significant at T5 ($P < .05$). No serious AEs were reported.

Conclusion: Monosensitized and polysensitized children exhibited similar beneficial efficacy and safety after 3 years of dust mite SCIT. Monosensitized children derived more benefits 2 years after discontinuation.

Keywords: allergic rhinitis; efficacy; monosensitized; polysensitized; subcutaneous immunotherapy.

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Am J Rhinol Allergy



. 2024 Mar;38(2):108-115.

doi: 10.1177/19458924231220763. Epub 2023 Dec 13.

[Genetic Association of Allergic Rhinitis with Sleep and Neuropsychological Disorders: A Mendelian Randomization Study](#)

[Chenxi Lin](#)¹, [Jia Li](#)¹, [Ye Deng](#)¹, [Xiongwen Li](#)¹, [Xiaofeng Wang](#)¹, [Jingcheng Lu](#)¹

Affiliations expand

- PMID: 38093177
- DOI: [10.1177/19458924231220763](https://doi.org/10.1177/19458924231220763)

Abstract

Background: The genetic association of allergic rhinitis (AR) with other physiological systems throughout the human body remains unknown.

Objective: The aim of this Mendelian randomization (MR) study was to explore the association of this respiratory disorder with multiple common sleep and neuropsychological disorders at the genetic level.

Methods: Summary data for total AR and pollen AR were collected from the most updated FinnGen genome-wide association studies involving more than 340 000 European subjects. Summary data for 12 sleep and neuropsychological disorders (including snoring) were included from UK Biobank studies involving 63 392 to 462 933 European subjects. Three MR methods, including inverse-variance weighting (IVW), weighted median and MR-Egger, were used to determine the relationships between the exposures and outcomes. Several sensitivity analyses, including Cochran's Q, MR-Egger intercept, MR-PRESSO, "leave-one-out" test and funnel plot, were used to detect heterogeneity and horizontal pleiotropy.

Results: IVW revealed that total and pollen AR were associated with an increased risk of snoring (odds ratio (OR) = 1.011, 95% confidence interval (CI) = 1.004~1.019, $P = .003$; OR = 1.006, 95% CI = 1.001~1.011, $P = .014$). Two other MR methods supported the results from the IVW analysis. No heterogeneity or horizontal pleiotropy was confirmed by sensitivity analyses. In addition, IVW did not reveal any association between AR and other included disorders.

Conclusion: AR (specifically AR caused by pollen) might be an independent risk factor for snoring at the genetic level, which should be verified in the future.

Keywords: FinnGen; Mendelian randomization; UK Biobank; allergic rhinitis; inverse-variance weighted; neuropsychological disorders; pollen; risk factor; sleep disorders; snoring.

Conflict of interest statement

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

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Sage Journals



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Eur Arch Otorhinolaryngol



. 2024 Mar;281(3):1317-1324.

doi: 10.1007/s00405-023-08309-x. Epub 2023 Nov 1.

Effectiveness of dupilumab versus endoscopic sinus surgery for the treatment of type-2 chronic rhinosinusitis with nasal polyps: a preliminary report

[Pietro Orlando](#)¹, [Giuseppe Licci](#)², [Donald Kuitche](#)², [Andrea Matucci](#)³, [Alessandra Vultaggio](#)³, [Oreste Gallo](#)^{2,4}, [Giandomenico Maggiore](#)²

Affiliations expand

- PMID: 37910208
- DOI: [10.1007/s00405-023-08309-x](https://doi.org/10.1007/s00405-023-08309-x)

Abstract

Purpose: Historically managed with intranasal corticosteroids (INCS) and endoscopic sinus surgery (ESS), type-2 Chronic RhinoSinusitis with Nasal Polyps (CRSwNP) treatment was revolutionized by the introduction of dupilumab but universally accepted guidelines are still lacking.

Methods: Patients treated at our University Hospital for type-2 CRSwNP were enrolled. Demographic data were collected, as well as laboratory (eosinophils, total IgE), endoscopic [nasal polyps score (NPS), modified Lund-Kennedy score (mLKS)], radiological [Lund-Mackay score (LMS) at CT scan], SNOT-22, and olfactory [Sniffin' Sticks identification test (SSIT)] features. Patients were treated with dupilumab or ESS and re-evaluated after 3 and 12 months.

Results: At 3 and 12 months, patients undergoing ESS achieved a higher reduction of NPS and mLKS, while patients receiving dupilumab experienced a higher improvement at SNOT-22 and SSIT with a greater positive variation in the prevalence of anosmia (- 57.7% vs - 42.9%) and normosmia (+ 37.8 vs + 28.5%). Mean mLKS and LMS were quite similar. Results were independent of clinical features known to contribute to CRSwNP severity, except for patients with ≥ 2 prior ESS who had a significantly lower smell improvement.

Conclusion: ESS and dupilumab were effective at reducing CRSwNP inflammatory burning. CRSwNP smell impairment cannot be attributed only to olfactory cleft obstruction and other mechanisms may be involved. Dupilumab acts systemically with poor correlation with NPS. As of today, dupilumab appears to be more suitable for elderly patients with anesthesiological contraindications and/or several previous surgeries, while ESS may represent the first-line choice in surgery-naive patients.

Keywords: Biologic drugs; CRSwNP; Dupilumab; Sinonasal outcomes; Transnasal endoscopic surgery.

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- [38 references](#)

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[Review](#)

Eur Arch Otorhinolaryngol

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. 2024 Mar;281(3):1131-1137.

doi: 10.1007/s00405-023-08307-z. Epub 2023 Oct 30.

Pediatric chronic rhinosinusitis

[Hassan H Ramadan](#)¹

Affiliations expand

- PMID: 37899371
- DOI: [10.1007/s00405-023-08307-z](https://doi.org/10.1007/s00405-023-08307-z)

Abstract

Purpose: An up-to-date overview of diagnosis, differential diagnosis, comorbidities, and current medical and surgical management of pediatric chronic rhinosinusitis (PCRS).

Methods: Review of current evidence-based literature on PCRS.

Results: Diagnosis of PCRS seems to be improving based on recent evidence using nasal endoscopy as well as computed tomography scanning. Recent literature supports the fact that chronic adenoiditis can be an independent etiology of symptoms of chronic sinusitis, that are very similar to chronic adenoiditis. Allergic rhinitis and immune deficiency play important roles in the management of PCRS. Surgery for PCRS has evolved significantly in the last 15–20 years to include adenoidectomy as well as endoscopic sinus surgery.

Conclusions: PCRS is very common in children causing poor QOL for these children. Medical management remains the main stay of treatment with attention to management of co-morbidities that may contribute to the disease severity. Making the correct diagnosis will help with the choice of surgical intervention if medical management fails.

Keywords: Adenoidectomy; Chronic adenoiditis; Chronic rhinosinusitis; Endoscopic sinus surgery; Pediatric.

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- [49 references](#)

SUPPLEMENTARY INFO

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12

J Asthma

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. 2024 Mar;61(3):177-183.

doi: 10.1080/02770903.2023.2255277. Epub 2023 Sep 14.

[Breathing pattern disorder in chronic rhinosinusitis with severe asthma: nasal obstruction and polyps do not increase prevalence](#)

[Rebecca Livingston](#)^{1,2}, [Helene Bellas](#)^{1,2}, [Jagdeep Sahota](#)^{2,3}, [Therese Bidder](#)^{2,4}, [Florian Vogt](#)², [Valerie J Lund](#)^{3,5}, [Simon B Gane](#)^{3,5}, [Douglas S Robinson](#)², [Harsha H Kariyawasam](#)^{2,4,5}

Affiliations expand

- PMID: 37668326
- DOI: [10.1080/02770903.2023.2255277](https://doi.org/10.1080/02770903.2023.2255277)

Abstract

Objectives: Chronic rhinosinusitis (CRS) with severe asthma are associated with breathing pattern disorder (BPD). Mouth breathing is a sign of breathing pattern disorder, and nose breathing a fundamental part of breathing pattern retraining for BPD. The prevalence of BPD in relation to CRS subtypes and the relationship of nasal obstruction to BPD in CRS

and associated severe asthma is unknown. The breathing pattern assessment tool (BPAT) can identify BPD. Our objective was to thus investigate the prevalence of BPD, nasal airflow obstruction and measures of airway disease severity in CRS with (CRSwNP) and without nasal polyps (CRSsNP) in severe asthma.

Methods: We determined whether CRS status, peak nasal inspiratory flow (PNIF) or polyp disease increased BPD prevalence. Demographic factors, measures of airway function and breathlessness in relation to BPD status and CRS subtypes were also evaluated.

Results: 130 Patients were evaluated ($n = 69$ had BPD). The prevalence of BPD in CRS with severe asthma was 53.1%. There was no difference between BPD occurrence between CRSwNP and CRSsNP. The mean polyp grade and PNIF were not statistically different between the BPD and non-BPD group. The presence of nasal polyps did not increase breathlessness.

Conclusions: BPD and CRS are commonly co-associated. CRS status and nasal obstruction per se does not increase BPD prevalence.

Keywords: Chronic rhinosinusitis; breathing pattern disorder; nasal obstruction; severe asthma.

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Review

Laryngoscope

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. 2024 Mar;134(3):1005-1013.

Non-Type 2 and Mixed Inflammation in Chronic Rhinosinusitis and Lower Airway Disease

[Austin Heffernan](#)¹, [Amir Shafiee](#)¹, [Teffran Chan](#)¹, [Sydney Sparanese](#)¹, [Andrew Thamboo](#)¹

Affiliations expand

- PMID: 37615304
- DOI: [10.1002/lary.30992](https://doi.org/10.1002/lary.30992)

Abstract

Objective: The aim was to discuss the role of non-type 2 inflammation in patients diagnosed with chronic rhinosinusitis (CRS) and comorbid lower airway disease.

Data sources: Medline, Embase, National Institute for Health and Care Excellence, TRIP Database, ProQuest, Clinicaltrials.gov, Cochrane Central Registry of Controlled Trials, Web of Science, government and health organizations, and graduate-level theses.

Review methods: This scoping review followed PRISMA-ScR guidelines. Search strategy was peer-reviewed by medical librarians. Studies were included if they utilized airway sampling, non-type 2 cytokines, and patients with CRS and lower airway disease.

Results: Twenty-seven from 7060 articles were included. In patients with CRS and comorbid asthma, aspirin-exacerbated respiratory disease (AERD), and chronic obstructive pulmonary disease (COPD)/bronchiectasis, 60% (n = 12), 33% (n = 2), and 100% (n = 1), respectively, demonstrated mixed or non-type 2 endotypes. Comorbid CRS and asthma produced type 1 (n = 1.5), type 2 (n = 8), type 3 (n = 1), mixed type 1/2 (n = 1), and mixed type 1/2/3 (n = 8.5) endotype shifts. AERD demonstrated type 2 (n = 4), mixed type 2/3 (n = 1), and mixed type 1/2/3 (n = 1) endotype shifts. CRS with COPD or bronchiectasis demonstrated a mixed 1/2 (n = 1) endotype shift.

Conclusion: Type 2 disease has been extensively reviewed due to advent biologics targeting type 2 inflammation, but outcomes may be suboptimal due to the presence of non-type 2 inflammation. A proportion of patients with CRS and comorbid lower airway disease demonstrated mixed and non-type 2 endotype shifts. This emphasizes that

patients with unified airway disease may have forms of inflammation beyond classical type 2 disease which could inform biologic development. *Laryngoscope*, 134:1005-1013, 2024.

Keywords: chronic rhinosinusitis; endotypes; mixed inflammation; non-type 2 inflammation; unified airway disease.

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- [62 references](#)

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Review

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. 2024 Feb 29;38(4):e23485.

doi: 10.1096/fj.202302584RR.

[Th2 cells in rapid immune responses and protective avoidance reactions](#)

[Edward J Goetzl](#)¹

Affiliations expand

- PMID: 38372961
- DOI: [10.1096/fj.202302584RR](https://doi.org/10.1096/fj.202302584RR)

Abstract

Type 2 helper cells (Th2 cells) differentiate from CD4 helper T cells under the influence of IL-4 and conventional or monocyte-derived CD11b⁺ dendritic cells. Th2 cells are capable of generating IL-4, IL-5, and IL-13, as well as evoking immunoglobulin class-switch to IgE. Three types of rapid immune responses are Th2 cell-dependent: (1) mast cell-IgE mediated allergic reactions, (2) Th2 cell-derived cytokine-mediated reactions that complement allergic reactions and protect the host from toxins, xenobiotics, environmental irritants, and helminthic parasites, and (3) IgE-stimulated mast cell-derived cysteinyl-leukotriene mediated avoidance of toxins. The contributions of Th2 cell-derived cytokines to eosinophilia (IL-5), IgE class-switch, and epithelial barrier activation, mucous secretion, and metaplasia (IL-4 and IL-13) in asthma, allergic rhinitis with polyps and atopic dermatitis have led to anti-cytokine monoclonal antibody treatments. Anti-IL-5 neutralizing monoclonal antibody in asthma and anti-IL-4/IL-13 receptor neutralizing monoclonal antibody in asthma and atopic dermatitis are proven successful therapies in appropriately selected patients who are not sufficiently improved by conventional treatments.

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- [17 references](#)

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Sleep Breath

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. 2024 Feb 28.

doi: 10.1007/s11325-024-03011-6. Online ahead of print.

Allergic rhinitis as a predictor of moderate-to-severe paediatric obstructive sleep apnoea

Bo Yang^{#1}, Qiyuan Zou^{#2}, Fan Wang², Ying Pang², Ping Wei², Yuhan Xing^{3,4,5}

Affiliations expand

- PMID: 38418766
- DOI: [10.1007/s11325-024-03011-6](https://doi.org/10.1007/s11325-024-03011-6)

Abstract

Purpose: Obstructive sleep apnoea (OSA) is a common sleep-related breathing disorder affecting children. This study aims to characterize factors associated with the development and progression of severe forms of paediatric OSA.

Methods: This study included children admitted to Children's Hospital of Chongqing Medical University, a tertiary children's hospital in southwest China between January 2020 and December 2020 with a discharge diagnosis of OSA. Each patient underwent polysomnography examination, following assessments of apnoea-hypopnea index (AHI) and lowest oxygen saturation (LSaO₂) by standardized techniques. Demographic and clinical information was collected from the hospital's electronic medical records. Associations between OSA severity and various factors were first examined in a univariate logistic model, with subsequent multivariate analysis to further identify independent risk factors.

Results: A total of 263 children were identified during the study period. Among patients presenting with OSA, 51.3% had mild and 48.7% had moderate to severe symptoms according to standardized guidelines. The incidence of mild and moderate to severe hypoxemia in our population was 39.2% and 60.8%, respectively. Allergic rhinitis (AR; adjusted odds ratio (aOR) = 1.75, 95% CI 1.03-2.96) and male gender (aOR = 1.77, 95% CI 1.03-3.06) were significantly associated with moderate-to-severe OSA (all P-values < 0.05) after adjustment for covariates. AR was also the only significant predictor of hypoxemia (P < 0.05).

Conclusion: Our results suggest that male gender and presence of AR may be associated with an increased likelihood of moderate-to-severe OSA in children. These findings underscore the importance of timely intervention and individualized management for at-risk individuals.

Keywords: Allergic rhinitis; Children; Obstructive sleep apnoea; Risk factor.

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- [33 references](#)

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Minerva Med

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. 2024 Feb 28.

doi: 10.23736/S0026-4806.24.09214-0. Online ahead of print.

[Budesonide aqueous nasal spray: an updated reappraisal in rhinitis management](#)

[Giorgio Ciprandi](#)¹

Affiliations expand

- PMID: 38414250

- DOI: [10.23736/S0026-4806.24.09214-0](https://doi.org/10.23736/S0026-4806.24.09214-0)

Abstract

Allergic rhinitis (AR) and nonallergic rhinitis are prevalent diseases. In western countries, type 2 inflammation usually characterizes these medical conditions and mainly sustains nasal obstruction. Budesonide aqueous nasal spray (BANS) is an intranasal corticosteroid (INCS) that has been available since the early 1980s. BANS is indicated for treating allergic rhinitis, nonallergic rhinitis, and nasal polyps (both as treatment and prevention after surgery). Consolidated evidence confirms its efficacy in treating seasonal and perennial AR, and nonallergic rhinitis. In addition, BANS is safe with negligible local and systemic side effects. Recent guidelines for patients with AR recommend using INCS as the first line in many situations. In particular, patients may assess the perception of symptoms' severity using the Visual Analog Scale. A score $\geq 5/10$ means uncontrolled symptoms and requires adequate treatment. BANS could appropriately be used in patients with uncontrolled symptoms and/or moderate/severe nasal obstruction. In conclusion, BANS represents a valuable option in managing patients with type 2 inflammation of the nose.

FULL TEXT LINKS



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17

Ann Otol Rhinol Laryngol

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. 2024 Feb 27:34894241234593.

doi: 10.1177/00034894241234593. Online ahead of print.

[Comparison of Allergen Immunotherapy Alone and in Conjunction With Turbinate Surgery for](#)

Nasal Obstruction in Perennial Allergic Rhinitis Patients

[Amaris Xin Jie Chong](#)^{1,2}, [Raquel Alvarado](#)¹, [Janet Rimmer](#)^{1,3,4}, [Raewyn G Campbell](#)^{1,5}, [Larry Kalish](#)^{1,6,7}, [Lu Hui Png](#)^{1,8,9}, [Richard J Harvey](#)^{1,8}

Affiliations expand

- PMID: 38414187
- DOI: [10.1177/00034894241234593](https://doi.org/10.1177/00034894241234593)

Abstract

Background: Nasal obstruction, triggered by allergic rhinitis, often does not resolve with allergen-specific immunotherapy (AIT) alone, thus inferior turbinate reduction surgery (ITR) may be required. This study aims to investigate the impact of combined treatment on nasal obstruction, as evidence is currently limited.

Methodology/principal: A retrospective cohort study of perennial allergic rhinitis patients experiencing nasal obstruction and undergoing ≥ 12 months AIT was conducted. Two groups were derived, those undergoing AIT-with or without an ITR. Patient reported nasal obstruction (evaluated with questionnaires) and nasal airway function (Nasal Peak Inspiratory Flow [NPIF] and Nasal Airflow Resistance [NAR]) were monitored. The change from baseline to 12 months post-treatment in each group were compared.

Results: A total of 118 patients (33.71 ± 14.43 years, 41.5% female) were recruited, 72% had AIT and 28% AIT&ITR. At baseline, the AIT&ITR group had a higher level of nasal obstruction (>moderate%; 63.6% vs 52.9%, $P = .048$). Post treatment, AIT&ITR group reported greater reduction in nasal obstruction (>1 category change: 75.8% vs 48.2%, $P = .002$). Similarly, the AIT&ITR group had greater improvement in nasal function by NPIF (-13.9 ± 110.3 L/minute vs -3.4 ± 78.1 L/minute, $P = .049$) and NAR (-0.120 ± 0.342 Pa/cm³/second vs -0.093 ± 0.224 Pa/cm³/second, $P = .050$).

Conclusions: Allergic rhinitis patients, with moderate to severe nasal obstruction, who undergo combined AIT&ITR have greater relief of nasal obstruction and improved airflow analysis compared to AIT alone.

Keywords: airway analysis; allergen immunotherapy; allergic rhinitis; nasal obstruction; patient reported outcomes; turbinate surgery.

Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Richard J Harvey is a consultant/advisory board with Medtronic, Novartis, GSK and Meda pharmaceuticals and received research grant funding from Glaxo-Smith-Kline. He has been on the speakers' bureau for Glaxo-Smith-Kline, Astra-zeneca, Meda Pharmaceuticals, and Seqirus. Both Richard J Harvey and Raquel Alvarado have affiliations to the School of Clinical Medicine, St Vincent's Healthcare Clinical Campus, Faculty of Medicine and Health, UNSW Sydney, Australia. Janet Rimmer has honoraria with Sanofi Aventis, Novartis, Mundipharma, BioCSL, Stallergenes. Raewyn Campbell has honoraria with Medtronic, Seqirus, Viartis, and Novartis steering committee. Larry Kalish is on the speakers' bureau for Care Pharmaceuticals, Mylan, and Seqirus Pharmaceuticals.

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Cite

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18

Inflamm Bowel Dis

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. 2024 Feb 27:izae027.

doi: 10.1093/ibd/izae027. Online ahead of print.

[Comorbidity Between Inflammatory Bowel Disease and Asthma and Allergic Diseases: A Genetically Informed Study](#)

[Tong Gong](#)¹, [Bronwyn K Brew](#)^{1,2}, [Cecilia Lundholm](#)¹, [Awad I Smew](#)¹, [Arvid Harder](#)¹, [Ralf Kuja-Halkola](#)¹, [Jonas F Ludvigsson](#)^{1,3}, [Yi Lu](#)¹, [Catarina Almqvist](#)^{1,4}

Affiliations expand

- PMID: 38412344

- DOI: [10.1093/ibd/izae027](https://doi.org/10.1093/ibd/izae027)

Abstract

Background: Little is known about shared origins between inflammatory bowel disease (IBD) and allergic diseases (asthma, allergic rhinitis, and eczema). We aimed to expand current knowledge on the etiological sources of comorbidities between these disorders using a range of genetically informed methods.

Methods: Within-individual and familial co-aggregation analysis was applied to 2 873 445 individuals born in Sweden from 1987 to 2014 and their first- and second-degree relatives. Quantitative genetic modeling was applied to 38 723 twin pairs to decompose the genetic and environmental sources for comorbidity. Polygenic risk score analysis between IBD and allergic diseases was conducted in 48 186 genotyped twins, and linkage disequilibrium score regression was applied using publicly available data to explore the genetic overlap.

Results: IBD was associated with asthma (adjusted odds ratio [aOR], 1.35; 95% confidence interval [CI], 1.30 to 1.40), allergic rhinitis (aOR, 1.27; 95% CI, 1.20 to 1.34), and eczema (aOR, 1.47; 95% CI, 1.38 to 1.56), with similar estimates for ulcerative colitis or Crohn's disease. The ORs for familial co-aggregation decreased with decreasing genetic relatedness. Quantitative genetic modeling revealed little evidence of common genetic factors between IBD and allergic diseases (eg, IBD and allergic rhinitis; genetic correlation $r_g = 0.06$; 95% CI, -0.03 to 0.15) but did reveal some evidence of unique environmental factors between IBD and eczema ($r_e = 0.16$; 95% CI, 0.00 to 0.32). Molecular genetic analyses were similarly null for IBD and allergic diseases, except for a slight association between Crohn's disease polygenic risk score and eczema (OR, 1.09; 95% CI, 1.06 to 1.12).

Conclusions: We found little evidence to support a shared origin between IBD and any allergic disease but weak evidence for shared genetic and unique environmental components for IBD and eczema.

Keywords: Crohn's disease; allergic rhinitis; asthma; eczema; familial co-aggregation; genetic correlation; ulcerative colitis.

Plain language summary

Comorbidities between inflammatory bowel disease (IBD) with asthma and allergic diseases have been documented, but shared origin remains unknown. Using multiple genetically informed approaches, we found little evidence of a shared origin explaining the comorbidities of IBD with asthma and allergic rhinitis but weak evidence for IBD and eczema.

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Review

Int Arch Allergy Immunol

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. 2024 Feb 26:1-16.

doi: 10.1159/000536335. Online ahead of print.

[The Role of Regulatory T Cells in Allergic Diseases: Collegium Internationale Allergologicum \(CIA\) Update 2024](#)

[Leticia Martín-Cruz](#)^{1,2}, [Cristina Benito-Villalvilla](#)^{1,3}, [Sofía Sirvent](#)¹, [Alba Angelina](#)¹, [Oscar Palomares](#)¹

Affiliations [expand](#)

- PMID: 38408438

- DOI: [10.1159/000536335](https://doi.org/10.1159/000536335)

Abstract

Background: Allergy represents a major health problem of increasing prevalence worldwide with a high socioeconomic impact. Our knowledge on the molecular mechanisms underlying allergic diseases and their treatments has significantly improved over the last years. The generation of allergen-specific regulatory T cells (Tregs) is crucial in the induction of healthy immune responses to allergens, preventing the development and worsening of allergic diseases.

Summary: In the last decades, intensive research has focused on the study of the molecular mechanisms involved in Treg development and Treg-mediated suppression. These mechanisms are essential for the induction of sustained tolerance by allergen-specific immunotherapy (AIT) after treatment discontinuation. Compelling experimental evidence demonstrated altered suppressive capacity of Tregs in patients suffering from allergic rhinitis, allergic asthma, food allergy, or atopic dermatitis, as well as the restoration of their numbers and functionality after successful AIT.

Key message: The better understanding of the molecular mechanisms involved in Treg generation during allergen tolerance induction might well contribute to the development of novel strategies for the prevention and treatment of allergic diseases.

Keywords: Allergen-specific immunotherapy; Allergic asthma; Allergic rhinitis; Atopic dermatitis; Food allergy; Regulatory T cells.

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Minerva Pediatr (Torino)



. 2024 Feb 26.

doi: 10.23736/S2724-5276.24.07538-4. Online ahead of print.

The updated role of budesonide in managing children and adolescents with allergic rhinitis

[Giorgio Ciprandi](#)¹

Affiliations expand

- PMID: 38407014
- DOI: [10.23736/S2724-5276.24.07538-4](https://doi.org/10.23736/S2724-5276.24.07538-4)

Abstract

Allergic rhinitis (AR) is a prevalent disease in childhood and adolescence. A type 2 inflammation characterizes AR and, mainly, sustains nasal obstruction. Budesonide aqueous nasal spray (BANS) is an intranasal corticosteroid (INCS) available since the early 1980s. BANS is indicated for treating allergic rhinitis. There is evidence about its efficacy in treating children and adolescents with seasonal and perennial AR. In addition, BANS is safe with negligible local and systemic side effects. Recent guidelines for patients with AR recommend the use of INCS as first line in many situations. In particular, AR patients (and their parents) may assess the perception of symptoms' severity using the Visual Analog Scale (VAS). A score $\geq 5/10$ means uncontrolled symptoms and requires adequate treatment. BANS could appropriately be used in patients with uncontrolled symptoms and/or moderate/severe nasal obstruction. In conclusion, BANS represents a valuable option in managing children and adolescents with AR.

FULL TEXT LINKS



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Allergy



. 2024 Feb 25.

doi: 10.1111/all.16068. Online ahead of print.

Immune signatures predict response to house dust mite subcutaneous immunotherapy in patients with allergic rhinitis

[Nan Wang](#)^{1,2}, [Jia Song](#)^{1,2}, [Shi-Ran Sun](#)^{1,2}, [Ke-Zhang Zhu](#)^{1,2}, [Jing-Xian Li](#)^{1,2}, [Zhi-Chao Wang](#)^{1,2}, [Cui-Lian Guo](#)^{1,2}, [Wen-Xuan Xiang](#)¹, [Yun-Long Tong](#)³, [Ming Zeng](#)^{1,2}, [Heng Wang](#)^{1,2}, [Xiao-Yan Xu](#)⁴, [Yin Yao](#)^{1,2,5}, [Zheng Liu](#)^{1,2,5}

Affiliations expand

- PMID: 38403941
- DOI: [10.1111/all.16068](https://doi.org/10.1111/all.16068)

Abstract

Background: Identifying predictive biomarkers for allergen immunotherapy response is crucial for enhancing clinical efficacy. This study aims to identify such biomarkers in patients with allergic rhinitis (AR) undergoing subcutaneous immunotherapy (SCIT) for house dust mite allergy.

Methods: The Tongji (discovery) cohort comprised 72 AR patients who completed 1-year SCIT follow-up. Circulating T and B cell subsets were characterized using multiplexed flow cytometry before SCIT. Serum immunoglobulin levels and combined symptom and medication score (CSMS) were assessed before and after 12-month SCIT. Responders, exhibiting $\geq 30\%$ CSMS improvement, were identified. The random forest algorithm and logistic regression analysis were used to select biomarkers and establish predictive models

for SCIT efficacy in the Tongji cohort, which was validated in another Wisco cohort with 43 AR patients.

Results: Positive SCIT response correlated with higher baseline CSMS, allergen-specific IgE (sIgE)/total IgE (tIgE) ratio, and frequencies of Type 2 helper T cells, Type 2 follicular helper T (T_{FH2}) cells, and CD23⁺ nonswitched memory B (B_{NSM}) and switched memory B (B_{SM}) cells, as well as lower follicular regulatory T (T_{FR}) cell frequency and T_{FR}/T_{FH2} cell ratio. The random forest algorithm identified sIgE/tIgE ratio, T_{FR}/T_{FH2} cell ratio, and B_{NSM} frequency as the key biomarkers discriminating responders from nonresponders in the Tongji cohort. Logistic regression analysis confirmed the predictive value of a combination model, including sIgE/tIgE ratio, T_{FR}/T_{FH2} cell ratio, and CD23⁺ B_{SM} frequency (AUC = 0.899 in Tongji; validated AUC = 0.893 in Wisco).

Conclusions: A T- and B-cell signature combination efficiently identified SCIT responders before treatment, enabling personalized approaches for AR patients.

Keywords: allergen immunotherapy; allergic rhinitis; biomarker; immune signature; prediction.

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- [39 references](#)

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Grants and funding [expand](#)

FULL TEXT LINKS



"chronic cough"[MeSH Terms] OR chronic cough[Text Word]

[Published Erratum](#)

Respir Med

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. 2024 Mar;223:107556.

doi: 10.1016/j.rmed.2024.107556. Epub 2024 Feb 14.

Corrigendum to "Burden of chronic cough on social participation, healthcare resource utilisation and activities of daily living in the Canadian Longitudinal Study on Aging (CLSA)" [Respir. Med. 219 (2013) 107431]

[Imran Satia](#)¹, [Alexandra J Mayhew](#)², [Nazmul Sohel](#)², [Om Kurmi](#)³, [Kieran J Killian](#)⁴, [Paul M O'Byrne](#)⁵, [Parminder Raina](#)⁶

Affiliations expand

- PMID: 38354487
- DOI: [10.1016/j.rmed.2024.107556](https://doi.org/10.1016/j.rmed.2024.107556)

No abstract available

Erratum for

- [Burden of chronic cough on social participation, healthcare resource utilisation and activities of daily living in the Canadian Longitudinal Study on Aging \(CLSA\)](#). Satia I, Mayhew AJ, Sohel N, Kurmi O, Killian KJ, O'Byrne PM, Raina P. *Respir Med*. 2023 Nov-Dec;219:107431. doi: 10.1016/j.rmed.2023.107431. Epub 2023 Oct 24. PMID: 37879447

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J Healthc Inform Res

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. 2023 Sep 27;8(1):50-64.

doi: 10.1007/s41666-023-00150-5. eCollection 2024 Mar.

[Chronic Cough: Characterizing and Quantifying Burden in Adults Using a Nationwide Electronic Health Records Database](#)

[Lindsey E Scierka](#)¹, [Brooklyn A Bradley](#)^{1,2}, [Earl Glynn](#)³, [Sierra Davis](#)³, [Mark Hoffman](#)³, [Jade B Tam-Williams](#)³, [Carlos Mena-Hurtado](#)¹, [Kim G Smolderen](#)^{1,2}

Affiliations expand

- PMID: 38273985
- PMID: PMC10805682 (available on 2025-03-01)
- DOI: [10.1007/s41666-023-00150-5](https://doi.org/10.1007/s41666-023-00150-5)

Abstract

Chronic cough is a common condition; until recently, no International Classification of Diseases (ICD) code for chronic cough existed; therefore, the true scope and burden of chronic cough is unclear. Using established algorithms, we examined chronic cough patients and their risk profiles, recurrent cough episodes, and subsequent 1-year health care utilization in the nationwide Cerner EHR data resource, compared with those with acute cough. An ICD-based algorithm was applied to the Cerner Health Facts EHR

database to derive a phenotype of chronic cough defined as three ICD-based "cough" encounters 14-days apart over a 56-to-120-day period from 2015 to 2017. Demographics, comorbidities, and outcomes (1-year outpatient, emergency, and inpatient encounters) were collected for the chronic cough cohort and acute cough cohort. The chronic cough cohort was 61.5% female, 70.4% white, and 15.2% African American, with 13.7% being of Asian, Native American, or unknown race. Compared with the acute cough cohort, chronic cough patients were more likely to be older, female, and have chronic pulmonary disease, obesity, and depression. Predictors of recurrent chronic cough were older age and race. Those with chronic cough had more outpatient (2.48 ± 2.10 vs. 1.48 ± 0.99 ; SMD = 0.94), emergency (1.90 ± 2.26 vs. 1.23 ± 0.68 ; SMD = 0.82), and inpatient (1.11 ± 0.36 vs. 1.05 ± 0.24 , SMD = 0.24) encounters compared with acute cough. While EHR-based data may provide a useful resource to identify chronic cough phenotypes, supplementary data approaches and screening methods for chronic cough can further identify the scope of the problem.

Keywords: Chronic cough; Clinical encounters; Clinical phenotype; Electronic health record; International classification of diseases.

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Conflict of interest statement

Competing Interests Dr. Smolderen reports unrestricted research grants from Cardiva Medical Inc., W. L. Gore & Associates, Inc., Abbott Laboratories, Merck & Co., Inc. and Janssen Pharmaceutical Companies of Johnson & Johnson. She is a consultant for Optum Labs, Inc. and Abbott Laboratories. Dr. Williams reports research support from Boehringer Ingelheim and the American Lung Association. Dr. Mena-Hurtado reports grant funding from Shockwave Medical, Inc. and is a consultant for Abbott Laboratories, Cook Medical, Inc., and Optum Labs, Inc. All other authors report no disclosures.

- [31 references](#)

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Respir Investig



. 2024 Mar;62(2):269-276.

doi: 10.1016/j.resinv.2024.01.003. Epub 2024 Jan 23.

Relevant factors associated with the development of chronic cough after recovery from COVID-19

[Yoshihiro Kanemitsu](#)¹, [Kensuke Fukumitsu](#)², [Akio Niimi](#)³

Affiliations expand

- PMID: 38262214
- DOI: [10.1016/j.resinv.2024.01.003](https://doi.org/10.1016/j.resinv.2024.01.003)

Abstract

Background: Cough is one of the symptoms of the post-COVID-19 condition. However, the factors associated with its development remain unclear. We evaluated the factors associated with chronic cough in the post-COVID-19 condition.

Methods: In this survey, 170 individuals who previously had COVID-19 and were admitted to Aichi Hospital between October 2020 and October 2021 were included. Using self-developed questionnaires and visual analog scales, 19 symptoms, including cough, were assessed. Cough-specific quality of life (QoL), reflux-related symptoms, and abnormal laryngeal sensations were also evaluated. The patients' clinical characteristics and indices, including cough-specific QoL, at admission were extracted from their medical records. Multivariate regression analyses were conducted to determine the factors associated with cough-related outcomes, such as prevalence, QoL, and severity, in the post-COVID-19 condition.

Results: The median length (range) of the survey after recovery from COVID-19 was 158 (95-467) days. Cough was prevalent (n = 41, 24 %) and often accompanied by other

symptoms, including gastrointestinal symptoms. Cough-specific QoL after recovery was correlated with reflux-related symptoms and abnormal laryngeal sensations. Multivariate analyses revealed that gastrointestinal symptoms, sputum, and chronic cough before contracting COVID-19 are significant predictors of cough-related outcomes in the post-COVID-19 condition. Meanwhile, other indices including cough-specific QoL on the acute phase were not reliable predictors in the post-COVID-19 condition.

Conclusions: Cough during the post-COVID-19 condition had a negative impact on daily life activities. Gastrointestinal symptoms could play a significant role in the pathophysiology of cough in such a condition.

Keywords: Abnormal laryngeal sensations; Chronic cough; Gastrointestinal symptoms; Post-COVID-19 condition; Quality of life.

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Conflict of interest statement

Declaration of competing interest Yoshihiro Kanemitsu received research grants from MSD Life Science Foundation and lecture fees from GSK outside the submitted work; Akio Niimi received lecture fees from AstraZeneca, Kyorin, Novartis, GSK and Sanofi outside the submitted work; Kensuke Fukumitsu has no conflict of interest.

SUPPLEMENTARY INFO

MeSH termsexpand

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Neurogastroenterol Motil

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. 2024 Feb 29:e14775.

Proximal esophageal impedance baseline increases the yield of impedance-pH and is associated with response to PPIs in chronic cough patients

[Mentore Ribolsi](#)¹, [Nicola De Bortoli](#)², [Marzio Frazzoni](#)³, [Lorenzo Marchetti](#)¹, [Edoardo Savarino](#)⁴, [Michele Cicala](#)¹

Affiliations expand

- PMID: 38424679
- DOI: [10.1111/nmo.14775](https://doi.org/10.1111/nmo.14775)

Abstract

Background: Chronic cough significantly impairs the quality of life. Although various studies focused on MNBI as assessed in the distal esophagus, scarce data are available on the clinical value of proximal measurements.

Aim: To investigate the role of proximal MNBI in the workup of patients with chronic cough and its ability to predict PPI response.

Methods: Demographic, clinical, endoscopy findings, impedance-pH and HRM tracings from consecutive cough patients were evaluated. MNBI was calculated at proximal and distal esophagus.

Results: One hundred and sixty four patients were included. In addition to traditional variables, when considering also the PSPW index or MNBI at 3 cm or 15 cm, the proportion of patients with pathological impedance-pH monitoring significantly increased. 70/164 patients were responders, while 94 (57.3%) were non-responder to double PPI dose ($p < 0.05$). Patients with pathologic MNBI at 3 cm and/or 15 cm as well as those with pathologic PSPW index were characterized by a significantly higher proportion of responders than that observed among patients with normal impedance-pH variables ($p < 0.001$). The proportion of responders with pathological MNBI at 15 cm was significantly higher than the proportion of responders with pathological MNBI at 3 cm (82.8% vs. 64.3%, $p < 0.05$). At multivariable model, pathological MNBI at both 3 cm and 15 cm as well as PSPW index

were associated with PPI responsiveness. The strongest association with PPI response was observed for MNBI at 15 cm.

Conclusions: The assessment of MNBI at proximal esophagus increases the diagnostic yield of impedance-pH monitoring and may represent a useful predictor of PPI responsiveness in the cumbersome clinical setting of suspected reflux-related cough.

Keywords: GERD; MNBI; PPI; PSPW; impedance-pH.

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- [37 references](#)

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Respir Med

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. 2024 Feb 28:107582.

doi: 10.1016/j.rmed.2024.107582. Online ahead of print.

[Validity and reliability of the Swedish version of the Leicester Cough Questionnaire in unexplained chronic cough](#)

[Ewa Ternesten Hasséus](#)¹, [Ewa-Lena Johansson](#)²

Affiliations expand

- PMID: 38428509

- DOI: [10.1016/j.rmed.2024.107582](https://doi.org/10.1016/j.rmed.2024.107582)

Abstract

Background: Cough is considered chronic when it lasts for >8 weeks. When no medical explanation can be found it is often called unexplained chronic cough (UCC), which may affect health-related quality of life (HRQOL). This study aimed to assess the validity and reliability of the Swedish version of the Leicester Cough Questionnaire (LCQ-S) in patients with UCC.

Methods: Seventy-six consecutively selected patients with UCC replied to: a local questionnaire; the LCQ-S; a Visual Analog Scale (VAS) for cough; the Swedish version of the Hull Airway Reflux Questionnaire (HARQ-S); and the Chemical Sensitivity Scale for Sensory Hyperreactivity (CSS-SHR). To evaluate the reproducibility of the LCQ-S, the VAS and LCQ-S were answered again after two to four weeks.

Results: Seventy-four patients (17 men) answered the questionnaires at baseline. Concurrent validity for LCQ-S was regarded as moderate with the VAS for cough and HARQ-S. Internal consistency using Cronbach's alpha was high for the LCQ-S total score (0.92) and satisfactory for the LCQ-S domains (0.78-0.83). Reliability and reproducibility were analysed in 57 patients (14 men). Intra-class correlation for the LCQ-S total score and domains showed strong reliability (≥ 0.92), without any significant differences over time. The standard error of measurement and the smallest real difference were 1.26 and 3.48, respectively. The Bland-Altman plot showed no systematic change in the mean values.

Conclusions: The LCQ-S has good validity and reliability and can be used in clinical settings to evaluate HRQOL in Swedish-speaking adult patients with UCC.

Keywords: Chronic cough; Health-related quality of life questionnaire; Patient-reported outcome; Unexplained chronic cough.

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Conflict of interest statement

Declaration of competing interest There is no conflict of interest. Kindly proceed.

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6

Lung



. 2024 Feb 27.

doi: 10.1007/s00408-024-00674-6. Online ahead of print.

Characterization of Codeine Treatment Responders Among Patients with Refractory or Unexplained Chronic Cough: A Prospective Real-World Cohort Study

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Collaborators, Affiliations expand

- PMID: 38411774
- DOI: [10.1007/s00408-024-00674-6](https://doi.org/10.1007/s00408-024-00674-6)

Abstract

Purpose: Codeine is a narcotic antitussive often considered for managing patients with refractory or unexplained chronic cough. This study aimed to evaluate the proportion and characteristics of patients who responded to codeine treatment in real-world practice.

Methods: Data from the Korean Chronic Cough Registry, a multicenter prospective cohort study, were analyzed. Physicians assessed the response to codeine based on the timing

and degree of improvement after treatment initiation. Follow-up assessments included the Leicester Cough Questionnaire and cough severity visual analog scale at six months. In a subset of subjects, objective cough frequency was evaluated following the initiation of codeine treatment.

Results: Of 305 patients, 124 (40.7%) responded to treatments based on anatomic diagnostic protocols, while 181 (59.3%) remained unexplained or refractory to etiological treatments. Fifty-one subjects (16.7%) were classified as codeine treatment responders (those showing a rapid and clear response), 57 (18.7%) as partial responders, and 62 (20.3%) as non-responders. Codeine responders showed rapid improvement in objective cough frequency and severity scores within a week of the treatment. At 6 months, responders showed significantly improved scores in cough scores, compared to non-responders. Several baseline parameters were associated with a more favorable treatment response, including older age, non-productive cough, and the absence of heartburn.

Conclusions: Approximately 60% of chronic cough patients in specialist clinics may require antitussive drugs. While codeine benefits some, only a limited proportion (about 20%) of patients may experience rapid and significant improvement. This underscores the urgent need for new antitussive drugs to address these unmet clinical needs.

Keywords: Codeine; Cough; Real-world study; Treatment responders.

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Respirology

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. 2024 Feb 27.

doi: 10.1111/resp.14686. Online ahead of print.

Chronic cough: New guidelines, new approaches and new treatments

[Richard Turner](#)^{1,2}, [Stuart Mazzone](#)³, [Surinder Birring](#)⁴

Affiliations expand

- PMID: 38410044
- DOI: [10.1111/resp.14686](https://doi.org/10.1111/resp.14686)

No abstract available

Keywords: chronic cough; cough.

- [17 references](#)

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BMJ Open Respir Res

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. 2024 Feb 26;11(1):e001704.

doi: 10.1136/bmjresp-2023-001704.

Clinical utility of elective paediatric flexible bronchoscopy and impact on

the quality of life: protocol for a single-centre, single-blind, randomised controlled trial

[Rahul Thomas](#)^{1,2}, [Julie M Marchant](#)^{2,3}, [Vikas Goyal](#)^{2,4}, [Ian Brent Masters](#)^{2,4}, [Stephanie T Yerkovich](#)^{2,5}, [Anne B Chang](#)^{6,5}

Affiliations expand

- PMID: 38413121
- PMCID: [PMC10900573](#)
- DOI: [10.1136/bmjresp-2023-001704](#)

Free PMC article

Abstract

Introduction: Elective flexible bronchoscopy (FB) is now widely available and standard practice for a variety of indications in children with respiratory conditions. However, there are no randomised controlled trials (RCTs) that have examined its benefits (or otherwise). Our primary aim is to determine the impact of FB on the parent-proxy quality-of-life (QoL) scores. Our secondary aims are to determine if undertaking FB leads to (a) change in management and (b) improvement of other relevant patient-reported outcome measures (PROMs). We also quantified the benefits of elective FB (using 10-point Likert scale). We hypothesised that undertaking elective FB will contribute to accurate diagnosis and therefore appropriate treatment, which will in turn improve QoL and will be deemed to be beneficial from patient and doctor perspectives.

Methods and analysis: Our parallel single-centre, single-blind RCT (commenced in May 2020) has a planned sample size of 114 children (aged <18 years) recruited from respiratory clinics at Queensland Children's Hospital, Brisbane, Australia. Children are randomised (1:1 concealed allocation) within two strata: age (≤ 2 vs > 2 years) and indication for FB (chronic cough vs other indications) to either (a) early arm (intervention where FB undertaken within 2 weeks) or (b) delayed (control, FB undertaken at usual wait time). Our primary outcome is the difference between groups in their change in QoL at the T2 timepoint when the intervention group has had the FB and the control group has not. Our secondary outcomes are change in management, change in PROMs, adverse events and the Likert scales.

Ethics and dissemination: The human research ethics committee of the Queensland Children's Hospital granted ethical clearance (HREC/20/QCHQ/62394). Our RCT is conducted in accordance with Good Clinical Practice and the Australian legislation. Results will be disseminated through conference presentations, teaching avenues, workshops, websites and publications.

Registration: Australia New Zealand Clinical Trial Registry ACTRN12620000610932.

Keywords: Bronchoscopy; Paediatric Physician.

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Conflict of interest statement

Competing interests: None declared.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS



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

1
Physiother Theory Pract

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. 2024 Mar 3;40(3):505-515.

doi: 10.1080/09593985.2022.2126741. Epub 2022 Sep 20.

Patient perspectives of airway clearance techniques in bronchiectasis

[Lisa J Franks](#)^{1,2}, [James R Walsh](#)^{1,2,3}, [Kathleen Hall](#)^{1,4}, [Julie A Adsett](#)⁵, [Norman R Morris](#)^{2,3,6}

Affiliations expand

- PMID: 36124537
- DOI: [10.1080/09593985.2022.2126741](https://doi.org/10.1080/09593985.2022.2126741)

Abstract

Introduction: While airway clearance techniques (ACTs) are recommended for individuals with bronchiectasis, data suggests the use of and adherence to ACTs is poor.

Objective: This study aimed to identify patient perceptions regarding ACTs, the barriers and facilitators to ACTs, and factors affecting adherence.

Methods: A multi-center qualitative study using in-depth semi-structured interviews of individuals with bronchiectasis was undertaken. All interviews were audio recorded and transcribed verbatim. Data was analyzed using the thematic framework approach described by Braun and Clark. NVIVO™ 12 software assisted with coding and thematic analysis of the interview transcripts. Data saturation was achieved when no new common themes were identified. Findings were summarized into major conceptual themes. Participant demographic data was also obtained.

Results: Twenty-four participants participated in semi-structured interviews. The main facilitators to using ACTs included a perceived health and quality of life benefit, a tailored approach to ACTs and the use of self-management strategies. Main barriers included lack of time and motivation, lack of access to resources, and a lack of perceived health benefit. A number of factors were identified by participants that may help promote adherence including combining and trialing different ACTs, receiving regular ACT reviews and education from physiotherapists, and having good social support.

Conclusion: To assist the personalized prescription of ACTs, these facilitators and barriers should be considered by clinicians to help promote adherence and improve patient outcomes.

Keywords: Airway clearance techniques; adherence; barriers; facilitators; patient perspectives.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Mycoses

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. 2024 Mar;67(3):e13711.

doi: 10.1111/myc.13711.

[Incidence and prevalence of chronic pulmonary aspergillosis in patients with post-tuberculosis lung abnormality: Results from a community survey in North India](#)

[Kathirvel Soundappan](#)¹, [Inderpaul Singh Sehgal](#)², [Nidhi Prabhakar](#)³, [Samriti Rana](#)², [Rajesh Raju](#)⁴, [Sahajal Dhooria](#)², [Kuruswamy Thurai Prasad](#)², [Valliappan Muthu](#)², [Shivaprakash M Rudramurthy](#)⁵, [Arunaloke Chakrabarti](#)⁶, [Mandeep Garg](#)³, [Ritesh Agarwal](#)²

Affiliations expand

- PMID: 38414309
- DOI: [10.1111/myc.13711](https://doi.org/10.1111/myc.13711)

Abstract

Background: Post-tuberculosis lung abnormality (PTLA) is the most common risk factor for developing chronic pulmonary aspergillosis (CPA). However, the prevalence and incidence of CPA in PTLA patients in India remain unknown.

Objectives: We aimed to ascertain the incidence and prevalence of CPA in subjects with PTLA.

Methods: We identified a cohort of pulmonary tuberculosis who completed anti-tuberculosis therapy (ATT) before November 2019 from the records of the 12 tuberculosis treatment centers attached to the national program. We recorded the clinical and demographic details. We performed computed tomography (CT) of the chest and estimated serum *A. fumigatus*-specific IgG. We categorised subjects as PTLA with or without CPA using a composite of clinical, radiological, and microbiological features. We resurveyed the subjects at 6 months (or earlier) for the presence of new symptoms. We calculated the prevalence and the incidence rate (per 100-person years) of CPA.

Results: We included 117 subjects with PTLA, with a median of 3 years after ATT completion. Eleven subjects had CPA in the initial survey, and one additional case developed CPA during the second survey. The prevalence of CPA in PTLA subjects was 10.3% (12/117). The total observation period was 286.7 person-years. The median (interquartile range) time to develop CPA after ATT completion was 12.5 (5-36.7) months. We found the CPA incidence rate (95% confidence interval) of 4.2 (1.8-6.5) per 100-person years.

Conclusion: Chronic pulmonary aspergillosis complicates 10% of PTLA subjects after successful outcomes with ATT. Four new CPA cases may develop per 100-persons years of observation after ATT completion. We suggest screening patients with PTLA who develop new symptoms for CPA.

Keywords: CFPAs; aspergilloma; bronchiectasis; chronic cavitary pulmonary aspergillosis; post-TB lung disease.

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- [22 references](#)

SUPPLEMENTARY INFO

MeSH terms, Grants and funding expand

FULL TEXT LINKS



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EClinicalMedicine



. 2024 Feb 17:69:102500.

doi: 10.1016/j.eclinm.2024.102500. eCollection 2024 Mar.

[Long-term risks of respiratory diseases in patients infected with SARS-CoV-2: a longitudinal, population-based cohort study](#)

[Meijun Meng](#)^{1,2,3}, [Rui Wei](#)², [YanJun Wu](#)^{2,3}, [Ruijie Zeng](#)^{2,4}, [Dongling Luo](#)¹, [Yuying Ma](#)^{2,3}, [Lijun Zhang](#)^{2,5}, [Wentao Huang](#)^{2,3}, [Hanshi Zeng](#)⁶, [Felix W Leung](#)^{7,8}, [Xinqi Qiu](#)⁹, [Weihong Sha](#)^{1,2,3,4,5}, [Hao Chen](#)^{1,2,3,4,5}

Affiliations expand

- PMID: 38389713
- PMCID: [PMC10882104](#)
- DOI: [10.1016/j.eclinm.2024.102500](#)

Free PMC article

Abstract

Background: In the post-pandemic era, growing apprehension exists regarding the potential sequelae of COVID-19. However, the risks of respiratory diseases following SARS-

CoV-2 infection have not been comprehensively understood. This study aimed to investigate whether COVID-19 increases the long-term risk of respiratory illness in patients with COVID-19.

Methods: In this longitudinal, population-based cohort study, we built three distinct cohorts age 37-73 years using the UK Biobank database; a COVID-19 group diagnosed in medical records between January 30th, 2020 and October 30th, 2022, and two control groups, a contemporary control group and a historical control group, with cutoff dates of October 30th, 2022 and October 30th, 2019, respectively. The follow-up period of all three groups was 2.7 years (the median (IQR) follow-up time was 0.8 years). Respiratory outcomes diagnosed in medical records included common chronic pulmonary diseases (asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), pulmonary vascular disease (PVD), and lung cancer. For the data analysis, we calculated hazard ratios (HRs) along with their 95% CIs using Cox regression models, following the application of inverse probability weights (IPTW).

Findings: A total of 3 cohorts were included in this study; 112,311 individuals in the COVID-19 group with a mean age (\pm SDs) of 56.2 (8.1) years, 359,671 in the contemporary control group, and 370,979 in the historical control group. Compared with the contemporary control group, those infected with SARS-CoV-2 exhibited elevated risks for developing respiratory diseases. This includes asthma, with a HR of 1.49 and a 95% CI 1.28-1.74; bronchiectasis (1.30; 1.06-1.61); COPD (1.59; 1.41-1.81); ILD (1.81; 1.38-2.21); PVD (1.59; 1.39-1.82); and lung cancer (1.39; 1.13-1.71). With the severity of the acute phase of COVID-19, the risk of pre-described respiratory outcomes increases progressively. Besides, during the 24-months follow-up, we observed an increasing trend in the risks of asthma and bronchiectasis over time. Additionally, the HR of lung cancer for 0-6 month follow-up was 3.07 (CI 1.73-5.44), and the association of lung cancer with COVID-19 disease disappeared at 6-12 month follow-up (1.06; 0.43-2.64) and at 12-24 months (1.02; 0.45-2.34). Compared to those with one SARS-CoV-2 infection, reinfected patients were at a higher risk of asthma (3.0; 1.32-6.84), COPD (3.07; 1.42-6.65), ILD (3.61; 1.11-11.8), and lung cancer (3.20; 1.59-6.45). Similar findings were noted when comparing with a historical cohort serving as a control group, including asthma (1.31; 1.13-1.52); bronchiectasis (1.53; 1.23-1.89); COPD (1.41; 1.24-1.59); ILD (2.53; 2.05-3.13); PVD (2.30; 1.98-2.66); and lung cancer (2.23; 1.78-2.79).

Interpretation: Our research suggests that patients with COVID-19 may have an increased risk of developing respiratory diseases, and the risk increases with the severity of infection and reinfection. Even during the 24-month follow-up, the risk of asthma and bronchiectasis continued to increase. Hence, implementing appropriate follow-up strategies for these individuals is crucial to monitor and manage potential long-term respiratory health issues. Additionally, the increased risk in lung cancer in the COVID-19 individuals was probably due to the diagnostic tests conducted and incidental diagnoses.

Funding: The National Natural Science Foundation of China of China Regional Innovation and Development Joint Foundation; National Natural Science Foundation of China;

Program for High-level Foreign Expert Introduction of China; Natural Science Foundation for Distinguished Young Scholars of Guangdong Province; Guangdong Basic and Applied Basic Research Foundation; Climbing Program of Introduced Talents and High-level Hospital Construction Project of Guangdong Provincial People's Hospital; VA Clinical Merit and ASGE clinical research funds.

Keywords: COVID-19 (coronavirus disease 2019); Epidemiological study; Respiratory diseases; SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).

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Conflict of interest statement

All authors declare no competing interests.

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

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Respir Med

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. 2024 Mar;223:107555.

doi: 10.1016/j.rmed.2024.107555. Epub 2024 Feb 1.

Severity of bronchiectasis predicts use of and adherence to high frequency chest wall oscillation therapy - Analysis

from the United States Bronchiectasis and NTM research registry

[Ashwin Basavaraj](#)¹, [Radmila Choate](#)², [Brian C Becker](#)³, [Timothy R Aksamit](#)⁴, [Mark L Metersky](#)⁵; [Bronchiectasis and NTM Research Registry Investigators](#)

Affiliations expand

- PMID: 38307319
- DOI: [10.1016/j.rmed.2024.107555](https://doi.org/10.1016/j.rmed.2024.107555)

Abstract

Background: High frequency chest wall oscillation (HFCWO) is a form of airway clearance therapy that has been available since the mid-1990s and is routinely used by patients suffering from retained pulmonary secretions. Patients with cystic fibrosis (CF), neuromuscular disease (NMD), and other disorders, including bronchiectasis (BE) and COPD (without BE), are commonly prescribed this therapy. Limited evidence exists describing HFCWO use in the BE population, its impact on long-term management of disease, and the specific patient populations most likely to benefit from this therapy. This study sought to characterize the clinical characteristics of patients with BE who have documented use of HFCWO at baseline and 1-year follow-up.

Methods: An analysis from a large national database registry of patients with BE was performed. Demographic and clinical characteristics of all patients receiving HFCWO therapy at baseline are reported. Patients were stratified into two groups based on continued or discontinued use of HFCWO therapy at 1-year follow-up.

Results: Over half (54.8 %) of patients who reported using HFCWO therapy had a Modified Bronchiectasis Severity Index (m-BSI) classified as severe, and the majority (81.4 %) experienced an exacerbation in the prior two years. Of patients with 1-year follow-up data, 73 % reported continued use of HFCWO. Compared to patients who discontinued therapy, these patients were more severe at baseline and at follow-up suggesting that patients with more severe disease are more likely to continue HFCWO therapy.

Conclusions: Patients who have more severe disease and continue to experience exacerbations and hospitalizations are more likely to continue HFCWO therapy.

Clinical trial registration: NA.

Keywords: Airway clearance therapy; Bronchiectasis; HFCWO.

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: Ashwin Basavaraj reports writing assistance was provided by LeeAnn Phipps. AB - Consultant and Advisory Board for Baxter, Insmad, Physio-Assist, Dymedso, Zambon. Medical education consulting for Tactile Medical. Principal investigator on clinical trial sponsored by Baxter with funding to institution. Educational grant funding received from Insmad to institution. RC - No disclosures to report. BB - Employee relationship with Baxter. MM - Grant funding from Insmad and COPD foundation. Consulting fees from Insmad, Boehringer-Ingelheim, and Tactile Medical. Payment/honoraria for presentations/lectures from Insmad. Participation on data safety monitoring/advisory board for AN2, Renovion. TA - Support as medical director of the Bronchiectasis and NTM research registry. Has participated in clinical trials sponsored by Bayer, Aradigm, Zambon.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS



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Respirology

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. 2024 Mar;29(3):209-216.

doi: 10.1111/resp.14664. Epub 2024 Jan 30.

[Increased exacerbations of bronchiectasis following recovery from](#)

mild COVID-19 in patients with non-cystic fibrosis bronchiectasis

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- DOI: [10.1111/resp.14664](https://doi.org/10.1111/resp.14664)

Free article

Abstract

Background and objective: Respiratory viral infection is a common trigger of bronchiectasis exacerbation. Knowledge of the intermediate to long-term effect of COVID-19 on bronchiectasis is poor.

Methods: A retrospective cohort study of patient records was conducted to assess the frequency of bronchiectasis exacerbation following recovery from mild-to-moderate COVID-19. The exacerbation frequency at baseline, using 2019 and 2019-2021 data, was compared with that during the 1 year following recovery.

Results: A total of 234 adult patient records who had a confirmed diagnosis of bronchiectasis were identified, of whom 52 (22.2%) were classified as the COVID-19 group. Patients with COVID-19 had significantly more frequent annual exacerbations of bronchiectasis (total exacerbations and hospitalizations). Compared with 2019-2021 data, the total exacerbation frequency decreased by 0.1 ± 0.51 per year among non-COVID-19 patients but increased by 0.68 ± 1.09 per year among the COVID-19 group ($p < 0.001$). Compared with 2019 only data, exacerbation frequency decreased by 0.14 ± 0.79 per year among non-COVID-19 patients but increased by 0.76 ± 1.17 per year in the COVID-19 group, $p < 0.001$. The annual frequency of hospitalization for bronchiectasis increased by 0.01 ± 0.32 per year among non-COVID-19 patients and increased by 0.39 ± 1.06 per year in the COVID-19 group ($p < 0.001$) compared with 2019 to 2021 data. When compared with only 2019 data, it remained unchanged at 0 ± 0.43 per year among non-COVID-19 patients but increased to 0.38 ± 1.12 per year among COVID-19 patients ($p < 0.001$).

Conclusion: Mild-to-moderate COVID-19 was associated with an increase in frequency of bronchiectasis exacerbation and frequency of hospitalizations following recovery.

Keywords: COVID-19; bronchiectasis control; bronchiectasis exacerbation; coronavirus disease.

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Ann Am Thorac Soc

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. 2024 Mar;21(3):393-401.

doi: 10.1513/AnnalsATS.202302-133OC.

Quality-of-Life Bronchiectasis Respiratory Symptom Scale Predicts the Risk of Exacerbations in Adults with Bronchiectasis: A Prospective Observational Study

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Abstract

Rationale: The relationship between symptoms, measured using a validated disease-specific questionnaire, and longitudinal exacerbation risk has not been demonstrated in bronchiectasis. **Objectives:** The aim of this study is to investigate whether baseline symptoms, assessed using the Quality-of-Life Bronchiectasis Respiratory Symptom Scale (QoL-B-RSS) and its individual component scores, could predict future exacerbation risk in patients with bronchiectasis. **Methods:** The study included 436 adults with bronchiectasis from three tertiary hospitals. Symptoms were measured using the QoL-B-RSS, with scores ranging from 0 to 100, where lower scores indicated more severe symptoms. We examined whether symptoms as continuous measures were associated with the risk of exacerbation over 12 months. The analysis was also repeated for individual components of the QoL-B-RSS score. **Results:** The baseline QoL-B-RSS score was associated with an increased risk of exacerbations (rate ratio, 1.25 for each 10-point decrease; 95% confidence interval [CI], 1.15-1.35; $P < 0.001$), hospitalizations (rate ratio, 1.24; 95% CI, 1.05-1.43; $P = 0.02$), and reduced time to the first exacerbation (hazard ratio, 1.12; 95% CI, 1.03-1.21; $P = 0.01$) over 12 months, even after adjusting for relevant confounders, including exacerbation history. The QoL-B-RSS score was comparable to exacerbation history in its association with future frequent exacerbations (defined as three or more exacerbations per year) and hospitalization (area under the curve, 0.86 vs. 0.84; $P = 0.46$; and area under the curve, 0.81 vs. 0.83; $P = 0.41$, respectively). Moreover, patients with more severe symptoms in the majority of individual components of the QoL-B-RSS were more likely to experience exacerbations. **Conclusions:** Symptoms can serve as useful indicators for identifying patients at increased risk of exacerbation in bronchiectasis. Beyond relying solely on exacerbation history, a comprehensive assessment of symptoms could facilitate timely and cost-effective implementation of interventions for exacerbation prevention.

Keywords: QoL-B-RSS; bronchiectasis; exacerbation; symptom.

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Review

Curr Opin Pulm Med



. 2024 Mar 1;30(2):156-166.

doi: 10.1097/MCP.0000000000001026. Epub 2023 Oct 30.

[Burden, clinical features, and outcomes of post-tuberculosis chronic obstructive lung diseases](#)

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- DOI: [10.1097/MCP.0000000000001026](https://doi.org/10.1097/MCP.0000000000001026)

Abstract

Purpose of review: Post-tuberculosis lung disease (PTLD) is an increasingly recognized and debilitating consequence of pulmonary tuberculosis (PTB). In this review, we provide a comprehensive overview of PTLD with airflow obstruction (PTLD-AFO), focusing on its burden, pathophysiology, clinical manifestations, diagnostic methods, and management strategies.

Recent findings: The relationship between PTLD and airflow obstruction is complex and multifactorial. Approximately 60% of the patients with PTLD have some spirometric abnormality. Obstruction is documented in 18-22% of PTLD patients. The host susceptibility and host response to mycobacterium drive the pathogenic mechanism of PTLD. A balance between inflammatory, anti-inflammatory, and fibrotic pathways decides whether an individual with PTB would have PTLD after microbiological cure. An obstructive abnormality in PTLD-AFO is primarily due to destruction of bronchial walls, aberrant healing, and reduction of mucosal glands. The most common finding on computed tomography (CT) of thorax in patients with PTLD-AFO is bronchiectasis and cavitation. Therefore, the 'Cole's vicious vortex' described in bronchiectasis applies to PTLD. A multidisciplinary approach is required for diagnosis and treatment. The disability-adjusted life-years (DALYs) attributed to PTLD represent about 50% of the total estimated burden of DALYs due to tuberculosis (TB). Patients with PTLD require comprehensive care that includes psychosocial support, pulmonary rehabilitation, and vaccination against respiratory pathogens. In the absence of trials evaluating different treatments for PTLD-AFO, therapy is primarily symptomatic.

Summary: PTLD with airflow obstruction has considerable burden and causes a significant morbidity and mortality. However, many aspects of PTLD-AFO still need to be answered. Studies are required to evaluate different phenotypes, especially concerning Aspergillus - related complications. The treatment should be personalized based on the predominant phenotype of airflow obstruction. Extensive studies to understand the exact burden, pathogenesis, and treatment of PTLD-AFO are needed.

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J Palliat Med

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. 2024 Mar;27(3):411-420.

doi: 10.1089/jpm.2023.0263. Epub 2023 Sep 13.

Prognostic Factors of Mortality in Nonchronic Obstructive Pulmonary Disease Chronic Lung Disease: A Scoping Review

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Affiliations expand

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- DOI: [10.1089/jpm.2023.0263](https://doi.org/10.1089/jpm.2023.0263)

Abstract

Introduction: Patients with chronic lung disease (CLD) experience a heavy symptom burden at the end of life, but their uptake of palliative care is notably low. Having an understanding of a patient's prognosis would facilitate shared decision making on treatment options and care planning between patients, families, and their clinicians, and complement clinicians' assessments of patients' unmet palliative needs. While literature on prognostication in patients with chronic obstructive pulmonary disease (COPD) has been established and summarized, information for other CLDs remains less consolidated. Summarizing the mortality risk factors for non-COPD CLDs would be a novel contribution to literature. Hence, we aimed to identify and summarize the prognostic factors associated with non-COPD CLDs from the literature. **Methods:** We conducted a scoping review following published guidelines. We searched MEDLINE, Embase, PubMed, CINAHL, Cochrane Library, and Web of Science for studies published between 2000 and 2020 that described non-COPD CLD populations with an all-cause mortality risk period of up to three

years. Only primary studies which reported associations with mortality adjusted through multivariable analysis were included. **Results:** Fifty-five studies were reviewed, with 53 based on interstitial lung disease (ILD) or connective tissue disease-associated ILD populations and two in bronchiectasis populations. Prognostic factors were classified into 10 domains, with pulmonary function and disease being the largest. Older age, lower forced vital capacity, and lower carbon monoxide diffusing capacity were most commonly investigated and associated with statistically significant increases in mortality risks. **Conclusions:** This comprehensive overview of prognostic factors for patients with non-COPD CLDs would facilitate the identification and prioritization of candidate factors to predict short-term mortality, supporting tool development for decision making and to identify high-risk patients for palliative needs assessments. Literature focused on patients with ILDs, and more studies should be conducted on other CLDs to bridge the knowledge gap.

Keywords: bronchiectasis; interstitial lung disease; palliative care; prognostic factors; scoping review.

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Laryngoscope

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. 2024 Mar;134(3):1005-1013.

doi: 10.1002/lary.30992. Epub 2023 Aug 24.

Non-Type 2 and Mixed Inflammation in Chronic Rhinosinusitis and Lower Airway Disease

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Affiliations expand

- PMID: 37615304
- DOI: [10.1002/lary.30992](https://doi.org/10.1002/lary.30992)

Abstract

Objective: The aim was to discuss the role of non-type 2 inflammation in patients diagnosed with chronic rhinosinusitis (CRS) and comorbid lower airway disease.

Data sources: Medline, Embase, National Institute for Health and Care Excellence, TRIP Database, ProQuest, Clinicaltrials.gov, Cochrane Central Registry of Controlled Trials, Web of Science, government and health organizations, and graduate-level theses.

Review methods: This scoping review followed PRISMA-ScR guidelines. Search strategy was peer-reviewed by medical librarians. Studies were included if they utilized airway sampling, non-type 2 cytokines, and patients with CRS and lower airway disease.

Results: Twenty-seven from 7060 articles were included. In patients with CRS and comorbid asthma, aspirin-exacerbated respiratory disease (AERD), and chronic obstructive pulmonary disease (COPD)/bronchiectasis, 60% (n = 12), 33% (n = 2), and 100% (n = 1), respectively, demonstrated mixed or non-type 2 endotypes. Comorbid CRS and asthma produced type 1 (n = 1.5), type 2 (n = 8), type 3 (n = 1), mixed type 1/2 (n = 1), and mixed type 1/2/3 (n = 8.5) endotype shifts. AERD demonstrated type 2 (n = 4), mixed type 2/3 (n = 1), and mixed type 1/2/3 (n = 1) endotype shifts. CRS with COPD or bronchiectasis demonstrated a mixed 1/2 (n = 1) endotype shift.

Conclusion: Type 2 disease has been extensively reviewed due to advent biologics targeting type 2 inflammation, but outcomes may be suboptimal due to the presence of non-type 2 inflammation. A proportion of patients with CRS and comorbid lower airway disease demonstrated mixed and non-type 2 endotype shifts. This emphasizes that patients with unified airway disease may have forms of inflammation beyond classical type 2 disease which could inform biologic development. *Laryngoscope*, 134:1005-1013, 2024.

Keywords: chronic rhinosinusitis; endotypes; mixed inflammation; non-type 2 inflammation; unified airway disease.

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. 2024 Feb 29;10(1):e003866.

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[Characterisation of airway disease associated with Sjögren disease](#)

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Affiliations expand

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- DOI: [10.1136/rmdopen-2023-003866](https://doi.org/10.1136/rmdopen-2023-003866)

Abstract

Objective: Although airway disease associated with Sjögren's disease (Sjo-AD) is common, it is poorly studied compared with interstitial lung disease (ILD). In this study, we aimed to assess factors associated with Sjo-AD, the characteristics and prognosis of this manifestation.

Methods: We performed a retrospective multicentric study involving nine centres. We included Sjo-AD patients confirmed by at least one clinician and one CT scan report. Clinical and biological data, pulmonary function test (PFT), and CT scans were collected. A single radiologist specialist in thoracic diseases reviewed CT scans. Sjo-AD patients were compared with Sjo controls without pulmonary involvement, randomly selected after matching for age and disease duration.

Results: We included 31 Sjo-AD and 62 Sjo controls without pulmonary history. Sjo-AD had a higher disease activity (ESSDAI) compared with controls, even when excluding the pulmonary domain of the score (7 vs 3.8, $p < 0.05$), mainly due to the biological activity. Sjo-AD was multilobar (72%) and associated with signs of both bronchiectasis and bronchiolitis (60%). Obstructive lung disease occurred in 32% at the time of Sjo-AD diagnosis. Overall, PFT was stable after 8.7 ± 7 years follow-up but repeated CT scans showed extended lesions in 41% of cases within 6 ± 3.2 years. No patient developed Sjo-ILD. Sjo-AD progression was independent of the global disease activity.

Conclusions: Sjo-AD preferentially affects Sjo patients with higher biological activity. It is often characterised as a diffuse disease, affecting both proximal and distal airways, with a slow evolution over time and no progression to Sjo-ILD.

Keywords: Autoimmune Diseases; Epidemiology; Risk Factors; Sjogren's Syndrome.

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Conflict of interest statement

Competing interests: GN received honorarium from Biogen, Pfizer, Novartis, Lilly and Amgen. XM received honorarium from Astra-Zeneca, BMS, Galapagos, GSK, Novartis, Pfizer. M-PD received honorarium from Boehringer-Ingelheim and GSK. P-AJ received honorarium from Galapagos. ED received honorarium from Abbvie, BMS, Janssen, Lilly, Medac, MSD, Novartis, Roche-Chugai, Sanofi, UCB, Celgène, Amgen and Galapagos.

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BMC Pulm Med



. 2024 Feb 26;24(1):98.

doi: 10.1186/s12890-024-02912-2.

[Eosinophilic bronchiectasis increases length and cost of hospitalization: a retrospective analysis in a hospital of southern China from 2012 to 2020](#)

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Affiliations expand

- PMID: 38408986
- PMCID: [PMC10895853](#)
- DOI: [10.1186/s12890-024-02912-2](#)

Free PMC article

Abstract

Background: The concept of eosinophilic bronchiectasis has received clinical attention recently, but the association between blood eosinophil count (BEC) and hospital

characteristics has rarely been reported yet. We aim to investigate the clinical impact of BEC on patients with acute bronchiectasis exacerbation.

Methods: A total of 1332 adult patients diagnosed with acute exacerbation of bronchiectasis from January 2012 to December 2020 were included in this retrospective study. A propensity-matched analysis was performed by matching age, sex and comorbidities in patients with high eosinophil count (≥ 300 cell/ μL) and low eosinophil count (< 300 cell/ μL). Clinical characteristics, length of hospital stay (LOS), hospitalization cost and inflammatory markers were compared between the two groups.

Results: Eosinophilic bronchiectasis occurred in approximately 11.7% of all patients. 156 propensity score-matched pairs were identified with and without high eosinophil count. Eosinophilic bronchiectasis presented with a longer LOS [9.0 (6.0-12.5) vs. 5.0 (4.0-6.0) days, $p < 0.0001$] and more hospitalization cost [15,011(9,753-27,404) vs. 9,109(6,402-12,287) RMB, $p < 0.0001$] compared to those in non-eosinophilic bronchiectasis. The median white blood cell (WBC), lymphocyte, platelet (PLT) and C-reactive protein (CRP) levels in eosinophilic bronchiectasis were significantly increased. Multivariate logistic regression analysis confirmed that the high levels of eosinophil count (OR = 13.95, $p < 0.0001$), worse FEV1% predicted (OR = 7.80, $p = 0.0003$) and PLT (OR = 1.01, $p = 0.035$) were independent prognostic factors for length of hospital (LOS) greater than 7 days.

Conclusion: Eosinophilic bronchiectasis patients had longer length of hospital stay and more hospitalization cost compared to those in non-eosinophilic bronchiectasis group, which might be associated with the stronger inflammatory reaction.

Keywords: Blood eosinophil count; Bronchiectasis; Hospitalization cost; Inflammation markers; Length of hospital stay (LOS).

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Conflict of interest statement

The authors declare no competing interests.

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- [3 figures](#)

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