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## COPD

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Review

Respir Med

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. 2023 Apr-May;210:107168.

doi: 10.1016/j.rmed.2023.107168. Epub 2023 Feb 21.

## Anatomical and histopathological approaches to asthma phenotyping

[Jonas S Erjefält](#)<sup>1</sup>

Affiliations expand

- PMID: 36822489

- DOI: [10.1016/j.rmed.2023.107168](https://doi.org/10.1016/j.rmed.2023.107168)

## Abstract

Asthma is typically characterized by variable respiratory symptoms and airflow limitation. Along with the pathophysiology and symptoms are immunological and inflammatory processes. The last decades research has revealed that the immunology of asthma is highly heterogeneous. This has clinical consequences and identification of immunological phenotypes is currently used to guide biological treatment. The focus of this review is on another dimension of asthma diversity, namely anatomical heterogeneity. Immunopathological alterations may go beyond the central airways to also involve the distal airways, the alveolar parenchyma, and pulmonary vessels. Also, extrapulmonary tissues are affected. The anatomical distribution of inflammation in asthma has remained relatively poorly discussed despite its potential implication on both clinical presentation and response to treatment. There is today evidence that a significant proportion of the asthma patients has small airway disease with type 2 immunity, eosinophilia and smooth muscle infiltration of mast cells. The small airways in asthma are also subjected to remodelling, constriction, and luminal plugging, events that are likely to contribute to the elevated distal airway resistance seen in some patients. In cases when the inflammation extends into the alveolar parenchyma alveolar FCER1-high mast cells, eosinophilia, type 2 immunity and activated alveolar macrophages, together with modest interstitial remodelling, create a complex immunopathological picture. Importantly, the distal lung inflammation in asthma can be pharmacologically targeted by use of inhalers with more distal drug deposition. Biological treatments, which are readily distributed to the distal lung, may also be beneficial in eligible patients with more severe and anatomically widespread disease.

**Keywords:** Alveolar; Anatomy; Asthma; Bronchiolar; Histology; Immunology; Inflammation; Phenotypes.

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### SUPPLEMENTARY INFO

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Respir Med

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. 2023 Apr;209:107150.

doi: 10.1016/j.rmed.2023.107150. Epub 2023 Feb 8.

# Identification of frequent acute exacerbations phenotype in COPD patients based on imaging and clinical characteristics

[Dan Zhu](#)<sup>1</sup>, [Huiling Dai](#)<sup>2</sup>, [Haiyan Zhu](#)<sup>3</sup>, [Yuang Fang](#)<sup>4</sup>, [Huihui Zhou](#)<sup>4</sup>, [Zhangwei Yang](#)<sup>4</sup>, [Shuguang Chu](#)<sup>5</sup>, [Qian Xi](#)<sup>6</sup>

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- PMID: 36758904
- DOI: [10.1016/j.rmed.2023.107150](https://doi.org/10.1016/j.rmed.2023.107150)

## Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a common disease with high morbidity, with acute exacerbations manifesting as a worsening of respiratory symptoms. This study aimed to identify the frequent acute exacerbation phenotype in patients with COPD based on imaging and clinical characteristics.

**Methods:** Patients with COPD (n = 201) were monitored for acute exacerbations one year after their initial hospital admission and further divided into frequent and non-frequent exacerbation groups according to the frequency and severity of acute exacerbations. All patients underwent high resolution CT scans and low attenuation area less than -950Hu (LAA-950) in the whole lung was measured. Differences in visual subtypes, LAA-950, and clinical basic characteristics were compared between groups. The clinical factors influencing frequent exacerbation were determined using binary logistic regression. Finally, based on imaging and clinical factors, the receiver operating characteristic curve was used to identify the phenotype of COPD with frequent acute exacerbations.

**Results:** Patients with frequent exacerbations had a larger LAA-950 than those non-frequent exacerbations patients ( $p < 0.001$ ). Frequent acute exacerbations were associated with worsening visual subtypes. Multivariate binary logistic regression illustrated that age, smoking status, BMI, FEV1 pred, and LAA-950 were associated with frequent exacerbations of COPD. The area under the receiver operating characteristic curve for predicting frequent exacerbations based on age, smoking status, BMI, FEV1 pred, and LAA-950 was 0.907 ( $p < 0.001$ ).

**Conclusion:** The combination of imaging and clinical characteristics reached high diagnostic efficacy in the identification of frequent acute exacerbations in patients with COPD.

**Keywords:** Acute exacerbation; Chronic obstructive pulmonary disease; High-resolution computed tomography; Low attenuation area; Pulmonary function test; Visual subtype.

## Conflict of interest statement

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

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. 2023 Apr;108(4):535-538.

doi: 10.1113/EP091078. Epub 2023 Feb 6.

# [A song of iron and oxygen: Hypoxic pulmonary vasoconstriction and gas exchange in chronic obstructive pulmonary disease](#)

[Jacob P Hartmann](#)<sup>1,2</sup>, [Damian M Bailey](#)<sup>3</sup>, [Ronan M G Berg](#)<sup>1,2,3,4</sup>

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- PMID: 36744659
- DOI: [10.1113/EP091078](#)

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Observational Study

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. 2023 Apr 1;37(5):745-752.

doi: 10.1097/QAD.00000000000003465. Epub 2022 Dec 23.

# Chronic obstructive pulmonary disease and the risk for myocardial infarction by type in people with HIV

[Kristina Crothers<sup>1</sup>](#), [Robin M Nance<sup>2,3</sup>](#), [Bridget M Whitney<sup>2</sup>](#), [Barbara N Harding<sup>4,5</sup>](#), [Susan R Heckbert<sup>3</sup>](#), [Matthew J Budoff<sup>6</sup>](#), [William C Mathews<sup>7</sup>](#), [Laura Bamford<sup>7</sup>](#), [Edward R Cachay<sup>7</sup>](#), [Joseph J Eron<sup>8</sup>](#), [Sonia Napravnik<sup>8</sup>](#), [Richard D Moore<sup>9</sup>](#), [Jeanne C Keruly<sup>9</sup>](#), [Amanda Willig<sup>10</sup>](#), [Greer Burkholder<sup>10</sup>](#), [Matthew J Feinstein<sup>11</sup>](#), [Michael S Saag<sup>10</sup>](#), [Mari M Kitahata<sup>2</sup>](#), [Heidi M Crane<sup>2</sup>](#), [Joseph A C Delaney<sup>3,12</sup>](#); [for CNICS](#)

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- PMID: 36728918
- PMCID: PMC10041661 (available on 2024-04-01)
- DOI: [10.1097/QAD.00000000000003465](https://doi.org/10.1097/QAD.00000000000003465)

## Abstract

**Objectives:** The relationship between chronic obstructive pulmonary disease (COPD) and cardiovascular disease in people with HIV (PWH) is incompletely understood. We determined whether COPD is associated with risk of myocardial infarction (MI) among PWH, and if this differs for type 1 (T1MI) and type 2 (T2MI).

**Design:** We utilized data from five sites in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort, a multisite observational study.

**Methods:** Our primary outcome was an adjudicated MI, classified as T1MI or T2MI. We defined COPD based on a validated algorithm requiring COPD diagnosis codes and at least 90-day continuous supply of inhalers. We conducted time-to-event analyses to first MI and used multivariable Cox proportional hazards models to measure associations between COPD and MI.

**Results:** Among 12 046 PWH, 945 had COPD. Overall, 309 PWH had an MI: 58% had T1MI (N = 178) and 42% T2MI (N = 131). In adjusted models, COPD was associated with a significantly increased risk of all MI [adjusted hazard ratio (aHR) 2.68 (95% confidence interval (CI) 1.99-3.60)] even after including self-reported smoking [aHR 2.40 (95% CI 1.76-3.26)]. COPD was also associated with significantly increased risk of T1MI and T2MI individually, and with sepsis and non-sepsis causes of T2MI. Associations were generally minimally changed adjusting for substance use.

**Conclusion:** COPD is associated with a substantially increased risk for MI, including both T1MI and T2MI, among PWH. Given the association with both T1MI and T2MI, diverse mechanistic pathways are involved. Future strategies to decrease risk of T1MI and T2MI in PWH who have COPD are needed.

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. 2023 Jan 25;32(167):220141.

doi: 10.1183/16000617.0141-2022. Print 2023 Mar 31.

# Mucolytics for acute exacerbations of chronic obstructive pulmonary disease: a meta-analysis

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Affiliations expand

- PMID: 36697209
- PMCID: [PMC9879332](#)
- DOI: [10.1183/16000617.0141-2022](#)

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## Abstract

This meta-analysis explored the safety and effectiveness of mucolytics as an add-on treatment for chronic obstructive pulmonary disease (COPD) exacerbations. Based on a pre-registered protocol and following Cochrane methods, we systematically searched for relevant randomised or quasi-randomised controlled trials (RCTs). We used the Risk of Bias v2 tool for appraising the studies and performed random-effect meta-analyses when appropriate. We assessed certainty of evidence using GRADE. This meta-analysis included 24 RCTs involving 2192 patients with COPD exacerbations, entailing at least some concerns of methodological bias. We demonstrated with moderate certainty that mucolytics increase the rate of treatment success (relative risk 1.37, 95% CI 1.08-1.73, n=383), while they also exert benefits on overall symptom scores (standardised mean difference 0.86, 95% CI 0.63-1.09, n=316), presence of cough at follow-up (relative risk 1.93, 95% CI 1.15-3.23) and ease of expectoration (relative risk 2.94, 95% CI 1.68-5.12). Furthermore, low or very low certainty evidence suggests mucolytics may also reduce future risk of exacerbations and improve health-related quality of life, but do not impact on breathlessness, length of hospital stay, indication for higher level of care or serious adverse events. Overall, mucolytics could be considered for COPD exacerbation management. These findings should be validated in further, rigorous RCTs.

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## Conflict of interest statement

Conflicts of interest: The authors declare no conflict of interest related to this work. E. Papadopoulos, J. Hansel, and Z. Lazar report no conflict of interest. K. Kostikas reports grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir, consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, ELPEN,

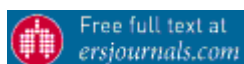
GSK, Menarini, Novartis and Sanofi Genzyme, honoraria from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GILEAD, GSK, Menarini, MSD, Novartis, Sanofi Genzyme and WebMD. S. Tryfon reports honoraria from Menarini, Boehringer-Ingelheim and ELPEN, support for attending meetings from Chiesi and Menarini, and patents with GSK, AstraZeneca and ELPEN, not related to this work. J. Vestbo reports consulting fees and/or honoraria from ALK-Abello, AstraZeneca, Boehringer Ingelheim, GSK and TEVA, not related to this work. A.G. Mathioudakis reports a research grant from Boehringer Ingelheim, not related to this work.

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. 2023 Jan 25;32(167):220109.

doi: 10.1183/16000617.0109-2022. Print 2023 Mar 31.

# [Physical activity promotion interventions in chronic airways disease: a systematic review and meta-analysis](#)

[Caroline Reilly](#)<sup>1</sup>, [Joe Sails](#)<sup>1</sup>, [Antonios Stavropoulos-Kalinoglou](#)<sup>1</sup>, [Rebecca J Birch](#)<sup>2</sup>, [Jim McKenna](#)<sup>1</sup>, [Ian J Clifton](#)<sup>2,3</sup>, [Daniel Peckham](#)<sup>2,3</sup>, [Karen M Birch](#)<sup>4</sup>, [Oliver J Price](#)<sup>3,4</sup>

[Affiliations expand](#)

- PMID: 36697208



- PMCID: [PMC9879326](#)
- DOI: [10.1183/16000617.0109-2022](#)

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## Abstract

Physical inactivity is common in people with chronic airways disease (pwCAD) and associated with worse clinical outcomes and impaired quality of life. We conducted a systematic review and meta-analysis to characterise and evaluate the effectiveness of interventions promoting step-based physical activity (PA) in pwCAD. We searched for studies that included a form of PA promotion and step-count outcome measure. A random-effects model was used to determine the overall effect size using post-intervention values. 38 studies (n=32 COPD; n=5 asthma; n=1 bronchiectasis; study population: n=3777) were included. Overall, implementing a form of PA promotion resulted in a significant increase in step-count: median (IQR) 705 (183-1210) when compared with usual standard care: -64 (-597-229), standardised mean difference (SMD) 0.24 (95% CI: 0.12-0.36),  $p<0.01$ . To explore the impact of specific interventions, studies were stratified into subgroups: PA promotion+wearable activity monitor-based interventions (n=17) (SMD 0.37,  $p<0.01$ ); PA promotion+step-count as an outcome measure (n=9) (SMD 0.18,  $p=0.09$ ); technology-based interventions (n=12) (SMD 0.16,  $p=0.01$ ). Interventions promoting PA, particularly those that incorporate wearable activity monitors, result in a significant and clinically meaningful improvement in daily step-count in pwCAD.

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## Conflict of interest statement

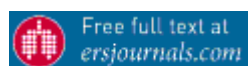
Conflict of interest: I.J. Clifton reports personal fees from GlaxoSmithKline, outside the submitted work. The remaining authors have no conflicts to declare.

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

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# Th2 high and mast cell gene signatures are associated with corticosteroid sensitivity in COPD

[Alen Faiz](#)<sup>1,2,3</sup>, [Stelios Pavlidis](#)<sup>4</sup>, [Chih-Hsi Kuo](#)<sup>4,5</sup>, [Anthony Rowe](#)<sup>6</sup>, [Pieter S Hiemstra](#)<sup>7</sup>, [Wim Timens](#)<sup>3,8</sup>, [Marijn Berg](#)<sup>3,8</sup>, [Marissa Wisman](#)<sup>3,8</sup>, [Yi-Ke Guo](#)<sup>4</sup>, [Ratko Djukanović](#)<sup>9</sup>, [Peter Sterk](#)<sup>10</sup>, [Kerstin B Meyer](#)<sup>11</sup>, [Martijn C Nawijn](#)<sup>3,8</sup>, [Ian Adcock](#)<sup>#4,5</sup>, [Kian Fan Chung](#)<sup>#4,5</sup>, [Maarten van den Berge](#)<sup>#2,3</sup>

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- PMID: 36598042
- DOI: [10.1136/thorax-2021-217736](https://doi.org/10.1136/thorax-2021-217736)

## Free article

## Abstract

**Rationale:** Severe asthma and chronic obstructive pulmonary disease (COPD) share common pathophysiological traits such as relative corticosteroid insensitivity. We recently published three transcriptome-associated clusters (TACs) using hierarchical analysis of the sputum transcriptome in asthmatics from the Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes (U-BIOPRED) cohort comprising one Th2-high inflammatory signature (TAC1) and two Th2-low signatures (TAC2 and TAC3).

**Objective:** We examined whether gene expression signatures obtained in asthma can be used to identify the subgroup of patients with COPD with steroid sensitivity.

**Methods:** Using gene set variation analysis, we examined the distribution and enrichment scores (ES) of the 3 TACs in the transcriptome of bronchial biopsies from 46 patients who participated in the Groningen Leiden Universities Corticosteroids in Obstructive Lung Disease COPD study that received 30 months of treatment with inhaled corticosteroids (ICS) with and without an added long-acting  $\beta$ -agonist (LABA). The identified signatures were then associated with longitudinal clinical variables after treatment. Differential gene expression and cellular convolution were used to define key regulated genes and cell types.

**Measurements and main results:** Bronchial biopsies in patients with COPD at baseline showed a wide range of expression of the 3 TAC signatures. After ICS $\pm$ LABA treatment, the ES of TAC1

was significantly reduced at 30 months, but those of TAC2 and TAC3 were unaffected. A corticosteroid-sensitive TAC1 signature was developed from the TAC1 ICS-responsive genes. This signature consisted of mast cell-specific genes identified by single-cell RNA-sequencing and positively correlated with bronchial biopsy mast cell numbers following ICS $\pm$ LABA. Baseline levels of gene transcription correlated with the change in RV/TLC %predicted following 30-month ICS $\pm$ LABA.

**Conclusion:** Sputum-derived transcriptomic signatures from an asthma cohort can be recapitulated in bronchial biopsies of patients with COPD and identified a signature of airway mast cells as a predictor of corticosteroid responsiveness.

**Keywords:** COPD pathology; airway epithelium; oxidative stress.

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## Conflict of interest statement

Competing interests: None declared.

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Eur J Intern Med

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. 2023 Apr;110:122-124.

doi: 10.1016/j.ejim.2022.12.022. Epub 2022 Dec 26.

# Long-term prognostic capacity of multi-comorbid indices in chronic obstructive pulmonary disease

[Rocio Reinoso-Arija](#)<sup>1</sup>, [Laura Carrasco-Hernandez](#)<sup>2</sup>, [Candelaria Caballero Eraso](#)<sup>2</sup>, [Esther Quintana-Gallego](#)<sup>2</sup>, [Jose Luis López-Campos](#)<sup>3</sup>

Affiliations expand

- PMID: 36577566

- DOI: [10.1016/j.ejim.2022.12.022](https://doi.org/10.1016/j.ejim.2022.12.022)

*No abstract available*

## 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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Ann Vasc Surg

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. 2023 Apr;91:10-19.

doi: 10.1016/j.avsg.2022.12.072. Epub 2022 Dec 19.

# [A Systematic Review and Meta-Analysis to Assess the Impact of Pre-existing Comorbidities on the 30-Day Readmission after Lower Extremity Bypass Surgery for Peripheral Artery Occlusive Disease](#)

- PMID: 36549476
- DOI: [10.1016/j.avsg.2022.12.072](https://doi.org/10.1016/j.avsg.2022.12.072)

## Abstract

**Background:** Unplanned hospital readmissions after surgical operations are considered a marker for suboptimal care during index hospitalizations and are associated with poor patient outcomes and increased healthcare resource utilization. Patients undergoing lower extremity bypass (LEB) operations for severe peripheral arterial disease (PAD) have one of the highest readmission rates, among all the vascular and nonvascular surgical operations. This review is meant to evaluate the impact of pre-existing comorbidities (diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), hypertension (HTN), and coronary artery disease (CAD))-on the 30-day readmission rates among patients who underwent LEB for severe PAD.

**Methods:** The review protocol was registered to the PROSPERO database (CRD42021261067). A systematic review of the English literature was performed using PubMed, Scopus, and the Cochrane Library databases from inception till April 2022. The review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and included only studies reporting on 30-day readmission following LEB for occlusive PAD. The quality of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach and was reported as high, moderate, or low. The risk of bias was evaluated utilizing the Risk of Bias in Nonrandomized Studies - of Interventions (ROBINS-I) tool. A pooled odds ratio (OR) for each study was computed, and a P-value of <0.05 was designated as statistically significant. Interstudy heterogeneity was evaluated by Q-metric and quantified using Higgins I<sup>2</sup> statistics.

**Results:** Five studies reported data on 30-day readmission after LEB for occlusive PAD. A total of 19,739 patients were included. Readmission occurred among 3,559 (18%) patients. DM and COPD were reported by all 5 selected studies, and CHF and HTN were reported by 4 studies. CAD was least reported among the selected 5 pre-existing conditions, with only 2 studies mentioning it. HTN (OR, 1.35; 95% confidence interval (CI), 1.10-1.64;  $P \leq 0.001$ ;  $I^2 = 52.20\%$ ), DM (OR, 1.52; 95% CI, 1.30-1.79;  $P \leq 0.001$ ;  $I^2 = 74.51\%$ ), and CHF (OR, 1.85; 95% CI, 1.51-2.25;  $P \leq 0.001$ ;  $I^2 = 50.48\%$ ) were all found to be associated with an increased risk of 30-day readmission, while the presence of COPD (OR, 1.16; 95% CI, 0.98-1.36;  $P = 0.09$ ;  $I^2 = 61.93\%$ ) and CAD (OR, 1.30; 95% CI, 0.94-1.78;  $P = 0.11$ ;  $I^2 = 51.01\%$ ) was not associated with early readmission on meta-analysis of the available studies.

**Conclusions:** The pre-existing comorbidities HTN, DM, and CHF increase the risk of 30-day readmission after LEB for occlusive PAD. The identification of these risk factors can help stratify the patients and further guide in understanding the variety of factors that contribute in hospital readmissions.

## SUPPLEMENTARY INFO

Publication types, MeSH terms, Supplementary conceptsexpand

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Editorial

Radiology



. 2023 Apr;307(1):e222675.

doi: 10.1148/radiol.222675. Epub 2022 Dec 13.

# Artificial Intelligence Analysis of Bronchiectasis Is Predictive of Outcomes in Chronic Obstructive Pulmonary Disease

[Mark L Schiebler<sup>1</sup>](#), [Joon Beom Seo<sup>1</sup>](#)

Affiliations expand

- PMID: 36511811
- DOI: [10.1148/radiol.222675](https://doi.org/10.1148/radiol.222675)

*No abstract available*

## Comment on

- [Artificial Intelligence-based CT Assessment of Bronchiectasis: The COPDGene Study.](#) Díaz AA, Nardelli P, Wang W, San José Estépar R, Yen A, Kligerman S, Maselli DJ, Dolliver WR, Tsao A, Orejas JL, Aliberti S, Aksamit TR, Young KA, Kinney GL, Washko GR, Silverman EK, San José Estépar R. *Radiology*. 2023 Apr;307(1):e221109. doi: 10.1148/radiol.221109. Epub 2022 Dec 13. PMID: 36511808

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[Multicenter Study](#)

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. 2023 Apr;307(1):e221109.

doi: 10.1148/radiol.221109. Epub 2022 Dec 13.

# Artificial Intelligence-based CT Assessment of Bronchiectasis: The COPDGene Study

[Alejandro A Díaz<sup>1</sup>](#), [Pietro Nardelli<sup>1</sup>](#), [Wei Wang<sup>1</sup>](#), [Rubén San José Estépar<sup>1</sup>](#), [Andrew Yen<sup>1</sup>](#), [Seth Kligerman<sup>1</sup>](#), [Diego J Maselli<sup>1</sup>](#), [Wojciech R Dolliver<sup>1</sup>](#), [Andrew Tsao<sup>1</sup>](#), [José L Orejas<sup>1</sup>](#), [Stefano Aliberti<sup>1</sup>](#), [Timothy R Aksamit<sup>1</sup>](#), [Kendra A Young<sup>1</sup>](#), [Gregory L Kinney<sup>1</sup>](#), [George R Washko<sup>1</sup>](#), [Edwin K Silverman<sup>1</sup>](#), [Raúl San José Estépar<sup>1</sup>](#)

Affiliations [expand](#)

- PMID: 36511808
- DOI: [10.1148/radiol.221109](https://doi.org/10.1148/radiol.221109)

## Abstract

Background CT is the standard method used to assess bronchiectasis. A higher airway-to-artery diameter ratio (AAR) is typically used to identify enlarged bronchi and bronchiectasis; however, current imaging methods are limited in assessing the extent of this metric in CT scans. Purpose To determine the extent of AARs using an artificial intelligence-based chest CT and assess the association of AARs with exacerbations over time. Materials and Methods In a secondary analysis of ever-smokers from the prospective, observational, multicenter COPDGene study, AARs were

quantified using an artificial intelligence tool. The percentage of airways with AAR greater than 1 (a measure of airway dilatation) in each participant on chest CT scans was determined. Pulmonary exacerbations were prospectively determined through biannual follow-up (from July 2009 to September 2021). Multivariable zero-inflated regression models were used to assess the association between the percentage of airways with AAR greater than 1 and the total number of pulmonary exacerbations over follow-up. Covariates included demographics, lung function, and conventional CT parameters. Results Among 4192 participants (median age, 59 years; IQR, 52-67 years; 1878 men [45%]), 1834 had chronic obstructive pulmonary disease (COPD). During a 10-year follow-up and in adjusted models, the percentage of airways with AARs greater than 1 (quartile 4 vs 1) was associated with a higher total number of exacerbations (risk ratio [RR], 1.08; 95% CI: 1.02, 1.15;  $P = .01$ ). In participants meeting clinical and imaging criteria of bronchiectasis (ie, clinical manifestations with  $\geq 3\%$  of AARs  $>1$ ) versus those who did not, the RR was 1.37 (95% CI: 1.31, 1.43;  $P < .001$ ). Among participants with COPD, the corresponding RRs were 1.10 (95% CI: 1.02, 1.18;  $P = .02$ ) and 1.32 (95% CI: 1.26, 1.39;  $P < .001$ ), respectively. Conclusion In ever-smokers with chronic obstructive pulmonary disease, artificial intelligence-based CT measures of bronchiectasis were associated with more exacerbations over time. Clinical trial registration no. [NCT00608764](#) © RSNA, 2022 *Supplemental material is available for this article.* See also the editorial by Schiebler and Seo in this issue.

## Comment in

- [Artificial Intelligence Analysis of Bronchiectasis Is Predictive of Outcomes in Chronic Obstructive Pulmonary Disease.](#)  
Schiebler ML, Seo JB. *Radiology*. 2023 Apr;307(1):e222675. doi: 10.1148/radiol.222675. Epub 2022 Dec 13. PMID: 36511811 No abstract available.

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. 2023 Apr;29(4):523-529.

doi: 10.1016/j.cmi.2022.11.029. Epub 2022 Dec 8.

# Hospitalization for chronic obstructive pulmonary disease and pneumonia:



# association with the dose of inhaled corticosteroids. A nation-wide cohort study of 52 100 outpatients

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## Abstract

**Objectives:** International guidelines only advocate the use of inhaled corticosteroids (ICSs) in patients with chronic obstructive pulmonary disease (COPD) experiencing recurring exacerbations and eosinophilic inflammation. However, ICSs are commonly used in patients with COPD and without exacerbations and signs of eosinophilic inflammation, thus possibly increasing the risk of hospitalization for pneumonia. Thus, we aimed to determine the risk of hospitalization for pneumonia associated with increasing cumulated ICS doses among patients with COPD to establish whether there is dose dependency.

**Methods:** A retrospective cohort study included all patients with COPD treated at a respiratory outpatient clinic in Denmark. The patients were divided into four groups based on their average daily ICS exposure. The dose-response relationship was investigated using a multivariable Cox proportional hazard regression analysis.

**Results:** In total, 52 100 patients were included, who were divided into the no-use (n = 15 755), low-dose (n = 12 050), moderate-dose (n = 12 488), and high-dose (n = 11 807) groups. ICS use was strongly associated with hospitalization for pneumonia (hazard ratio [HR], 1.3; CI, 1.2-1.3) (ICS vs. no ICS). The risk of hospitalization for pneumonia increased with every dosing group step: low dose: HR, 1.1 (CI, 1.0-1.2); moderate dose: HR, 1.2 (CI, 1.1-1.3), and high dose: HR, 1.5 (CI, 1.4-1.6); "no use" was the reference. Sensitivity analyses confirmed these findings.

**Conclusions:** In the dose-response relationship analysis, ICS dose were associated with a substantially increased risk of hospitalization for pneumonia of up to 50%. Our data support that ICSs should be administered at the lowest possible dose and only to patients with COPD who have a documented need.

**Keywords:** Corticosteroid; Hospitalization; Inhalation; Pneumonia.

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Am J Respir Crit Care Med

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. 2023 Apr 1;207(7):865-875.

doi: 10.1164/rccm.202204-0643OC.

# Long-term Telerehabilitation or Unsupervised Training at Home for Patients with Chronic Obstructive Pulmonary Disease: A Randomized Controlled Trial

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Affiliations expand

- PMID: 36480957
- DOI: [10.1164/rccm.202204-0643OC](https://doi.org/10.1164/rccm.202204-0643OC)

## Abstract

**Rationale:** Despite the benefits of pulmonary rehabilitation in chronic obstructive pulmonary disease (COPD), many patients do not access or complete pulmonary rehabilitation, and long-term maintenance of exercise is difficult. **Objectives:** To compare long-term telerehabilitation or unsupervised treadmill training at home with standard care. **Methods:** In an international randomized controlled trial, patients with COPD were assigned to three groups (telerehabilitation, unsupervised training, or control) and followed up for 2 years. Telerehabilitation consisted of individualized treadmill training at home supervised by a physiotherapist and self-management. The

unsupervised training group performed unsupervised treadmill exercise at home. The control group received standard care. The primary outcome was the combined number of hospitalizations and emergency department presentations. Secondary outcomes included time free from the first event; exercise capacity; dyspnea; health status; quality of life; anxiety; depression; self-efficacy; and subjective impression of change. **Measurements and Main Results:** A total of 120 participants were randomized. The incidence rate of hospitalizations and emergency department presentations was lower in telerehabilitation (1.18 events per person-year; 95% confidence interval [CI], 0.94-1.46) and unsupervised training group (1.14; 95% CI, 0.92-1.41) than in the control group (1.88; 95% CI, 1.58-2.21;  $P < 0.001$  compared with intervention groups). Telerehabilitation and unsupervised training groups experienced better health status for 1 year. Intervention participants reached and maintained clinically significant improvements in exercise capacity. **Conclusions:** Long-term telerehabilitation and unsupervised training at home in COPD are both successful in reducing hospital readmissions and can broaden the availability of pulmonary rehabilitation and maintenance strategies.

**Keywords:** COPD; clinical trial; exercise; telemedicine.

## Comment in

- [Constructing Modern Pulmonary Rehabilitation: Another Brick from the Wall.](#) Bourbeau J, Bhatt SP. *Am J Respir Crit Care Med*. 2023 Apr 1;207(7):804-805. doi: 10.1164/rccm.202301-0007ED.PMID: 36656552 No abstract available.

## SUPPLEMENTARY INFO

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Ann Am Thorac Soc

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. 2023 Apr;20(4):516-522.

doi: 10.1513/AnnalsATS.202204-318OC.

# [Access to Pulmonary Rehabilitation among Medicare Beneficiaries with Chronic Obstructive Pulmonary Disease](#)

[Gargya Malla](#)<sup>1,2,3</sup>, [Sandeep Bodduluri](#)<sup>1,2</sup>, [Vivek Sthanam](#)<sup>1,2</sup>, [Gulshan Sharma](#)<sup>4</sup>, [Surya P Bhatt](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36476450
- DOI: [10.1513/AnnalsATS.202204-318OC](https://doi.org/10.1513/AnnalsATS.202204-318OC)

## Abstract

**Rationale:** Pulmonary rehabilitation (PR) remains substantially underused as a treatment modality for chronic obstructive pulmonary disease (COPD). A major barrier to the uptake of PR is the poor availability of and access to PR. **Objectives:** To quantify patients' access to PR centers in the United States. **Methods:** Using the 100% Medicare population with coverage for 2018, four geodesic distance-based buffers of 10-, 15-, 25-, and 50-mi radii around the geographic centroid of each ZIP code with at least one beneficiary with COPD were created. Street addresses of PR centers across the continental United States were geocoded. We calculated the distance between the residential ZIP code centroid and the closest PR center. The proportions of individuals with at least one PR center available within the four distance buffers were calculated overall as well as in metropolitan, micropolitan, small-town, and rural areas. **Results:** Of 62,930,784 Medicare beneficiaries, 10,376,949 (16.5%) had COPD. There were 1,696 PR centers across the United States, with one PR center for every 6,030 individuals with COPD. Mean distance to the nearest PR center was 12.4 (standard deviation, 16.6) mi. Overall, the proportions of individuals with COPD who had PR centers available within 10-, 15-, 25-, and 50-mi radii were 61.5%, 73.2%, 86.6%, and 97.1%, respectively. Proportions for rural areas were 11.3%, 24.3%, 53.4%, and 88.6%, respectively. Compared with those living in metropolitan areas, those living in rural areas were 95% less likely to have PR centers within 10 mi of their residences (odds ratio, 0.048 [95% confidence interval, 0.039-0.057]). **Conclusions:** In a nationally representative sample of Medicare beneficiaries, we found that two-fifths of adults with COPD overall, and eight in nine of those in rural areas, have poor access to PR.

**Keywords:** COPD; PR; access.

## Comment in

- [Insufficient Patient Access to Pulmonary Rehabilitation: A Multifaceted Problem.](#) Rochester CL. *Ann Am Thorac Soc.* 2023 Apr;20(4):510-512. doi: [10.1513/AnnalsATS.202301-032ED](https://doi.org/10.1513/AnnalsATS.202301-032ED). PMID: 37000146 No abstract available.

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Ann Am Thorac Soc

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. 2023 Apr;20(4):532-538.

doi: 10.1513/AnnalsATS.202203-237OC.

# Promoting Participation in Pulmonary Rehabilitation after Hospitalization for Chronic Obstructive Pulmonary Disease, Strategies of Top-performing Systems: A Qualitative Study

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Affiliations expand

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## Abstract

**Rationale:** Pulmonary rehabilitation (PR) after hospitalization for chronic obstructive pulmonary disease (COPD) is recommended by guidelines; however, few patients participate, and rates vary between hospitals. **Objectives:** To identify contextual factors and strategies that may promote participation in PR after hospitalization for COPD. **Methods:** Using a positive-deviance approach, we calculated hospital-specific rates of PR after hospitalization for COPD among a cohort of Medicare beneficiaries. At a purposive sample of high-performing and innovative hospitals in the United States, we conducted in-depth interviews with key stakeholders. We defined high-performing hospitals as having a PR rate above the 95th percentile, at least 6.58%. To learn from hospitals that demonstrated a commitment to improving rates of PR, regardless of PR rates after discharge, we identified innovative hospitals on the basis of a review of American Thoracic Society conference research presentations from prior years. Interviews were audio-recorded and transcribed verbatim. Using a directed content analysis approach, transcripts were coded iteratively to identify themes. **Results:** Interviews were conducted with 38 stakeholders at nine hospitals (seven high-performers and two innovators). Hospitals were diverse regarding size, teaching status, PR program characteristics, and geographic location. Participants included PR medical directors, PR managers,

respiratory therapists, inpatient and outpatient providers, and others. We found that high-performing hospitals were broadly focused on improving care for patients with COPD, and several had recently implemented new initiatives to reduce rehospitalizations after admission for COPD in response to the Centers for Medicare and Medicaid Services/Medicare's Hospital Readmission Reduction Program. Innovative and high-performing hospitals had systems in place to identify patients with COPD that enabled them to provide patient education and targeted discharge planning. Strategies took several forms, including the use of a COPD navigator or educator. In addition, we found that high-performing hospitals reported effective interprofessional and patient communication, had clinical champions or external change agents, and received support from hospital leadership. Specific strategies to promote PR included education of referring providers, education of patients to increase awareness of PR and its benefits, and direct assistance in overcoming barriers. **Conclusions:** Our findings suggest that successful efforts to increase participation in PR may be most effective when part of a larger strategy to improve outcomes for patients with COPD. Further research is necessary to test the generalizability of our findings.

**Keywords:** Medicare; chronic obstructive pulmonary disease; positive deviance; pulmonary rehabilitation; qualitative.

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Respir Care

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. 2023 Apr;68(4):445-451.

doi: 10.4187/respcare.10495. Epub 2022 Nov 18.

## [Evaluation of Over-the-Counter Portable Oxygen Concentrators Utilizing a Metabolic Simulator](#)

[Richard Casaburi](#)<sup>1</sup>, [Michael Hess](#)<sup>2</sup>, [Janos Porszasz](#)<sup>3</sup>, [William Clark](#)<sup>4</sup>, [Ryan Diesem](#)<sup>4</sup>, [Ruth Tal-Singer](#)<sup>2</sup>, [Carrie Ferguson](#)<sup>3</sup>

Affiliations expand

- PMID: 36400446

- DOI: [10.4187/respcare.10495](https://doi.org/10.4187/respcare.10495)

## Abstract

**Background:** Supplemental oxygen is designed to raise alveolar  $P_{O_2}$  to facilitate diffusion into arterial blood. Oxygen is generally delivered by nasal cannula either by continuous or pulsatile flow. Battery-powered portable oxygen concentrators (POCs) facilitate ambulation in patients experiencing exertional hypoxemia. In the United States, the Food and Drug Administration (FDA) clears these devices to be sold by physician prescription. Recently, however, lower-cost devices described as POCs have been advertised by online retailers. These devices lack FDA clearance and are obtained over the counter (OTC) without prescription. This study determined whether a selected group of OTC POCs have oxygen delivery characteristics suitable for use by hypoxemic patients.

**Methods:** A metabolic simulator, capable of simulating a range of metabolic rates and minute ventilations, determined effects of oxygen supplementation delivered by a variety of devices on alveolar  $P_{O_2}$ . Devices tested included 3 OTC POCs, an FDA-cleared POC, and continuous-flow oxygen from a compressed oxygen cylinder. End-tidal  $P_{ETO_2}$ , a surrogate of alveolar  $P_{O_2}$ , was determined at each of each device's flow settings at 3 metabolic rates.

**Results:** Continuous-flow tank oxygen yielded a linear  $P_{ETO_2}$  increase as flow increased, with progressively lower slope of increase for higher metabolic rate. The prescription POC device yielded similar  $P_{ETO_2}$  elevations, though with somewhat smaller elevations in pulse-dose operation. One OTC POC was only technically portable (no on-board battery); it provided only modest  $P_{ETO_2}$  elevation that failed to increase as flow setting was incremented. A second OTC POC produced only minimal  $P_{ETO_2}$  elevation. A third OTC POC, a pulsed-dose device, produced meaningful  $P_{ETO_2}$  increases, though not as great as the prescription device.

**Conclusions:** Only one of 3 OTC POCs tested was potentially of use by patients requiring ambulatory oxygen. Physicians and respiratory therapists should inform patients requiring portable oxygen that OTC devices may not meet their oxygenation requirements.

**Keywords:** exertional hypoxemia; long-term oxygen therapy; metabolic simulator; nasal cannula; online store; portable oxygen concentrator; supplemental oxygen.

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## Conflict of interest statement

Dr Casaburi discloses relationships with Inogen, Boehringer-Ingelheim, GlaxoSmithKline, and Regeneron. Mr Hess discloses relationships with the COPD Foundation and Inogen. Dr Porszasz discloses relationships with United Therapeutics, Genentech, and Regeneron. Dr Tal-Singer discloses relationships with GlaxoSmithKline, ENA Respiratory Board on behalf of the COPD Foundation, Teva, ImmunoMet, Vocalis Health, and ENA Respiratory. Dr Ferguson discloses relationships with United Therapeutics, Genentech, and Regeneron. The remaining authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

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Radiology

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. 2023 Apr;307(1):e212611.

doi: 10.1148/radiol.212611. Epub 2022 Nov 15.

## Chest CT Findings in Marijuana Smokers

[Luke Murtha](#)<sup>1</sup>, [Paul Sathiadoss](#)<sup>1</sup>, [Jean-Paul Salameh](#)<sup>1</sup>, [Matthew D F Mcinnes](#)<sup>1</sup>, [Giselle Revah](#)<sup>1</sup>

Affiliations expand

- PMID: 36378033
- DOI: [10.1148/radiol.212611](https://doi.org/10.1148/radiol.212611)

### Abstract

**Background** Global consumption of marijuana is increasing, but there is a paucity of evidence concerning associated lung imaging findings. **Purpose** To use chest CT to investigate the effects of marijuana smoking in the lung. **Materials and Methods** This retrospective case-control study evaluated results of chest CT examinations (from October 2005 to July 2020) in marijuana smokers, nonsmoker control patients, and tobacco-only smokers. We compared rates of emphysema, airway changes, gynecomastia, and coronary artery calcification. Age- and sex-matched subgroups were created for comparison with tobacco-only smokers older than 50 years. Results were analyzed using  $\chi^2$  tests. **Results** A total of 56 marijuana smokers (34 male; mean age, 49 years  $\pm$  14 [SD]), 57 nonsmoker control patients (32 male; mean age, 49 years  $\pm$  14), and 33 tobacco-only smokers (18 male; mean age, 60 years  $\pm$  6) were evaluated. Higher rates of emphysema were seen among marijuana smokers (42 of 56 [75%]) than nonsmokers (three of 57 [5%]) ( $P < .001$ ) but not tobacco-only smokers (22 of 33 [67%]) ( $P = .40$ ). Rates of bronchial thickening, bronchiectasis, and mucoid impaction were higher among marijuana smokers compared with the other groups ( $P < .001$  to  $P = .04$ ). Gynecomastia was more common in marijuana smokers (13 of 34 [38%]) than in control patients (five of 32 [16%]) ( $P = .039$ ) and tobacco-only smokers (two of 18 [11%]) ( $P = .040$ ). In age-matched subgroup analysis of 30 marijuana smokers (23 male), 29 nonsmoker control



patients (17 male), and 33 tobacco-only smokers (18 male), rates of bronchial thickening, bronchiectasis, and mucoid impaction were again higher in the marijuana smokers than in the tobacco-only smokers ( $P < .001$  to  $P = .006$ ). Emphysema rates were higher in age-matched marijuana smokers (28 of 30 [93%]) than in tobacco-only smokers (22 of 33 [67%]) ( $P = .009$ ). There was no difference in rate of coronary artery calcification between age-matched marijuana smokers (21 of 30 [70%]) and tobacco-only smokers (28 of 33 [85%]) ( $P = .16$ ). Conclusion Airway inflammation and emphysema were more common in marijuana smokers than in nonsmokers and tobacco-only smokers, although variable interobserver agreement and concomitant cigarette smoking among the marijuana-smoking cohort limits our ability to draw strong conclusions. © RSNA, 2022 See also the editorial by Galvin and Franks in this issue.

## Comment in

- [Marijuana and the Vulnerable Lung: The Role of Imaging and the Need to Move Quickly.](#) Galvin J, Franks T. *Radiology*. 2023 Apr;307(1):e222745. doi: 10.1148/radiol.222745. Epub 2022 Nov 15. PMID: 36378035 No abstract available.

## SUPPLEMENTARY INFO

MeSH termsexpand

## FULL TEXT LINKS



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Respirology

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. 2023 Apr;28(4):350-356.

doi: 10.1111/resp.14400. Epub 2022 Nov 6.

# Contribution of obesity to breathlessness in a large nationally representative sample of Australian adults

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Affiliations expand

- PMID: 36336647
- DOI: [10.1111/resp.14400](https://doi.org/10.1111/resp.14400)

## Abstract

**Background and objective:** Breathlessness is prevalent and associated with medical consequences. Obesity is related to breathlessness. However, the magnitude of its contribution has not been clearly documented. This investigation aimed to determine the contribution of obesity to breathlessness by estimating the population attributable fraction (PAF) in a representative sample of Australian adults.

**Methods:** A cross-sectional, nationally representative survey of Australian residents aged  $\geq 18$  years was conducted in October 2019. Breathlessness was defined as modified Medical Research Council (mMRC) dyspnoea scale grade  $\geq 2$ . BMI was calculated from self-reported height and weight. Adjusted relative risks (aRRs) were estimated using a generalized linear model with Poisson distribution, adjusted for age group and/or participant-reported diagnosed illnesses. Adjusted PAFs were estimated using aRR and obesity prevalence in Australian adults.

**Results:** Among those who completed the National Breathlessness Survey, 9769 participants (51.4% female) were included in the analysis; 28.1% of participants were obese. The prevalence of breathlessness was 9.54%. The aRR of obesity for breathlessness was 2.04, adjusted for age. Adjusting for various co-morbid conditions, the aRR was slightly attenuated to around 1.85-1.98. The PAF, adjusted only for age, was 24.6% (95% CI 20.1-29.1) and after further adjustment for co-morbid conditions, the PAF ranged from 21.1% to 23.6%. Obesity accounted for a higher proportion of breathlessness in women than in men.

**Conclusion:** Our results demonstrate that obesity accounts for around a quarter of breathlessness symptoms in Australian adults. This has important implications for health policy in light of the global trend in increasing obesity.

**Keywords:** COPD; asthma; breathlessness; chronic obstructive pulmonary disease; dyspnoea; obesity; population attributable fraction.

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Respirology

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. 2023 Apr;28(4):357-365.

doi: 10.1111/resp.14394. Epub 2022 Oct 21.

# Promotion of physical activity after hospitalization for COPD exacerbation: A randomized control trial

[Beatriz Valeiro](#)<sup>1</sup>, [Esther Rodríguez](#)<sup>1,2</sup>, [Paula Pérez](#)<sup>3</sup>, [Alba Gómez](#)<sup>4</sup>, [Ana Isabel Mayer](#)<sup>4</sup>, [Alejandro Pasarín](#)<sup>5</sup>, [Jordi Ibañez](#)<sup>6</sup>, [Jaume Ferrer](#)<sup>1,2</sup>, [Maria Antonia Ramon](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36270673
- DOI: [10.1111/resp.14394](https://doi.org/10.1111/resp.14394)

Free article

## Abstract

**Background and objective:** Physical activity worsens during exacerbations of chronic obstructive pulmonary disease (COPD) and notably after hospitalizations. Pedometer-based interventions are useful to increase physical activity in stable patients with COPD. However, there is little information concerning the implementation of such programs following severe exacerbation. This study assessed the efficacy of a physical activity program after hospitalization for a COPD exacerbation.

**Methods:** We performed a prospective, 12-week, parallel group, assessor-blinded, randomized control trial in COPD patients hospitalized for an exacerbation. After discharge, physical activity and other secondary variables were assessed. Patients were allocated (1:1) to a physical activity promotion program (intervention group, IG) or usual care (control group, CG). Based on a motivational interview and accelerometer physical activity assessment, a patient-tailored, pedometer-based, progressive and target-driven program was designed. Linear mixed effect models were used to analyse between-group differences.

**Results:** Forty-six out of 61 patients recruited were randomized and 43 (IG = 20, CG = 23) completed the study. In-hospital and baseline characteristics were similar in both groups. After 12 weeks of intervention, the mean steps difference between groups was 2093 steps/day,  $p = 0.018$ , 95% CI 376-4012, favouring the IG. Only the IG significantly increased the number of steps/day

compared to baseline (mean difference [95% CI] 2932 [1069-4795] steps;  $p = 0.004$ ). There were no other between-group differences.

**Conclusion:** After hospitalization for a COPD exacerbation, a patient-tailored physical activity program based on a motivational interview and the use of pedometers, with progressive and customized targets, improved the number of steps/day.

**Keywords:** COPD exacerbation; clinical trial; hospitalization; pedometer; physical activity; sedentary behaviour.

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West J Nurs Res

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. 2023 Apr;45(4):316-326.

doi: 10.1177/01939459221129949. Epub 2022 Oct 16.

## Anxiety and Depressive Symptoms in Patients with COPD: Modifiable Explanatory Factors

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Affiliations expand

- PMID: 36250352

- DOI: [10.1177/01939459221129949](https://doi.org/10.1177/01939459221129949)

## Abstract

Anxiety and depressive symptoms affect up to 80% of people with chronic obstructive pulmonary disease (COPD). To reduce this symptom burden, clinicians should target modifiable explanatory factors while accounting for nonmodifiable explanatory factors of these symptoms. The purpose of this secondary data analysis was to examine which modifiable factors explain anxiety and depressive symptoms in COPD. This secondary data analysis of 1,760 COPD patients used multiple regression to explain anxiety and depressive symptoms from sets of modifiable patient characteristics and demographic controls. Clinically significant symptoms of anxiety or depression presented in 29.6% ( $n = 526$ ) of participants, and 20.6% ( $n = 363$ ) had both. Significant modifiable explanatory factors of both disorder symptoms were perceived functional status, functional capacity, psychosocial impact, symptom self-management, and significant symptoms for the other. Somatic symptom burden and dyspnea explained anxiety and depressive symptoms, respectively. Addressing these modifiable factors may reduce anxiety and depressive symptoms in patients with COPD.

**Keywords:** COPD; anxiety symptoms; depressive symptoms; modifiable factors; symptom self-management.

SUPPLEMENTARY INFO

MeSH termsexpand

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. 2023 Apr;78(4):344-353.

doi: 10.1136/thoraxjnl-2021-218288. Epub 2022 Jun 29.

## [Subtyping emphysematous COPD by respiratory volume change distributions on CT](#)

[Hiroshi Shima](#)<sup>1</sup>, [Naoya Tanabe](#)<sup>2</sup>, [Akira Oguma](#)<sup>3</sup>, [Kaoruko Shimizu](#)<sup>3</sup>, [Shizuo Kaji](#)<sup>4</sup>, [Kunihiko Terada](#)<sup>5</sup>, [Tsuyoshi Oguma](#)<sup>1</sup>, [Takeshi Kubo](#)<sup>6</sup>, [Masaru Suzuki](#)<sup>3</sup>, [Hironi Makita](#)<sup>3,7</sup>, [Atsuyasu Sato](#)<sup>1</sup>, [Masaharu Nishimura](#)<sup>3,7</sup>, [Susumu Sato](#)<sup>1</sup>, [Satoshi Konno](#)<sup>3</sup>, [Toyohiro Hirai](#)<sup>1</sup>

Affiliations expand

- PMID: 35768196
- DOI: [10.1136/thoraxjnl-2021-218288](https://doi.org/10.1136/thoraxjnl-2021-218288)

## Abstract

**Background:** There is considerable heterogeneity among patients with emphysematous chronic obstructive pulmonary disease (COPD). We hypothesised that in addition to emphysema severity, ventilation distribution in emphysematous regions would be associated with clinical-physiological impairments in these patients.

**Objective:** To evaluate whether the discordance between respiratory volume change distributions (from expiration to inspiration) in emphysematous and non-emphysematous regions affects COPD outcomes using two cohorts.

**Methods:** Emphysema was quantified using a low attenuation volume percentage on inspiratory CT (iLAV%). Local respiratory volume changes were calculated using non-rigidly registered expiratory/inspiratory CT. The Ventilation Discordance Index (VDI) represented the log-transformed Wasserstein distance quantifying discordance between respiratory volume change distributions in emphysematous and non-emphysematous regions.

**Results:** Patients with COPD in the first cohort (n=221) were classified into minimal emphysema (iLAV% <10%; n=113) and established emphysema with high VDI and low VDI groups (n=46 and 62, respectively). Forced expiratory volume in 1 s (FEV<sub>1</sub>) was lower in the low VDI group than in the other groups, with no difference between the high VDI and minimal emphysema groups. Higher iLAV%, more severe airway disease and hyperventilated emphysematous regions in the upper-middle lobes were independently associated with lower VDI. The second cohort analyses (n=93) confirmed these findings and showed greater annual FEV<sub>1</sub> decline and higher mortality in the low VDI group than in the high VDI group independent of iLAV% and airway disease on CT.

**Conclusion:** Lower VDI is associated with severe airflow limitation and higher mortality independent of emphysema severity and airway morphological changes in patients with emphysematous COPD.

**Keywords:** COPD Pathology; Emphysema; Imaging/CT MRI etc; Lung Physiology.

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## Conflict of interest statement

Competing interests: None declared.

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MeSH termsexpand

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J Asthma

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. 2023 Apr;60(4):718-726.

doi: 10.1080/02770903.2022.2089997. Epub 2022 Jun 25.

# [Asthma, chronic obstructive pulmonary disease, and asthma-COPD overlap among US working adults](#)

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

[Affiliations expand](#)

- PMID: 35696621
- DOI: [10.1080/02770903.2022.2089997](https://doi.org/10.1080/02770903.2022.2089997)

## Abstract

**Background:** Asthma-COPD overlap (ACO) is a respiratory condition with more severe respiratory symptoms, poorer quality of life, and increased hospital admissions compared with asthma or COPD alone.

**Objectives:** Estimate asthma, chronic obstructive pulmonary disease (COPD), and ACO prevalence among workers by industry and occupation and assess physical and mental health status, healthcare utilization, among workers with ACO.

**Methods:** The 2014-2018 National Health Interview Survey (NHIS) data for working adults aged  $\geq 18$  years employed (sample  $n = 99,424$ ) in the 12 months prior to the survey were analyzed. Age-adjusted ACO, COPD and asthma prevalence and prevalence ratios adjusted for age, sex, race and smoking status were estimated.

**Results:** During 2014-2018, of the estimated 166 million (annual average) US workers, age-adjusted asthma, COPD, and ACO prevalence was 6.9%, 4.0%, and 1.1%, respectively. ACO prevalence was highest among workers aged  $\geq 65$  years (2.0%), females (1.6%), current smokers (1.9%), those living below the federal poverty level (2.3%), and workers in the accommodation and food services (1.6%) industry and personal care and service (2.3%) occupations. Workers with ACO had more frequent ( $p < 0.05$ ) physician office visits, emergency department visits; and were more likely to be in poorer mental health, obese, have more lost workdays, more bed days, and comorbidities compared to workers with asthma alone and workers with COPD alone. **Conclusion:** Higher ACO prevalence among worker groups and increased healthcare utilization underscores the need for early identification of asthma and COPD, assessment of potential workplace exposures, and implementation of tailored interventions to reduce ACO among working adults.

**Keywords:** Asthma-COPD overlap; exposures; occupation; prevalence industry; workers; workplace.

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MeSH termsexpand

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Acad Radiol

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. 2023 Apr;30(4):707-716.

doi: 10.1016/j.acra.2022.05.009. Epub 2022 Jun 8.

## [Quantitative CT Lung Imaging and Machine Learning Improves Prediction of Emergency Room Visits and Hospitalizations in COPD](#)



- PMID: 35690537
- DOI: [10.1016/j.acra.2022.05.009](https://doi.org/10.1016/j.acra.2022.05.009)

## Abstract

**Rationale:** Predicting increased risk of future healthcare utilization in chronic obstructive pulmonary disease (COPD) patients is an important goal for improving patient management.

**Objective:** Our objective was to determine the importance of computed tomography (CT) lung imaging measurements relative to other demographic and clinical measurements for predicting future health services use with machine learning in COPD.

**Materials and methods:** In this retrospective study, lung function measurements and chest CT images were acquired from Canadian Cohort of Obstructive Lung Disease study participants from 2010 to 2017 (<https://clinicaltrials.gov>, [NCT00920348](https://clinicaltrials.gov/ct2/show/study?term=NCT00920348)). Up to two follow-up visits (1.5- and 3-year follow-up) were performed and participants were asked for details related to healthcare utilization. Healthcare utilization was defined as any COPD hospitalization or emergency room visit due to respiratory problems in the 12 months prior to the follow-up visits. CT analysis was performed (VIDA Diagnostics Inc.); a total of 108 CT quantitative emphysema, airway and vascular measurements were investigated. A hybrid feature selection method with support vector machine classifier was used to predict healthcare utilization. Performance was determined using accuracy, F1-measure and area under the receiver operating characteristic curve (AUC) and Matthews's correlation coefficient (MC).

**Results:** Of the 527 COPD participants evaluated, 179 (35%) used healthcare services at follow-up. There were no significant differences between the participants with or without healthcare utilization at follow-up for age ( $p = 0.50$ ), sex ( $p = 0.44$ ), BMI ( $p = 0.05$ ) or pack-years ( $p = 0.76$ ). The accuracy for predicting subsequent healthcare utilization was  $80\% \pm 3\%$  (F1-measure = 74%, AUC = 0.80, MC = 0.6) when all measurements were considered,  $76\% \pm 6\%$  (F1-measure = 72%, AUC = 0.77, MC = 0.55) for CT measurements alone and  $65\% \pm 5\%$  (F1-measure = 60%, AUC = 0.67, MC = 0.34) for demographic and lung function measurements alone.

**Conclusion:** The combination of CT lung imaging and conventional measurements leads to greater prediction accuracy of subsequent health services use than conventional measurements alone, and may provide needed prognostic information for patients suffering from COPD.

**Keywords:** COPD; Computed tomography; Hospitalization; Machine learning; Quantitative imaging.

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MeSH terms, Associated dataexpand

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Clin Rev Allergy Immunol

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. 2023 Apr;64(2):161-178.

doi: 10.1007/s12016-022-08928-y. Epub 2022 Mar 11.

# The Airway Microbiome-IL-17 Axis: a Critical Regulator of Chronic Inflammatory Disease

[Jenny M Mannion](#)<sup>1</sup>, [Rachel M McLoughlin](#)<sup>1</sup>, [Stephen J Lalor](#)<sup>2</sup>

Affiliations expand

- PMID: 35275333
- PMCID: [PMC10017631](#)
- DOI: [10.1007/s12016-022-08928-y](#)

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## Abstract

The respiratory tract is home to a diverse microbial community whose influence on local and systemic immune responses is only beginning to be appreciated. Increasing reports have linked changes in this microbiome to a range of pulmonary and extrapulmonary disorders, including asthma, chronic obstructive pulmonary disease and rheumatoid arthritis. Central to many of these findings is the role of IL-17-type immunity as an important driver of inflammation. Despite the crucial role played by IL-17-mediated immune responses in protection against infection, overt Th17 cell responses have been implicated in the pathogenesis of several chronic inflammatory diseases. However, our knowledge of the influence of bacteria that commonly colonise the respiratory tract on IL-17-driven inflammatory responses remains sparse. In this article, we review the current knowledge on the role of specific members of the airway microbiota in the modulation of IL-17-

type immunity and discuss how this line of research may support the testing of susceptible individuals and targeting of inflammation at its earliest stages in the hope of preventing the development of chronic disease.

**Keywords:** Airway microbiota; Chronic inflammatory disease; IL-17; Respiratory tract; Th17 cells.

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## Conflict of interest statement

The authors declare no competing interests.

- [Cited by 2 articles](#)
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## SUPPLEMENTARY INFO

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. 2023 Apr;78(4):394-401.

doi: 10.1136/thoraxjnl-2021-217710. Epub 2021 Dec 1.

# [CT pectoralis muscle area is associated with DXA lean mass and correlates with emphysema progression in a tobacco-exposed cohort](#)

[Michael Emmet O'Brien](#)<sup>#1</sup>, [Richard H Zou](#)<sup>#1</sup>, [Nathan Hyre](#)<sup>2</sup>, [Joseph K Leader](#)<sup>3</sup>, [Carl R Fuhrman](#)<sup>3</sup>, [Frank C Sciurba](#)<sup>1</sup>, [Mehdi Nouraie](#)<sup>1</sup>, [Jessica Bon](#)<sup>4</sup>

Affiliations [expand](#)

- PMID: 34853157
- PMCID: [PMC9156725](#)
- DOI: [10.1136/thoraxjnl-2021-217710](#)

## Abstract

**Introduction:** Muscle loss is an important extrapulmonary manifestation of COPD. Dual energy X-ray absorptiometry (DXA) is the method of choice for body composition measurement but is not widely used for muscle mass evaluation. The pectoralis muscle area (PMA) is quantifiable by CT and predicts cross-sectional COPD-related morbidity. There are no studies that compare PMA with DXA measures or that evaluate longitudinal relationships between PMA and lung disease progression.

**Methods:** Participants from our longitudinal tobacco-exposed cohort had baseline and 6-year chest CT (n=259) and DXA (n=164) data. Emphysema was quantified by CT density histogram parenchymal scoring using the 15th percentile technique. Fat-free mass index (FFMI) and appendicular skeletal mass index (ASMI) were calculated from DXA measurements. Linear regression model relationships were reported using standardised coefficient ( $\beta$ ) with 95% CI.

**Results:** PMA was more strongly associated with DXA measures than with body mass index (BMI) in both cross-sectional (FFMI:  $\beta=0.76$  (95% CI 0.65 to 0.86),  $p<0.001$ ; ASMI:  $\beta=0.76$  (95% CI 0.66 to 0.86),  $p<0.001$ ; BMI:  $\beta=0.36$  (95% CI 0.25 to 0.47),  $p<0.001$ ) and longitudinal ( $\Delta$ FFMI:  $\beta=0.43$  (95% CI 0.28 to 0.57),  $p<0.001$ ;  $\Delta$ ASMI:  $\beta=0.42$  (95% CI 0.27 to 0.57),  $p<0.001$ ;  $\Delta$ BMI:  $\beta=0.34$  (95% CI 0.22 to 0.46),  $p<0.001$ ) models. Six-year change in PMA was associated with 6-year change in emphysema ( $\beta=0.39$  (95% CI 0.23 to 0.56),  $p<0.001$ ) but not with 6-year change in airflow obstruction.

**Conclusions:** PMA is an accessible measure of muscle mass and may serve as a useful clinical surrogate for assessing skeletal muscle loss in smokers. Decreased PMA correlated with emphysema progression but not lung function decline, suggesting a difference in the pathophysiology driving emphysema, airflow obstruction and comorbidity risk.

**Keywords:** emphysema; imaging/CT MRI etc; respiratory muscles; tobacco and the lung.

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## Conflict of interest statement

Competing interests: None declared.

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Randomized Controlled Trial

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. 2023 Apr;78(4):326-334.

doi: 10.1136/thoraxjnl-2020-216509. Epub 2021 Oct 16.

# [Automatic oxygen titration versus constant oxygen flow rates during walking in COPD: a randomised controlled, double-blind, crossover trial](#)

[Tessa Schneeberger](#)<sup>1,2</sup>, [Inga Jarosch](#)<sup>3,2</sup>, [Daniela Leidl](#)<sup>3,2</sup>, [Rainer Gloeckl](#)<sup>3,2</sup>, [Wolfgang Hitzl](#)<sup>4,5,6</sup>, [Clancy John Dennis](#)<sup>7</sup>, [Tatjana Geyer](#)<sup>8</sup>, [Carl-Peter Criée](#)<sup>9</sup>, [Andreas Rembert Koczulla](#)<sup>3,2,10,11</sup>, [Klaus Kenn](#)<sup>3,2,10</sup>

Affiliations expand

- PMID: 34656996
- DOI: [10.1136/thoraxjnl-2020-216509](https://doi.org/10.1136/thoraxjnl-2020-216509)

Free article

## Abstract

**Rationale:** In patients with COPD, oxygen (O<sub>2</sub>)-supplementation via a constant flow oxygen system (CFOS) can result in insufficient oxygen saturation (SpO<sub>2</sub> <90%) during exercise. An automatically titrating O<sub>2</sub>-system (ATOS) has been shown to be beneficial compared with an untitrated CFOS, however, it is unknown if ATOS is superior to CFOS, titrated during exercise as

stipulated by guidelines. The aim was to investigate the effects of ATOS compared with titrated CFOS on walking capacity in people with hypoxaemic COPD.

**Methods:** Fifty participants completed this prospective randomised controlled, double-blind, crossover trial. Participants performed two endurance shuttle walk tests (ESWTs) with: (1) exercise titrated CFOS (ESWT<sub>CFOS</sub>) and (2) ATOS targeting an SpO<sub>2</sub> of 92% (ESWT<sub>ATOS</sub>). Primary outcome measure was walking time. Secondary measures were SpO<sub>2</sub>, transcutaneous-PCO<sub>2</sub> (TcPCO<sub>2</sub>), respiratory rate (RR), heart rate (HR) at isotime (end of shortest ESWT) with blood gases and dyspnoea at rest and end exercise.

**Results:** Participants (median (IQR): age 66 (59, 70) years, FEV<sub>1</sub> 28.8 (24.8, 35.1) % predicted, PO<sub>2</sub> 54.7 (51.0, 57.7) mm Hg, PCO<sub>2</sub> 44.2 (38.2, 47.8) mm Hg) walked significantly longer with ESWT<sub>ATOS</sub> in comparison to ESWT<sub>CFOS</sub> (median effect (95% CI) +144.5 (54 to 241.5) s, p<0.001). At isotime, SpO<sub>2</sub> was significantly higher (+3 (95% CI 1 to 4) %, p<0.001) with ATOS while TcPCO<sub>2</sub>, RR and HR were comparable. End exercise, PO<sub>2</sub> (+8.85 (95% CI 6.35 to 11.9) mm Hg) and dyspnoea (-0.5 (95% CI -1.0 to -0.5) points) differed significantly in favour of ATOS (each p<0.001) while PCO<sub>2</sub> was comparable.

**Conclusion:** In patients with hypoxaemia with severe COPD the use of ATOS leads to significant, clinically relevant improvements in walking endurance time, SpO<sub>2</sub>, PO<sub>2</sub> and dyspnoea with no impact on PCO<sub>2</sub>.

**Trial registration number:** [NCT03803384](https://www.clinicaltrials.gov/ct2/show/study?term=NCT03803384).

**Keywords:** COPD pathology; ambulatory oxygen therapy; exercise.

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## Conflict of interest statement

Competing interests: None declared.

- [Cited by 2 articles](#)

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Publication types, MeSH terms, Substances, Associated dataexpand

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# ASTHMA

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. 2023 Mar 31;4(1):36.

doi: 10.1186/s43058-023-00417-3.

## Creating implementable clinical practice guidelines: the 2020 Focused Updates to the National Heart, Lung, and Blood Institute's Asthma Management Guidelines

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Affiliations expand

- PMID: 37003961
- DOI: [10.1186/s43058-023-00417-3](https://doi.org/10.1186/s43058-023-00417-3)

## Abstract

**Background:** The 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group provides the first new clinical practice recommendations from the National Heart, Lung, and Blood Institute (NHLBI) since the previous 2007 asthma management guidelines. Guideline implementability was a high priority for the expert panel, and many approaches were undertaken to enhance the implementability of this clinical guideline update. Within the report, specific implementation guidance sections provide expanded summaries for each recommendation to quickly assist users. The implementation guidance incorporates findings from NHLBI-sponsored focus groups conducted with people who have asthma, caregivers, and health care providers. The

findings were used to identify the types of information and tools that individuals with asthma, their caregivers, and their health care providers would find most helpful; ensure that the new asthma guidelines reflect the voices of individuals with asthma and their caregivers; and identify potential barriers to uptake by individuals with asthma and their caregivers. The expert panel used a GRADE-based approach to develop evidence-to-decision tables that provided a framework for assessing the evidence and consideration of a range of contextual factors that influenced the recommendations such as desirable and undesirable effects, certainty of evidence, values, balance of effects, acceptability, feasibility, and equity. To facilitate uptake in clinical care workflow, selected recommendations were converted into structured, computer-based clinical decision support artifacts, and the new recommendations were integrated into existing treatment tables used in the 2007 asthma management guidelines, with which many users are familiar. A comprehensive approach to improve guidelines dissemination and implementation included scientific publications, patient materials, media activities, stakeholder engagement, and professional education.

**Conclusion:** We developed evidence-based clinical practice guideline updates for asthma management focused on six topic areas. The guideline development processes and implementation and dissemination activities undertaken sought to enhance implementability by focusing on intrinsic factors as described by Kastner, Gagliardi, and others to produce usable, adoptable, and adaptable guidelines. Enhanced collaboration during guideline development between authors, informaticists, and implementation scientists may facilitate the development of tools that support the application of recommendations to further improve implementability.

**Keywords:** Asthma; Clinical decision support; Guidelines; Implementability.

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J Healthc Qual Res

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. 2023 Mar 30;S2603-6479(23)00018-0.



# Quality indicators in the rational management of severe asthma: A Spanish multidisciplinary consensus

[A Crespo-Lessmann](#)<sup>1</sup>, [J A Marqués-Espi](#)<sup>2</sup>, [J Dominguez-Ortega](#)<sup>3</sup>, [L Perez de Llano](#)<sup>4</sup>, [M Blanco-Aparicio](#)<sup>5</sup>, [M Santiñá](#)<sup>6</sup>, [M Palop-Cervera](#)<sup>7</sup>, [F J Álvarez](#)<sup>8</sup>, [J Fraj](#)<sup>9</sup>

Affiliations expand

- PMID: 37003928
- DOI: [10.1016/j.jhqr.2023.03.003](https://doi.org/10.1016/j.jhqr.2023.03.003)

## Abstract

**Aim:** Severe asthma is a complex, heterogeneous condition that can be difficult to control despite currently available treatments. Multidisciplinary severe asthma units (SAU) improve control in these patients and are cost-effective in our setting; however, their implementation and development can represent an organizational challenge. The aim of this study was to validate a set of quality care indicators in severe asthma for SAU in Spain.

**Methods:** The Carabela initiative, sponsored by SEPAR, SEAIC, SECA and SEDISA and implemented by leading specialists, analyzed the care processes followed in 6 pilot centers in Spain to describe the ideal care pathway for severe asthma. This analysis, together with clinical guidelines and SEPAR and SEAIC accreditation criteria for asthma units, were used to draw up a set of 11 quality of care indicators, which were validated by a panel of 60 experts (pulmonologists, allergologists, and health-policy decision-makers) using a modified Delphi method.

**Results:** All 11 indicators achieved a high level of consensus after just one Delphi round.

**Conclusions:** Experts in severe asthma agree on a series of minimum requirements for the future optimization, standardization, and excellence of current SAUs in Spain. This proposal is well grounded on evidence and professional experience, but the validity of these consensus indicators must be evaluated in clinical practice.

**Keywords:** Asma; Asthma; Calidad asistencial; Care units; Consenso Delphi; Delphi consensus; Indicadores; Indicators; Quality of care; Unidades asistenciales.

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Chest

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. 2023 Mar 30;S0012-3692(23)00462-2.

doi: 10.1016/j.chest.2023.03.034. Online ahead of print.

# The fungal microbiome of the upper airway is associated with future loss of asthma control and exacerbation among children with asthma

[Hanshu Yuan](#)<sup>1</sup>, [Zhongmao Liu](#)<sup>2</sup>, [Jinhong Dong](#)<sup>1</sup>, [Leonard B Bacharier](#)<sup>3</sup>, [Daniel Jackson](#)<sup>4</sup>, [David Mauger](#)<sup>5</sup>, [Homer Boushey](#)<sup>6</sup>, [Mario Castro](#)<sup>7</sup>, [Juliana Durack](#)<sup>8</sup>, [Yvonne J Huang](#)<sup>9</sup>, [Robert F Lemanske Jr](#)<sup>4</sup>, [Gregory A Storch](#)<sup>10</sup>, [George M Weinstock](#)<sup>11</sup>, [Kristine Wylie](#)<sup>10</sup>, [Ronina Covar](#)<sup>12</sup>, [Anne M Fitzpatrick](#)<sup>13</sup>, [Wanda Phipatanakul](#)<sup>14</sup>, [Rachel G Robison](#)<sup>3</sup>, [Avraham Beigelman](#)<sup>15</sup>, [Yanjiao Zhou](#)<sup>1</sup>

Affiliations expand

- PMID: 37003356
- DOI: [10.1016/j.chest.2023.03.034](https://doi.org/10.1016/j.chest.2023.03.034)

## Abstract

**Background:** Accumulating evidence suggests that the upper airway bacterial microbiota is implicated in asthma inception, severity, and exacerbation. Unlike bacterial microbiota, the role of the upper airway fungal microbiome (mycobiome) in asthma control is poorly understood.

**Research question:** What are the upper-airway fungal colonization patterns among asthmatic children and their relationship with subsequent loss of asthma control and exacerbation of asthma?

**Study design and methods:** The study was coupled with the Step Up Yellow Zone Inhaled Corticosteroids to Prevent Exacerbations (STICS; [NCT02066129](#)) clinical trial. The upper airway mycobiome was investigated using ITS1 sequencing of nasal blow samples collected from children with asthma when asthma was well controlled (baseline, n=194) and during early signs of loss of asthma control (yellow zone (YZ), n=107).

**Results:** At baseline, 499 fungal genera were detected in the upper-airway samples, with two commensal fungal species *Malassezia globosa* and *Malassezia restricta* being most dominant. The relative abundance of *Malassezia* species vary by age, BMI, and race. Higher relative abundance of *Malassezia globosa* at baseline were associated with lower risk of future YZ episodes ( $p=0.038$ ), and longer time to develop first episode of YZ ( $p=0.022$ ). Higher relative abundance of *Malassezia globosa* at YZ was associated with lower risk of progression from YZ to severe asthma exacerbation ( $p=0.04$ ). The upper airway mycobiome underwent significant changes from baseline to YZ, and increased fungal diversity was highly correlated with increased bacterial diversity ( $\rho=0.41$ ).

**Interpretation:** The upper airway commensal mycobiome is associated with future asthma control. This work highlights the importance of the mycobiota in asthma control and may contribute to the development of fungi-based markers to predict asthma exacerbation.

**Keywords:** Fungi; *Malassezia*; asthma; mycobiome; upper airway.

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Chest

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. 2023 Mar 30;S0012-3692(23)00463-4.

doi: 10.1016/j.chest.2023.03.035. Online ahead of print.

## [Albuterol-budesonide pressurized metered dose inhaler in patients with mild-to-moderate asthma: results of](#)

# the DENALI double-blind randomized controlled trial

[Bradley E Chipps](#)<sup>1</sup>, [Elliot Israel](#)<sup>2</sup>, [Richard Beasley](#)<sup>3</sup>, [Reynold A Panettieri Jr](#)<sup>4</sup>, [Frank C Albers](#)<sup>5</sup>, [Robert Rees](#)<sup>6</sup>, [Lynn Dunsire](#)<sup>7</sup>, [Anna Danilewicz](#)<sup>6</sup>, [Eva Johnsson](#)<sup>8</sup>, [Christy Cappelletti](#)<sup>9</sup>, [Alberto Papi](#)<sup>10</sup>

Affiliations expand

- PMID: 37003355
- DOI: [10.1016/j.chest.2023.03.035](https://doi.org/10.1016/j.chest.2023.03.035)

## Abstract

**Background:** In the Phase 3 MANDALA trial, as-needed albuterol-budesonide pressurized metered-dose inhaler (pMDI) significantly reduced severe exacerbation risk versus as-needed albuterol in patients with moderate-to-severe asthma receiving inhaled corticosteroid-containing maintenance therapy. This study (DENALI) was conducted to address the US Food and Drug Administration Combination Rule which requires a combination product demonstrate that each component contributes to its safety or efficacy.

**Research question:** Do both albuterol and budesonide contribute to the efficacy of albuterol-budesonide combination pMDI in patients with asthma?

**Study design and methods:** This Phase 3 double-blind trial randomized patients aged  $\geq 12$  years with mild-to-moderate asthma 1:1:1:1 to four-times-daily albuterol-budesonide 180/160  $\mu\text{g}$  or 180/80  $\mu\text{g}$ , albuterol 180  $\mu\text{g}$ , budesonide 160  $\mu\text{g}$ , or placebo for 12 weeks. Dual-primary efficacy endpoints were change from baseline in forced expiratory volume area under the curve from 0-6 hours ( $\text{FEV}_1 \text{ AUC}_{0-6\text{h}}$ ) over 12 weeks (assessing albuterol effect) and trough  $\text{FEV}_1$  at Week 12 (assessing budesonide effect).

**Results:** Of 1001 patients randomized, 989 were  $\geq 12$  years and evaluable for efficacy. Change from baseline in  $\text{FEV}_1 \text{ AUC}_{0-6\text{h}}$  over 12 weeks was greater with albuterol-budesonide 180/160  $\mu\text{g}$  versus budesonide 160  $\mu\text{g}$  (least squares mean [LSM] difference [95%CI] 80.7 [28.4-132.9] mL;  $p=0.003$ ). Change in trough  $\text{FEV}_1$  at Week 12 was greater with albuterol-budesonide 180/160 and 180/80  $\mu\text{g}$  versus albuterol 180  $\mu\text{g}$  (LSM difference [95%CI] 132.8 [63.6-201.9] mL and 120.8 [51.5-190.1] mL, respectively; both  $p<0.001$ ). Day 1 time to onset and duration of bronchodilation with albuterol-budesonide was similar to albuterol. Albuterol-budesonide adverse event profile was similar to the mono-components.

**Interpretation:** Both mono-components contributed to albuterol-budesonide lung function efficacy. Albuterol-budesonide was well-tolerated, even at regular relatively high daily doses for 12 weeks, with no new safety findings, supporting its use as a novel rescue therapy.

**Keywords:** albuterol-ICS; albuterol–budesonide; asthma; bronchodilators; inflammation; inhaled corticosteroid; rescue therapy; short-acting  $\beta(2)$ -agonist.

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J Allergy Clin Immunol

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. 2023 Mar 29;S0091-6749(23)00373-1.

doi: 10.1016/j.jaci.2023.03.021. Online ahead of print.

## Type-2 inflammation reduces SARS-CoV-2 replication in the airway epithelium in allergic asthma through functional alteration of ciliated epithelial cells

[Naresh Doni Jayavelu](#)<sup>1</sup>, [Matthew C Altman](#)<sup>2</sup>, [Basilin Benson](#)<sup>3</sup>, [Matthew Dufort](#)<sup>1</sup>, [Elizabeth R Vanderwall](#)<sup>4</sup>, [Lucille M Rich](#)<sup>4</sup>, [Maria P White](#)<sup>4</sup>, [Patrice M Becker](#)<sup>5</sup>, [Alkis Togias](#)<sup>5</sup>, [Daniel J Jackson](#)<sup>6</sup>, [Jason S Debley](#)<sup>7</sup>

Affiliations expand

- PMID: 37001649

- DOI: [10.1016/j.jaci.2023.03.021](https://doi.org/10.1016/j.jaci.2023.03.021)

## Abstract

**Background:** Despite well-known susceptibilities to other respiratory viral infections, individuals with allergic asthma have shown reduced susceptibility to severe COVID-19.

**Objective:** We sought to identify mechanisms whereby type-2 inflammation in the airway protects against SARS-CoV-2 using bronchial airway epithelial cells (AECs) from aeroallergen-sensitized children with asthma and healthy non-sensitized children.

**Methods:** We measured SARS-CoV-2 replication and ACE2 protein, and performed bulk and single cell RNA-sequencing of ex vivo infected AEC samples with SARS-CoV-2 infection and with or without IL-13 treatment.

**Results:** We observed that viral replication was lower in AECs from children with allergic asthma compared to healthy non-sensitized children and that IL-13 treatment reduced viral replication only in allergic asthma but not in healthy. Lower viral transcript levels were associated with a down-regulation of functional pathways of the ciliated epithelium related to differentiation as well as cilia and axoneme production and function, rather than lower ACE2 expression or increases in goblet cells or mucus secretion pathways. Moreover, single cell RNA-sequencing identified specific subsets of relatively undifferentiated ciliated epithelium, common in allergic asthma and highly responsive to IL-13, that directly accounted for impaired viral replication.

**Conclusion:** Our results identify a novel mechanism of innate protection against SARS-CoV-2 in allergic asthma that provides important molecular and clinical insights during the ongoing COVID-19 pandemic.

**Keywords:** COVID-19; IL-13; SARS-CoV-2; airway epithelial cells; asthma; children; epithelium.

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Am J Respir Cell Mol Biol

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. 2023 Apr;68(4):456-458.

doi: 10.1165/rcmb.2022-0430LE.

# A Between-Sex Comparison of the Genomic Architecture of Asthma

[Joe G Zein](#)<sup>1</sup>, [Peter Bazeley](#)<sup>1</sup>, [Deborah Meyers](#)<sup>2</sup>, [Eugene Bleecker](#)<sup>2</sup>, [Benjamin Gaston](#)<sup>3</sup>, [Bo Hu](#)<sup>1</sup>, [Amy Attaway](#)<sup>1</sup>, [Victor Ortega](#)<sup>4</sup>

Affiliations expand

- PMID: 37000440
- DOI: [10.1165/rcmb.2022-0430LE](https://doi.org/10.1165/rcmb.2022-0430LE)

*No abstract available*

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Cancer Med

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. 2023 Mar 31.

doi: 10.1002/cam4.5875. Online ahead of print.

# Cancer incidence after asthma diagnosis: Evidence from a large clinical research network in the United States

[Yi Guo](#)<sup>1,2</sup>, [Jiang Bian](#)<sup>1,2</sup>, [Zhaoyi Chen](#)<sup>1</sup>, [Jennifer N Fiske](#)<sup>3</sup>, [Dongyu Zhang](#)<sup>2,4</sup>, [Dejana Braithwaite](#)<sup>2,4</sup>, [Thomas J George](#)<sup>1,2,5</sup>, [Elizabeth A Shenkman](#)<sup>1,2</sup>, [Jonathan D Licht](#)<sup>2,5</sup>

Affiliations expand

- PMID: 36999938

- DOI: [10.1002/cam4.5875](https://doi.org/10.1002/cam4.5875)

## Abstract

**Background:** Prior studies on the association between asthma and cancer show inconsistent results. This study aimed to generate additional evidence on the association between asthma and cancer, both overall, and by cancer type, in the United States.

**Method:** We conducted a retrospective cohort study using 2012–2020 electronic health records and claims data in the OneFlorida+ clinical research network. Our study population included a cohort of adult patients with asthma ( $n = 90,021$ ) and a matching cohort of adult patients without asthma ( $n = 270,063$ ). We built Cox proportional hazards models to examine the association between asthma diagnosis and subsequent cancer risk.

**Results:** Our results showed that asthma patients were more likely to develop cancer compared to patients without asthma in multivariable analysis (hazard ratio [HR] = 1.36, 99% confidence interval [CI] = 1.29–1.44). Elevated cancer risk was observed in asthma patients without (HR = 1.60; 99% CI: 1.50–1.71) or with (HR = 1.11; 99% CI: 1.03–1.21) inhaled steroid use. However, in analyses of specific cancer types, cancer risk was elevated for nine of 13 cancers in asthma patients without inhaled steroid use but only for two of 13 cancers in asthma patients with inhaled steroid use, suggesting a protective effect of inhaled steroid use on cancer.

**Conclusion:** This is the first study to report a positive association between asthma and overall cancer risk in the US population. More in-depth studies using real-world data are needed to further explore the causal mechanisms of asthma on cancer risk.

**Keywords:** electronic health records; inhaled steroid; prediction; real-world data; survival analysis.

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- [25 references](#)

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Rhinology

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. 2023 Mar 31.

doi: 10.4193/Rhin22.489. Online ahead of print.

# EPOS/EUFOREA update on indication and evaluation of Biologics in Chronic Rhinosinusitis with Nasal Polyps 2023

[W J Fokkens](#)<sup>1,2</sup>, [A-S Viskens](#)<sup>3,4</sup>, [V Backer](#)<sup>5</sup>, [D Conti](#)<sup>6</sup>, [E De Corso](#)<sup>6</sup>, [P Gevaert](#)<sup>7</sup>, [G K Scadding](#)<sup>8</sup>, [M Wagemann](#)<sup>9</sup>, [M Bernal-Sprekelsen](#)<sup>10,11</sup>, [A Chaker](#)<sup>12</sup>, [E Heffler](#)<sup>13,14</sup>, [J K Han](#)<sup>15</sup>, [E Van Staeyen](#)<sup>6</sup>, [C Hopkins](#)<sup>16</sup>, [J Mullol](#)<sup>17</sup>, [A Peters](#)<sup>18</sup>, [S Reitsma](#)<sup>1</sup>, [B A Senior](#)<sup>15</sup>, [P W Hellings](#)<sup>1,3,6,19</sup>

Affiliations expand

- PMID: 36999780

- DOI: [10.4193/Rhin22.489](https://doi.org/10.4193/Rhin22.489)

## Abstract

Severe chronic rhinosinusitis with nasal polyps (CRSwNP) is a debilitating disease with a significant impact on the quality of life (QoL). It is typically characterized by a type 2 inflammatory reaction and by comorbidities such as asthma, allergies and NSAID-Exacerbated Respiratory Disease (N-ERD). Here, the European Forum for Research and Education in Allergy and Airway diseases discusses practical guidelines for patients on biologic treatment. Criteria for the selection of patients who would benefit from biologics were updated. Guidelines are proposed concerning the monitoring of the drug effects that provide recognition of responders to the therapy and, subsequently, the decision about continuation, switching or discontinuation of a biologic. Furthermore, gaps in the current knowledge and unmet needs were discussed.

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[Review](#)

Eur J Med Res

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# The relationship between obstructive sleep apnea and asthma severity and vice versa: a systematic review and meta-analysis

[Donghao Wang](#)<sup>#1</sup>, [Yanyan Zhou](#)<sup>#1</sup>, [Riken Chen](#)<sup>#1,2</sup>, [Xiangxia Zeng](#)<sup>#1</sup>, [Sun Zhang](#)<sup>1</sup>, [Xiaofen Su](#)<sup>1</sup>, [Yateng Luo](#)<sup>1</sup>, [Yongkang Tang](#)<sup>1</sup>, [Shiwei Li](#)<sup>1</sup>, [Zhiyang Zhuang](#)<sup>1</sup>, [Dongxing Zhao](#)<sup>1</sup>, [Yingying Ren](#)<sup>3</sup>, [Nuofu Zhang](#)<sup>4</sup>

Affiliations expand

- PMID: 36998095
- PMCID: [PMC10062016](#)
- DOI: [10.1186/s40001-023-01097-4](#)

## Abstract

**Background:** There is a great association between the prevalence of obstructive sleep apnea (OSA) and asthma. Nonetheless, whether OSA impacts lung function, symptoms, and control in asthma and whether asthma increases the respiratory events in OSA are unknown. This meta-analysis aimed to examine the relationship between obstructive sleep apnea and asthma severity and vice versa.

**Methods:** We carried out a systematic search of PubMed, EMBASE, and Scopus from inception to September 2022. Primary outcomes were lung function, parameters of polysomnography, the risk of OSA in more severe or difficult-to-control asthmatic patients, and the risk of asthma in patients with more severe OSA. Heterogeneity was examined with the Q test and  $I^2$  statistics. We also performed subgroup analysis, Meta-regression, and Egger's test for bias analysis.

**Results:** 34 studies with 27,912 subjects were totally included. The results showed that the comorbidity of OSA aggravated lung function in asthmatic patients with a consequent decreased forced expiratory volume in one second %predicted (%FEV1) and the effect was particularly evident in children. %FEV1 tended to decrease in adult asthma patients

complicated with OSA, but did not reach statistical significance. Interestingly, the risk of asthma seemed to be slightly lower in patients with more severe OSA (OR = 0.87, 95%CI 0.763-0.998). Asthma had no significant effect on polysomnography, but increased daytime sleepiness assessed by the Epworth Sleepiness Scale in OSA patients (WMD = 0.60, 95%CI 0.16-1.04). More severe asthma or difficult-to-control asthma was independently associated with OSA (odds ratio (OR) = 4.36, 95%CI 2.49-7.64).

**Conclusion:** OSA was associated with more severe or difficult-to-control asthma with decreased %FEV<sub>1</sub> in children. The effect of OSA on lung function in adult patients should be further confirmed. Asthma increased daytime sleepiness in OSA patients. More studies are warranted to investigate the effect of asthma on OSA severity and the impact of different OSA severity on the prevalence of asthma. It is strongly recommended that people with moderate-to-severe or difficult-to-control asthma screen for OSA and get the appropriate treatment.

**Keywords:** Asthma; Daytime sleepiness; Lung function; Obstructive sleep apnea; Polysomnography.

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## Conflict of interest statement

Non-financial disclosure. All authors declared no competing interests. All authors have seen and approved the manuscript. The authors have no competing interests.

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

## SUPPLEMENTARY INFO

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Allergy Asthma Clin Immunol

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. 2023 Mar 30;19(1):26.

doi: 10.1186/s13223-023-00782-7.

# Clinical outcomes of dupilumab therapy in chronic rhinosinusitis with nasal polyps in a Canadian tertiary care rhinology practice

[Elysia Grose](#) <sup>#1</sup>, [Alyssa Y Li](#) <sup>#2</sup>, [John M Lee](#) <sup>3</sup>

Affiliations expand

- PMID: 36998065
- PMCID: [PMC10061739](#)
- DOI: [10.1186/s13223-023-00782-7](#)

## Abstract

**Background:** In 2020, dupilumab became the first monoclonal antibody therapy to be approved by Health Canada for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP). The primary aim of this study was to characterize the outcomes in an initial cohort of patients with CRSwNP who have undergone dupilumab therapy.

**Methods:** A retrospective study was conducted of patients with CRSwNP who were treated with dupilumab. Demographic information, comorbidities, number of previous surgeries, and insurance information were collected. The primary outcome were changes in the sinonasal outcome test (SNOT-22) scores from baseline to timepoints after receiving dupilumab.

**Results:** Forty-eight patients were considered for dupilumab therapy, and 27 (56%) received coverage or were able to fund the medication independently. Patients waited an average of 3.6 months to obtain access to the medication. The mean age of the patients was 43. Forty-one percent (11/27) of patients had aspirin exacerbated respiratory disease, and 96% (26/27) had a diagnosis of asthma. The mean length of time on dupilumab was 12.1 months. The baseline SNOT-22 score was 60.6. The mean decrease at 1 month, 3 months, 6 months, and 12 months after starting dupilumab was 8.8, 26.5, 42.8, and 33.8, respectively. There were no serious adverse events.

**Conclusion:** Patients treated with dupilumab in a Canadian tertiary care rhinology clinic demonstrated substantial clinical improvement as measured by disease-specific sinonasal

outcomes. Further studies are needed to determine the longer-term effectiveness and adverse event profile of this novel therapy.

**Keywords:** Asthma; Biologics; Chronic rhinosinusitis; Endoscopic sinus surgery; Sinonasal outcomes.

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## Conflict of interest statement

J.M.L. has received research grants and honoraria from Baxter corporation. All other authors declare no potential competing interest.

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

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BMJ Open

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. 2023 Mar 30;13(3):e064311.

doi: 10.1136/bmjopen-2022-064311.

# Loss to 5-year follow-up in the population-based Telemark Study: risk factors and potential for bias

[Nikola Zivadinovic](#)<sup>1,2</sup>, [Regine Abrahamsen](#)<sup>3</sup>, [Maiju Pesonen](#)<sup>4</sup>, [Anthony Wagstaff](#)<sup>2,5</sup>, [Kjell Torén](#)<sup>6</sup>, [Paul K Henneberger](#)<sup>7</sup>, [Johny Kongerud](#)<sup>8</sup>, [Anne Kristin Moeller Fell](#)<sup>3,2</sup>

Affiliations expand

- PMID: 36997259
- DOI: [10.1136/bmjopen-2022-064311](https://doi.org/10.1136/bmjopen-2022-064311)

**Free article**

# Abstract

**Objectives:** This study aimed to characterise participants lost to follow-up and identify possible factors associated with non-participation in a prospective population-based study of respiratory health in Norway. We also aimed to analyse the impact of potentially biased risk estimates associated with a high proportion of non-responders.

**Design:** Prospective 5-year follow-up study.

**Setting:** Randomly selected inhabitants from the general population of Telemark County in south-eastern Norway were invited to fill in a postal questionnaire in 2013. Responders in 2013 were followed-up in 2018.

**Participants:** 16 099 participants aged 16–50 years completed the baseline study. 7958 responded at the 5-year follow-up, while 7723 did not.

**Main outcome measures:**  $\chi^2$  test was performed to compare demographic and respiratory health-related characteristics between those who participated in 2018 and those who were lost to follow-up. Adjusted multivariable logistic regression models were used to assess the relationship between loss to follow-up, background variables, respiratory symptoms, occupational exposure and interactions, and to analyse whether loss to follow-up leads to biased risk estimates.

**Results:** 7723 (49%) participants were lost to follow-up. Loss to follow-up was significantly higher for male participants, those in the youngest age group (16–30 years), those in lowest education level category and among current smokers (all  $p < 0.001$ ). In multivariable logistic regression analysis, loss to follow-up was significantly associated with unemployment (OR 1.34, 95% CI 1.22 to 1.46), reduced work ability (1.48, 1.35 to 1.60), asthma (1.22, 1.10 to 1.35), being woken by chest tightness (1.22, 1.11 to 1.34) and chronic obstructive pulmonary disease (1.81, 1.30 to 2.52). Participants with more respiratory symptoms and exposure to vapour, gas, dust and fumes (VGDF) (1.07 to 1.00–1.15), low-molecular weight (LMW) agents (1.19, 1.00 to 1.41) and irritating agents (1.15, 1.05 to 1.26) were more likely to be lost to follow-up. We found no statistically significant association of wheezing and exposure to LMW agents for all participants at baseline (1.11, 0.90 to 1.36), responders in 2018 (1.12, 0.83 to 1.53) and those lost to follow-up (1.07, 0.81 to 1.42).

**Conclusion:** The risk factors for loss to 5-year follow-up were comparable to those reported in other population-based studies and included younger age, male gender, current smoking, lower educational level and higher symptom prevalence and morbidity. We found that exposure to VGDF, irritating and LMW agents can be risk factors associated with loss to follow-up. Results suggest that loss to follow-up did not affect estimates of occupational exposure as a risk factor for respiratory symptoms.

**Keywords:** EPIDEMIOLOGY; OCCUPATIONAL & INDUSTRIAL MEDICINE; RESPIRATORY MEDICINE (see Thoracic Medicine).

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## Conflict of interest statement

Competing interests: None declared.

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Editorial

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. 2023 Mar 30;61(3):2202307.

doi: 10.1183/13993003.02307-2022. Print 2023 Mar.

# If your patient with asthma wheezes when sitting or lying quietly, lung function testing may reveal small airway disease

[Peter B Noble](#)<sup>1</sup>, [Graham M Donovan](#)<sup>2</sup>

Affiliations expand

- PMID: 36997235
- DOI: [10.1183/13993003.02307-2022](https://doi.org/10.1183/13993003.02307-2022)

*No abstract available*

## Conflict of interest statement

Conflict of interest: None declared.

## Comment on

- [Development of a tool to detect small airways dysfunction in asthma clinical practice.](#)

Kocks J, van der Molen T, Voorham J, Baldi S, van den Berge M, Brightling C, Fabbri LM, Kraft M, Nicolini G, Papi A, Rabe KF, Siddiqui S, Singh D, Vonk J, Leving M, Flokstra-de Blok B. *Eur Respir J*. 2023 Mar 30;61(3):2200558. doi: 10.1183/13993003.00558-2022. Print 2023 Mar. PMID: 36517179 **Free PMC article.**

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. 2023 Mar 30;61(3):2202202.

doi: 10.1183/13993003.02202-2022. Print 2023 Mar.

# Not just an anti-eosinophil drug: tezepelumab treatment for type 2 asthma and beyond

[Jonathan Corren](#)<sup>1</sup>, [Christopher E Brightling](#)<sup>2</sup>, [Louis-Philippe Boulet](#)<sup>3</sup>, [Celeste Porsbjerg](#)<sup>4</sup>, [Michael E Wechsler](#)<sup>5</sup>, [Andrew Menzies-Gow](#)<sup>6</sup>, [Christopher S Ambrose](#)<sup>7</sup>, [Bill Cook](#)<sup>7</sup>, [Neil Martin](#)<sup>2,8</sup>, [Joseph Spahn](#)<sup>9</sup>, [Jean-Pierre Llanos](#)<sup>10</sup>

Affiliations [expand](#)

- PMID: 36997233



- DOI: [10.1183/13993003.02202-2022](https://doi.org/10.1183/13993003.02202-2022)

*No abstract available*

## Conflict of interest statement

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## Comment on

- [Combination therapy with long-acting bronchodilators and the risk of major adverse cardiovascular events in patients with COPD: a systematic review and meta-analysis.](#)

Yang M, Li Y, Jiang Y, Guo S, He JQ, Sin DD. *Eur Respir J*. 2023 Feb 9;61(2):2200302. doi: 10.1183/13993003.00302-2022. Print 2023 Feb. PMID: 36137586

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J Allergy Clin Immunol Pract

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. 2023 Mar 28;S2213-2198(23)00344-6.

doi: 10.1016/j.jaip.2023.03.034. Online ahead of print.

# [A systematic review of patient-reported adherence measures in asthma: Which questionnaire is most useful in clinical practice?](#)

[Sophia Quirke-McFarlane](#)<sup>1</sup>, [John Weinman](#)<sup>2</sup>, [Gráinne d'Ancona](#)<sup>3</sup>

Affiliations expand

- PMID: 36997118
- DOI: [10.1016/j.jaip.2023.03.034](https://doi.org/10.1016/j.jaip.2023.03.034)

## Abstract

**Background:** Suboptimal adherence to inhaled corticosteroid (ICS) in asthma is a worryingly prevalent yet modifiable factor in uncontrolled disease. Several objective measures of adherence exist, but they are time consuming. The use of patient-reported adherence measures (PRAMs) could therefore offer a time-efficient pragmatic approach to adherence assessment in clinical practice and potentially the appropriate interventions to improve it.

**Objectives:** To identify the PRAMs available for asthma and assess their psychometric quality, accessibility and usefulness in clinical practice. Moreover, to provide recommendations for clinicians based on the aforementioned findings.

**Methods:** A systematic review of six databases was conducted. Articles included in this study were: English language full-text original asthma-specific PRAMs or development/validation studies of a generic PRAM that had been administered to adults with asthma; investigated ICS adherence in adults ( $\geq 18$  years old); and assessed at least one CONsensus-based Standards for the selection of health Measurement INstruments (COSMIN) measurement property.

**Results:** 15 PRAM developmental and/or validation studies were included in this systematic review. Studies evaluated a range of COSMIN measurement properties, but none evaluated them all.

**Conclusion:** On the basis of this review, we recommend that if a PRAM is used, that it be the Test of the Adherence to Inhalers (TAI). However, the Adherence Starts with Knowledge-20 (ASK-20), and Adherence Starts with Knowledge-12 (ASK-12) may also be useful. Our results highlight the need for PRAM developers to robustly assess questionnaires and to provide guidance for clinicians on how to act upon PRAM answers by developing materials such as decision support toolkits.

**Keywords:** Adherence; Adults; Assessment; Asthma; COSMIN; Compliance; Inhaled corticosteroid; Patient-reported outcome instrument; Recommendations; Systematic Review.

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Int Arch Allergy Immunol

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. 2023 Mar 30;1-8.

doi: 10.1159/000529760. Online ahead of print.

## [Evaluation of the Clinical Features and Laboratory Data of Patients with Severe Eosinophilic Asthma Classified as Super-Responders, Partial Responders,](#)

# or Nonresponders to Mepolizumab Treatment: A Real-Life Study

[Mehmet Erdem Cakmak](#)<sup>1</sup>, [Nida Öztop](#)<sup>1</sup>, [Osman Ozan Yeğit](#)<sup>1</sup>, [Özlem Özdedeoğlu](#)<sup>1</sup>

Affiliations expand

- PMID: 36996772
- DOI: [10.1159/000529760](https://doi.org/10.1159/000529760)

## Abstract

**Introduction:** Mepolizumab is a treatment option in patients with severe eosinophilic asthma, which inhibits interleukin-5. The aim of this study was to evaluate the clinical features and laboratory data of patients with severe eosinophilic asthma who were classified as super-responders, partial responders, or nonresponders to mepolizumab treatment.

**Methods:** In this retrospective real-life study, the clinical features and laboratory data were compared between groups of patients with severe eosinophilic asthma who were classified as super-responders, partial responders, or nonresponders to mepolizumab treatment.

**Results:** Evaluation was made of a total of 55 patients, comprising 17 (30.9%) males and 38 (69.1%) females with a mean age of  $51.28 \pm 14.32$  years. All the patients were receiving mepolizumab treatment for severe eosinophilic asthma, with 17 (30.9%) patients evaluated as super-responders, 26 (47.3%) as partial responders, and 12 (21.8%) as nonresponders. After mepolizumab treatment, there was a statistically significant decrease in asthma exacerbations, the number of oral corticosteroids (OCSs) used, the rate of hospitalization due to asthma attacks, and the eosinophil count (cells/ $\mu$ L) ( $p < 0.001$ ,  $p < 0.001$ ,  $p < 0.001$ , and  $<0.001$ , respectively). A statistically significant increase was determined in the forced expiratory volume in 1 s (FEV1) value ( $p = 0.010$ ) and asthma control test (ACT) score ( $p < 0.001$ ) after mepolizumab treatment. The baseline eosinophil count, eosinophil/lymphocyte ratio and FEV1 (%) values were significantly higher in the super-responder and partial responder groups ( $p < 0.001$ ,  $p = 0.002$ , and  $p = 0.002$ , respectively). The baseline ACT score and the rate of chronic sinusitis with nasal polyps were significantly higher in the partial responder group ( $p = 0.004$ ,  $p = 0.015$ , respectively). The rate of regular OCS use before mepolizumab treatment was significantly higher in the nonresponder group ( $p = 0.049$ ). As a result of the receiver operating characteristics curve analysis, the blood eosinophil count (area under the curve [AUC]: 0.967,  $p < 0.001$ ), eosinophil/lymphocyte ratio (AUC: 0.921,  $p < 0.001$ ), and FEV1 (%) (AUC: 0.828,  $p = 0.002$ ) were found to have

diagnostic value in predicting the response to mepolizumab treatment in patients with severe eosinophilic asthma.

**Conclusion:** Baseline eosinophil count, eosinophil/lymphocyte ratio, and FEV1 (%) were found to be important predictors of response to mepolizumab treatment. Further studies are needed to define the characterization of mepolizumab responders in the real world.

**Keywords:** Antiasthmatic agents; Asthma; Interleukin 5; Mepolizumab; Treatment efficacy.

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PLoS One

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. 2023 Mar 30;18(3):e0283349.

doi: 10.1371/journal.pone.0283349. eCollection 2023.

## Acute chest syndrome, airway inflammation and lung function in sickle cell disease

[Aliva De<sup>1</sup>](#), [Sanford Williams<sup>2</sup>](#), [Yujing Yao<sup>3</sup>](#), [Zhezhen Jin<sup>3</sup>](#), [Gary M Brittenham<sup>4</sup>](#), [Meyer Kattan<sup>1</sup>](#), [Stephanie Lovinsky-Desir<sup>1</sup>](#), [Margaret T Lee<sup>4</sup>](#)

Affiliations [expand](#)

- PMID: 36996064
- PMCID: [PMC10062579](#)
- DOI: [10.1371/journal.pone.0283349](#)

## Abstract

**Background:** Acute chest syndrome (ACS) is an acute complication in SCD but its effects on lung function are not well understood. Inflammation is a key component of SCD pathophysiology but with an unclear association with lung function. We hypothesized that children with ACS had worse lung function than children without ACS and aimed to investigate the association of lung function deficits with inflammatory cytokines.

**Methods:** Patients enrolled in a previous 2-year randomized clinical trial who had consented to future data use, were enrolled for the present exploratory study. Patients were categorized into ACS and non-ACS groups. Demographic and clinical information were collected. Serum samples were used for quantification of serum cytokines and leukotriene B4 levels and pulmonary function tests (PFTs) were assessed.

**Results:** Children with ACS had lower total lung capacity (TLC) at baseline and at 2 years, with a significant decline in forced expiratory volume in 1 sec (FEV1) and mid-maximal expiratory flow rate (FEF25-75%) in the 2 year period ( $p = 0.015$  and  $p = 0.039$  respectively). For children with ACS, serum cytokines IL-5, and IL-13 were higher at baseline and at 2 years compared to children with no ACS. IP-10 and IL-6 were negatively correlated with PFT markers. In multivariable regression using generalized estimating equation approach for factors predicting lung function, age was significantly associated FEV1 ( $p = 0.047$ ) and ratio of FEV1 and forced vital capacity (FVC)- FEV1/FVC ratio ( $p = 0.006$ ); males had lower FEV1/FVC ( $p = 0.035$ ) and higher TLC ( $p = 0.031$ ). Asthma status was associated with FEV1 ( $p = 0.017$ ) and FVC ( $p = 0.022$ ); history of ACS was significantly associated with TLC ( $p = 0.027$ ).

**Conclusion:** Pulmonary function abnormalities were more common and inflammatory markers were elevated in patients with ACS, compared with those without ACS. These findings suggest airway inflammation is present in children with SCD and ACS, which could be contributing to impaired pulmonary function.

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## Conflict of interest statement

No authors have competing interests.

- [50 references](#)
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Review

Curr Allergy Asthma Rep

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. 2023 Mar 30.

doi: 10.1007/s11882-023-01074-1. Online ahead of print.

# The Comorbid Patient in the Spotlight: Efficacy of Benralizumab on Chronic Rhinosinusitis with Nasal Polyp Outcomes in Presence of Severe Asthma

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- PMID: 36995525
- DOI: [10.1007/s11882-023-01074-1](https://doi.org/10.1007/s11882-023-01074-1)

## Abstract

**Purpose of review:** The present review aims to systematically assess published data to elucidate benralizumab efficacy on nasal outcomes in comorbid patients.

**Recent findings:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is a heterogeneous inflammatory disease of the nasal cavity often associated with severe asthma (SA), contributing to a global disease burden in asthmatics. The two pathologies share common underlying mechanisms (e.g., type-2 inflammation), which sustain symptoms and poor comorbid patient quality of life. Therefore, it is of primary importance to identify the correct therapeutic option in order to achieve the optimal management of patients affected by both pathologies. Benralizumab is a humanized monoclonal antibody directed at the  $\alpha$  subunit of the interleukin-5 receptor (IL-5R $\alpha$ ) approved for the treatment of severe eosinophilic asthma. Increasing body of literature provides data on its efficacy also on

CRSwNP in the comorbid SA patient. Based on the data described in this review, when benralizumab is administered to comorbid patients, it does not only control severe asthma but also improves CRSwNP clinical outcomes, although we need further studies to add stronger evidence and to improve the correct pheno-endotyping of the comorbid patient.

**Keywords:** Benralizumab; CRSwNP; Comorbid patient; Eosinophilic inflammation; Nasal outcomes; Severe asthma.

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. 2023 Mar 30.

doi: 10.1111/all.15728. Online ahead of print.

## Innate lymphoid cells type 2 and CD8<sup>+</sup> T cells are perturbed in overweight and obese individuals with asthma

[Sophia Björkander](#)<sup>1</sup>, [Paul Maier](#)<sup>2</sup>, [Maura Kere](#)<sup>1</sup>, [Simon Kebede Merid](#)<sup>1</sup>, [Lorenz Wirth](#)<sup>3</sup>, [Whitney Wiegel](#)<sup>2</sup>, [Sandra Ekström](#)<sup>4,5</sup>, [Inger Kull](#)<sup>1,6</sup>, [Anna Bergström](#)<sup>4,5</sup>, [Erik Melén](#)<sup>1,6</sup>, [Jenny Mjösberg](#)<sup>2,7</sup>, [Christopher Andrew Tibbitt](#)<sup>2,7</sup>

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- PMID: 36994759
- DOI: [10.1111/all.15728](https://doi.org/10.1111/all.15728)



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. 2023 Mar 27;9(2):00605-2022.

doi: 10.1183/23120541.00605-2022. eCollection 2023 Mar.

# Nebulised interferon- $\beta$ 1a (SNG001) in hospitalised COVID-19: SPRINTER phase III study

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- PMID: 36994453
- PMCID: [PMC9790107](#)
- DOI: [10.1183/23120541.00605-2022](#)

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## Abstract

**Background:** Despite the availability of vaccines and therapies, patients are being hospitalised with coronavirus disease 2019 (COVID-19). Interferon (IFN)- $\beta$  is a naturally occurring protein that stimulates host immune responses against most viruses, including severe acute respiratory syndrome coronavirus 2. SNG001 is a recombinant IFN- $\beta$ 1a formulation delivered to the lungs *via* nebuliser. SPRINTER assessed the efficacy and safety of SNG001 in adults hospitalised due to COVID-19 who required oxygen *via* nasal prongs or mask.

**Methods:** Patients were randomised double-blind to SNG001 (n=309) or placebo (n=314) once daily for 14 days plus standard of care (SoC). The primary objective was to evaluate recovery after administration of SNG001 *versus* placebo, in terms of times to hospital discharge and recovery to no limitation of activity. Key secondary end-points were progression to severe disease or death, progression to intubation or death and death.

**Results:** Median time to hospital discharge was 7.0 and 8.0 days with SNG001 and placebo, respectively (hazard ratio (HR) 1.06 (95% CI 0.89-1.27); p=0.51); time to recovery was 25.0 days in both groups (HR 1.02 (95% CI 0.81-1.28); p=0.89). There were no significant SNG001-placebo differences for the key secondary end-points, with a 25.7% relative risk reduction in progression to severe disease or death (10.7% and 14.4%, respectively; OR 0.71 (95% CI 0.44-1.15); p=0.161). Serious adverse events were reported by 12.6% and 18.2% patients with SNG001 and placebo, respectively.

**Conclusions:** Although the primary objective of the study was not met, SNG001 had a favourable safety profile, and the key secondary end-points analysis suggested that SNG001 may have prevented progression to severe disease.

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## Conflict of interest statement

This study is registered at the ISRCTN registry with identifier number ISRCTN85436698. The data analysed and presented in this study are available from the corresponding author on reasonable request, providing the request meets local ethical and research governance criteria after publication. Patient-level data will be anonymised and study documents will be redacted to protect the privacy of trial participants. Conflict of interest: In addition to the writing support declared above, the authors have the following conflicts of interest to declare. P.D. Monk is an employee of Synairgen Research plc, the parent company of Synairgen Research Ltd (and such costs are met by Synairgen Research Ltd), the sponsor of this trial, and owns shares and has options on shares in Synairgen plc. J.L. Brookes is an employee of Synairgen Research Ltd, the sponsor of this trial, and has options on shares in Synairgen plc. V.J. Tear is an employee of Synairgen Research Ltd, the sponsor of this trial, and owns shares and has options on shares in Synairgen plc. T.N. Batten provided statistical support, programming and consultancy to Synairgen Research Ltd via a contract with his employer, Veramed Ltd. M. Mankowski provided consulting services to Synairgen Research Ltd, the sponsor of this trial, with all payments made to tranScrip Ltd. T. Adzic-

Vukicevic has no other conflicts of interest to disclose. M.G. Crooks has no other conflicts of interest to disclose. D.P.S. Dosanjh declares grants from GlaxoSmithKline (Supported Studies Programme) and Birmingham Health Partners CARP Fellowship, honorarium for meeting and podcast from Boehringer Ingelheim, support to attend congresses from Boehringer Ingelheim (no payment received), patent 0406271.7, filed 21 March 2005 (Mycobacterium tuberculosis infection diagnostic text), and participation in a data safety monitoring board or advisory board from AstraZeneca, Boehringer Ingelheim and the HAP-FAST trial, all outside the scope of this manuscript. M. Kraft declares the receipt of funding to her institution from Synairgen Research Ltd, the sponsor of this trial. Outside the scope of the trial she declares funds paid to her institution from the National Institutes of Health, American Lung Association, Sanofi-Regeneron and AstraZeneca, consulting fees from AstraZeneca, Sanofi-Regeneron and Genentech, one patent issued and one pending for which she received no funds directly (she is Chief Medical Officer and Co-founder of RaeSedo, Inc.), funds for the participation in a data safety monitoring board for the ALUND Study, funds for a leadership role of the National Heart, Lung and Blood Scientific Advisory Council (NIH), and the future receipt of stock options in RaeSedo, Inc. C.E. Brightling declares grants and consulting fees paid to his institution from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Novartis, Chiesi, Genentech, Roche, Sanofi, Regeneron, Mologic and 4DPharma, all outside the scope of this manuscript. F.J. Gabbay declares the receipt of consulting fees paid to tranScrip Ltd from Synairgen Research plc, the sponsor of this trial, and participation in a data safety monitoring board for Synairgen. She is also president of the Faculty of Pharmaceutical Medicine of the UK Royal College of Physicians. S.T. Holgate received payments as nonexecutive director of, and owns shares in, Synairgen plc, the parent company of the sponsor of this trial. R. Djukanovic declares the receipt of consulting fees and payment for participation in a data safety monitoring board or advisory board from Synairgen Research Ltd, the sponsor of this trial; and owns shares in Synairgen plc, the parent company of the sponsor of this trial. Outside the trial, he declares payment or honoraria from Regeneron, GlaxoSmithKline and Kymab. T.M.A. Wilkinson received research funding and consultancy fees from Synairgen Research Ltd, the sponsor of this trial. Outside the trial, he declares research grants from the National Institute for Health and Care Research, Medical Research Council, Bergenbio, AstraZeneca, UCB and Janssen, consultancy fees from AstraZeneca, Valneva, Olam Pharma, Janssen and My mHealth, lecture fees from AstraZeneca, Boehringer Ingelheim and Roche, participation on a data safety monitoring board for Valneva, and that he holds stock in My mHealth.

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. 2023 Mar 29.

doi: 10.1038/s41440-023-01257-3. Online ahead of print.

# Asthma and increased risk of myocardial infarction and mortality among hypertensive Korean patients

[Chan Joo Lee](#)<sup>#1</sup>, [Jinseub Hwang](#)<sup>#2</sup>, [Chae Young Kang](#)<sup>2</sup>, [Dayoung Kang](#)<sup>2</sup>, [Do Hyang Kim](#)<sup>2</sup>, [Hye Jung Park](#)<sup>3</sup>, [Hyeon-Chang Kim](#)<sup>4</sup>, [Sang-Hyun Ihm](#)<sup>5</sup>, [Yong-Jin Kim](#)<sup>6</sup>, [Jin-Ho Shin](#)<sup>7</sup>, [Wook Bum Pyun](#)<sup>8</sup>, [Sungha Park](#)<sup>9 10</sup>

Affiliations expand

- PMID: 36991063

- DOI: [10.1038/s41440-023-01257-3](https://doi.org/10.1038/s41440-023-01257-3)

## Abstract

This study aimed to evaluate the effects of asthma on cardiovascular disease incidence in patients with hypertension. A total of 639,784 patients with hypertension from the Korea National Health Insurance Service database were included, of whom 62,517 had history of asthma after propensity score matching. The risks of all-cause mortality, myocardial infarction (MI), stroke, and end-stage renal disease (ESRD) were assessed according to the presence of asthma, long-acting  $\beta$ 2-agonist (LABA) inhaler usage, and/or systemic corticosteroid usage for up to 11 years. In addition, whether these risks were modified by average blood pressure (BP) levels during the follow-up period was examined. Asthma was associated with an increased risk of all-cause mortality (hazard ratio [HR], 1.203; 95% confidence interval [CI], 1.165-1.241) and MI (HR, 1.244; 95% CI, 1.182-1.310) but not the risk of stroke or ESRD. LABA inhaler usage was associated with a higher risk of all-cause mortality and MI, and systemic corticosteroids usage showed a higher risk of ESRD as well as all-cause mortality and MI among hypertensive patients with asthma. Compared to patients without asthma, there was a graded increase in the risk of all-cause mortality and MI in those with asthma without LABA inhaler/systemic corticosteroid usage and in those with asthma with LABA inhaler/systemic corticosteroid usage. These associations were not significantly modified by BP levels. This nationwide population-based study supports that

asthma may be a clinical factor that increases the risk of poor outcomes in patients with hypertension.

**Keywords:** Asthma; Hypertension; Mortality; Myocardial infarction; Risk factor.

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. 2023 Mar 29;2201763.

doi: 10.1183/13993003.01763-2022. Online ahead of print.

## [Preterm birth and asthma and COPD in adulthood: a nationwide register study from two Nordic countries](#)

[Anna Pulakka](#)<sup>1,2</sup>, [Kari Risnes](#)<sup>3,4</sup>, [Johanna Metsälä](#)<sup>5</sup>, [Suvi Alenius](#)<sup>5,6</sup>, [Katriina Heikkilä](#)<sup>5</sup>, [Sara Marie Nilsen](#)<sup>3,7</sup>, [Pieta Näsänen-Gilmore](#)<sup>5,8,9</sup>, [Peija Haaramo](#)<sup>10</sup>, [Mika Gissler](#)<sup>11</sup>, [Signe Opdahl](#)<sup>12</sup>, [Eero Kajantie](#)<sup>5,9,12</sup>

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- PMID: 36990472
- DOI: [10.1183/13993003.01763-2022](https://doi.org/10.1183/13993003.01763-2022)

## Abstract

Preterm birth affects lungs in several ways but only few studies have follow-up until adulthood. We investigated the association of the entire spectrum of gestational ages with specialist care episodes for obstructive airway disease (asthma and chronic obstructive pulmonary disease, COPD) at age 18-50 years. We used nationwide register data on 706

717 people born 1987-1998 in Finland (4.8% preterm) and 1 669 528 born 1967-1999 in Norway (5.0% preterm). Care episodes of asthma and COPD were obtained from specialised healthcare registers, available in Finland 2005-2016 and in Norway 2008-2017. We used logistic regression to estimate odds ratios (OR) for having a care episode with either disease outcome. Odds of any obstructive airway disease in adulthood were 2-3-fold for those born <28 or 28-31 completed weeks, compared with those born full-term (39-41 completed weeks), persisting after adjustments. For individuals born at 32-33, 34-36 or 37-38 weeks, the odds were 1.1- to 1.5-fold. Associations were similar in the Finnish and the Norwegian data and among people aged 18-29 and 30-50 years. For COPD at age 30-50 years, the OR was 7.44 (95% CI 3.49-15.85) for those born <28 weeks, 3.18 (2.23-4.54) for those born 28-31 weeks, and 2.32 (1.72-3.12) for those born 32-33 weeks. Bronchopulmonary dysplasia in infancy increased the odds further for those born <28 and 32-31 weeks. Preterm birth is a risk factor for asthma and COPD in adulthood. The high odds of COPD calls for diagnostic vigilance when adults born very preterm present with respiratory symptoms.

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. 2023 Mar 30.

doi: 10.1515/cclm-2022-1323. Online ahead of print.

## [Serum biomarkers of remodeling in severe asthma with fixed airway obstruction and the potential role of KL-6](#)

[Andrea Vianello](#)<sup>1</sup>, [Gabriella Guarnieri](#)<sup>1</sup>, [Alessia Achille](#)<sup>1</sup>, [Federico Lionello](#)<sup>1</sup>, [Sara Lococo](#)<sup>1</sup>, [Martina Zaninotto](#)<sup>2</sup>, [Marco Caminati](#)<sup>3</sup>, [Gianenrico Senna](#)<sup>3</sup>

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- PMID: 36989607
- DOI: [10.1515/cclm-2022-1323](https://doi.org/10.1515/cclm-2022-1323)

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## Abstract

Over 3% of asthmatic patients are affected by a particularly severe form of the disease ("severe asthma", SA) which is often refractory to standard treatment. Airway remodeling (AR), which can be considered a critical characteristic of approximately half of all patients with SA and currently thought to be the main mechanism triggering fixed airway obstruction (FAO), seems to be a key factor affecting a patient's outcome. Despite the collective efforts of internationally renowned experts, to date only a few biomarkers indicative of AR and no recognizable biomarkers of lung parenchymal remodeling have been identified. This work examines the pathogenesis of airway and lung parenchymal remodeling and the serum biomarkers that may be able to identify the severe asthmatic patients who may develop FAO. The study also aims to examine if Krebs von den Lungen-6 (KL-6) could be considered a diagnostic biomarker of lung structural damage in SA.

**Keywords:** airway remodeling; asthma; biomarkers.

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. 2023 Mar 29.

doi: 10.1164/rccm.202302-0317LE. Online ahead of print.

## How Can Allergen Immunotherapy Protect Against COVID-19?

[Milena Sokolowska](#)<sup>1,2</sup>, [Urszula Radzikowska](#)<sup>1,3</sup>

Affiliations expand

- PMID: 36989503
- DOI: [10.1164/rccm.202302-0317LE](https://doi.org/10.1164/rccm.202302-0317LE)

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. 2023 Apr 1;98(4):455.

doi: 10.1097/ACM.00000000000005139. Epub 2023 Mar 24.

## Artist's Statement: Asthma

[Minsoo Kim](#)<sup>1</sup>

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- PMID: 36989410



- DOI: [10.1097/ACM.00000000000005139](https://doi.org/10.1097/ACM.00000000000005139)

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Respirology

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. 2023 Mar 28.

doi: 10.1111/resp.14498. Online ahead of print.

# Monoclonal antibody therapy in cystic fibrosis and asthma

[Huy Duc Vu](#)<sup>1</sup>, [Eskandarain Shafuddin](#)<sup>1,2</sup>, [Jane Willis](#)<sup>1</sup>, [Michael Pallin](#)<sup>1</sup>, [David Armstrong](#)<sup>1</sup>, [Christopher Daley](#)<sup>1</sup>

Affiliations expand

- PMID: 36978257
- DOI: [10.1111/resp.14498](https://doi.org/10.1111/resp.14498)

*No abstract available*

**Keywords:** asthma; cystic fibrosis; monoclonal antibodies.

- [14 references](#)

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Am J Respir Crit Care Med

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. 2023 Mar 28.

doi: 10.1164/rccm.202210-1852LE. Online ahead of print.

## **RV versus FRC CT Assessment of Functional Small Airways Disease in Smokers with and without COPD**

[Alejandro P Comellas](#)<sup>1</sup>, [John D Newell Jr](#)<sup>2</sup>, [Miranda Kirby](#)<sup>3</sup>, [Jered P Sieren](#)<sup>4</sup>, [Sam Peterson](#)<sup>5</sup>, [Charles Hatt](#)<sup>6</sup>, [Craig J Galban](#)<sup>7</sup>, [Ella A Kazerooni](#)<sup>8</sup>, [David A Lynch](#)<sup>9</sup>, [MeiLan K Han](#)<sup>10</sup>, [Eric A Hoffman](#)<sup>11</sup>

Affiliations expand

- PMID: 36977314
- DOI: [10.1164/rccm.202210-1852LE](https://doi.org/10.1164/rccm.202210-1852LE)

*No abstract available*

**Keywords:** Air Trapping; Asthma; COPD; Quantitative Computed Tomography; Small Airways.

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J Asthma

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. 2023 Mar 28;1-12.

doi: 10.1080/02770903.2023.2196563. Online ahead of print.

# Anti-IL-5/5Ra biologics improve work productivity and activity in severe asthma: A RAPSODI registry-based cohort study

[J P M van der Valk<sup>1</sup>](#), [P P Hekking<sup>1</sup>](#), [S P Rauh<sup>2</sup>](#), [K W Patberg<sup>3</sup>](#), [H P A A van Veen<sup>4</sup>](#), [A Van Huisstede<sup>5</sup>](#), [F W J M Smeenk<sup>6</sup>](#), [M J T van de Ven<sup>7</sup>](#), [M E A C Broeders<sup>8</sup>](#), [B Hilvering<sup>9</sup>](#), [J van Exsel<sup>10</sup>](#), [K T M Oud<sup>11</sup>](#), [B Langeveld<sup>12</sup>](#), [K B Fieten<sup>13</sup>](#), [A van Veen<sup>14</sup>](#), [S Hashimoto<sup>9</sup>](#), [J K Sont<sup>15</sup>](#), [A Ten Brinke<sup>16</sup>](#), [G J Braunstahl<sup>1 17</sup>](#), [RAPSODI team.](#)

Affiliations expand

- PMID: 36976568
- DOI: [10.1080/02770903.2023.2196563](https://doi.org/10.1080/02770903.2023.2196563)

## Abstract

**Introduction:** Severe asthma is associated with a serious disease burden, partially caused by limitations in activity and work impairment (1,2).

**Aims and objectives:** This study aims to relate treatment with biologics targeting IL-5/5Ra to work productivity and activity in the long term in a real-world context.

**Material and methods:** This is a registry-based multi-center cohort study evaluating data from adults with severe eosinophilic asthma included in the Dutch Register of Adult Patients with Severe Asthma for Optimal Disease management (RAPSODI). Patients that started with anti-IL-5/5Ra biologics and completed the work productivity and activity

improvement questionnaire, were included. Study and patient characteristics were compared between the employed and unemployed patients. Work productivity and activity impairment are related to accompanying improvements in clinical outcomes.

**Results:** At baseline, 91 of 137 patients (66%) were employed which remained stable throughout the follow-up period. Patients in the working age category were younger and had significantly better asthma control ( $p = 0.02$ ). Mean overall work impairment due to health decreased significantly from 25.5% (SD 2.6) to 17.6% (SD 2.8) during 12 months anti-IL-5/5Ra biologics treatment ( $P = 0.010$ ). There was a significant association between ACQ6 and overall work improvement after targeted therapy ( $\beta = 8.7$ , CI 2.1-15.4,  $P = 0.01$ ). The improvement of asthma control of 0.5 points on the asthma Control Questionnaire was associated with an overall work impairment of - 9%.

**Conclusions:** Work productivity and activity in severe eosinophilic asthma improved after starting anti-IL-5/5Ra biologics. Clinically relevant improvement in asthma control was associated with an overall work impairment score of - 9% in this study.

**Keywords:** ACQ6; AQLQ; Anti-IL-5/5Ra biologics; Asthma; MCID; WPAI; activity; work productivity.

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. 2023 Mar 28.

doi: 10.1111/cea.14306. Online ahead of print.

## [Increased inhaled corticosteroids for treating acute asthma exacerbations](#)

[Manisha Ramphul](#)<sup>1</sup>

[Affiliations expand](#)

- PMID: 36974609

- DOI: [10.1111/cea.14306](https://doi.org/10.1111/cea.14306)

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. 2023 Mar 28.

doi: [10.1007/s12098-023-04521-z](https://doi.org/10.1007/s12098-023-04521-z). Online ahead of print.

## [Best Spirometry Index for Assessment of Severity in Asthma: The Debate Still Continues](#)

[Samriti Gupta](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 36973610

- DOI: [10.1007/s12098-023-04521-z](https://doi.org/10.1007/s12098-023-04521-z)

*No abstract available*

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Thorax

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. 2023 Mar 27;thorax-2023-220030.

doi: 10.1136/thorax-2023-220030. Online ahead of print.

## [Respiratory effects of air pollution: time to stop this deadly trajectory](#)

[Sara De Matteis](#)<sup>1,2</sup>

Affiliations [expand](#)

- PMID: 36972978
- DOI: [10.1136/thorax-2023-220030](https://doi.org/10.1136/thorax-2023-220030)

*No abstract available*

**Keywords:** Asthma; Asthma Epidemiology; COPD epidemiology; Lung Cancer.

## Conflict of interest statement

Competing interests: None declared.

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J Asthma

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. 2023 Mar 27;1-18.

doi: 10.1080/02770903.2023.2196560. Online ahead of print.

# [The Relationship between Social Support, Self-Efficacy, and Asthma Outcomes in Older Adults](#)

[Naomi Greenfield](#)<sup>1</sup>, [Jacqueline Becker](#)<sup>2</sup>, [Sunit Jariwala](#)<sup>3</sup>, [Juan Wisnivesky](#)<sup>2</sup>, [Alex Federman](#)<sup>2</sup>, [Jonathan M Feldman](#)<sup>1,4</sup>

Affiliations expand

- PMID: 36972524
- DOI: [10.1080/02770903.2023.2196560](https://doi.org/10.1080/02770903.2023.2196560)

## Abstract

*Objective* There has been a call for research examining factors that influence asthma outcomes in older adults because of the notable disparities observed in this age group. Social support and self-efficacy are resources that factor into asthma outcomes. The

current study aimed to examine the relationship between these resources (independently and jointly) and asthma control and quality of life. *Methods* Older adults with moderate-severe asthma were recruited from NYC. Data were obtained during in-person interviews via validated measures of social support, asthma self-efficacy, asthma control, and asthma quality of life. Linear regression evaluated self-efficacy in the relationship between social support and asthma outcomes. *Results* In a sample of 359 older adults ( $M = 68.04$ , 47.9% Hispanic, 26.5% Black, and 25.6% other), social support had an inverse association with asthma control. As social support increased, asthma control decreased ( $\beta = .95$ ,  $t(356) = -3.13$ ,  $p = .002$ ). Self-efficacy significantly moderated this relationship ( $\beta = .01$ ,  $t(356) = 2.37$ ,  $p = .018$ ). For individuals with low or moderate asthma self-efficacy, more received social support was associated with worse asthma control ( $\beta = -.33$ ,  $t(356) = -4.66$ ,  $p < .0001$ ;  $\beta = -.20$ ;  $t(356) = -3.21$ ,  $p = .0014$ , respectively). For individuals with high self-efficacy, no relationship was found between received social support and asthma control ( $\beta = -.10$ ,  $t(356) = -1.20$ ,  $p = .23$ ). For asthma quality of life, higher levels of received social support were associated with worse quality of life ( $\beta = -.88$ ,  $t(356) = -2.64$ ,  $p = .009$ ), but this association was not significantly moderated by self-efficacy ( $\beta = .01$ ,  $t(356) = 1.90$ ,  $p = .0582$ ). *Conclusions* For older adults with asthma, receiving more social support is associated with worse asthma outcomes, especially for older adults with lower asthma self-efficacy.

**Keywords:** Asthma Control; Asthma Quality of Life; Geriatric Asthma; Personal Resources; Social Resources; Social-Cognitive.

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. 2023 Mar 27.

doi: 10.1007/s00408-023-00611-z. Online ahead of print.

## [The Association Between Insulin Use and Asthma: An Epidemiological](#)



# Observational Analysis and Mendelian Randomization Study

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- DOI: [10.1007/s00408-023-00611-z](https://doi.org/10.1007/s00408-023-00611-z)

## Abstract

**Background:** Asthma is a common respiratory disease caused by genetic and environmental factors, but the contribution of insulin use to the risk of asthma remains unclear. This study aimed to investigate the association between insulin use and asthma in a large population-based cohort, and further explore their causal relationship by Mendelian randomization (MR) analysis.

**Methods:** An epidemiological study including 85,887 participants from the National Health and Nutrition Examination Survey (NHANES) 2001-2018 was performed to evaluate the association between insulin use and asthma. Based on the inverse-variance weighted approach, MR analysis were conducted to estimate the causal effect of insulin use on asthma from the UKB and FinnGen datasets, respectively.

**Results:** In the NHANES cohort, we found that insulin use was associated with an increased risk of asthma [odd ratio (OR) 1.38; 95% CI 1.16-1.64;  $p < 0.001$ ]. For the MR analysis, we found a causal relationship between insulin use and a higher risk of asthma in both Finn (OR 1.10;  $p < 0.001$ ) and UK Biobank cohorts (OR 1.18;  $p < 0.001$ ). Meanwhile, there was no causal association between diabetes and asthma. After multivariable adjustment for diabetes in UKB cohort, the insulin use remained significantly associated with an increased risk of asthma (OR 1.17,  $p < 0.001$ ).

**Conclusions:** An association between insulin use and an increased risk of asthma was found via the real-world data from the NHANES. In addition, the current study identified a causal effect and provided a genetic evidence of insulin use and asthma. More studies are needed to elucidate the mechanisms underlying the association between insulin use and asthma.

**Keywords:** Asthma; Insulin use; Mendelian randomization; NHANES.

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. 2023 Mar 27;1-10.

doi: 10.1080/02770903.2023.2196562. Online ahead of print.

# [Evaluation of the clinical features and laboratory data of patients with severe asthma classified as super-responder or non super-responder to omalizumab treatment: a single-centre real-life study](#)

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- PMID: 36971065

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# Abstract

**Introduction** Omalizumab is used for the treatment of severe allergic asthma. **Objective** The aim of this study was to evaluate the clinical features and laboratory data of patients with severe allergic asthma classified as super-responder or non super-responder to omalizumab. **Methods** Comparisons were made of the laboratory data and clinical features of patients with severe allergic asthma. Patients who had no asthma exacerbation, no oral corticosteroid (OCS) use, asthma control test (ACT) score >20 and forced expiratory volume in 1 second (FEV1) >80% were considered super-responder after omalizumab. **Results** A total of 90 patients were included in the study, comprising 19 (21.1%) males. The age at onset of asthma, allergic rhinitis rate, number of endoscopic sinus surgeries (ESS), intranasal corticosteroid (INS) use, baseline FEV 1 (%) and ACT score were significantly higher in the omalizumab super-responder group ( $p = 0.013$ ,  $p = 0.015$ ,  $p = 0.002$ ,  $p = 0.001$ ,  $p = 0.001$  and  $p < 0.001$ , respectively). The duration of asthma, rate of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP), regular use of OCS, baseline eosinophil count and eosinophil/lymphocyte ratio were significantly higher in the omalizumab non super-responder group ( $p = 0.015$ ,  $p < 0.001$ ,  $p = 0.004$ ,  $p < 0.001$  and  $p < 0.001$ , respectively). Blood eosinophil count (AUC: 0.187,  $p < 0.001$ ), Eosinophil/Lymphocyte ratio (AUC: 0.150,  $p < 0.001$ ) and FEV1 (%) (AUC: 0.779,  $p = 0.001$ ) were determined to have diagnostic value in predicting the treatment response to omalizumab of patients with severe allergic asthma. **Conclusion** High blood eosinophil levels, CRSwNP, and low pre-treatment lung capacity may affect omalizumab treatment response in patients with severe allergic asthma. These results should be supported by further multicentre real-life studies.

**Keywords:** Omalizumab; anti IgE; anti asthmatic agents; asthma; treatment efficacy.

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doi: 10.1080/02770903.2023.2196689. Online ahead of print.

# Male-biased association of endothelial nitric oxide synthase Asp298Glu substitution ( NOS3-c.894G/T) with asthma risk and severity

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Affiliations expand

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## Abstract

**Objective:** The nitric-oxide pathway plays a crucial role in the pathogenesis of asthma and NOS3-encoded endothelial nitric oxide synthase is one of the main components of the pathway. Variants of NOS3 are known to contribute to asthma development and pathophysiology. **Methods:** We investigated the association of NOS3-c.894G/T (rs1799983) with asthma risk and severity by studying frequencies of its genotypes and alleles in 555 asthmatics (93 intermittent, 240 mild, 158 moderate, and 64 severe asthma cases) and 351 control participants using the PCR-FRLP method, logistic regression analysis and generalized ordered logit estimates. **Results:** GT genotype (OR<sub>adj</sub>:1.39; CI:1.04-1.85; P = 0.026), dominant model GT + TT (OR<sub>adj</sub>:1.41; CI:1.07-1.87; P = 0.015), and T allele (OR<sub>adj</sub>:1.32; CI:1.05-1.67; P = 0.018) was associated with increased ORs in asthmatics. Also, the frequency of GT + TT (OR<sub>adj</sub>:1.55; CI:1.01-2.38; P = 0.044) was significantly higher in males. Furthermore, GT genotype (OR<sub>adj</sub>:1.39; CI:1.04-1.85; P = 0.024), GT + TT (OR<sub>adj</sub>:1.42; CI:1.07-1.87; P = 0.014), and T allele (OR<sub>adj</sub>:1.32; CI:1.05-1.66; P = 0.018) in total population and GT + TT (OR<sub>adj</sub>:1.56; CI:1.02-2.37; P = 0.04) in males were significantly associated with increased risk of severe, moderate, mild, intermittent asthma vs. controls. Also, GT genotype (OR<sub>adj</sub>:1.39; CI:1.02-1.91; P = 0.039) was significantly more frequent in severe, moderate grades vs. lower severity grades in the total population. Frequencies of GT genotype (OR<sub>adj</sub>:1.77; CI:1.05-3.00; P = 0.032) and GT + TT (OR<sub>adj</sub>:1.74; CI:1.04-2.90; P = 0.036) in total population and GT genotype (OR<sub>adj</sub>:2.40; CI:1.16-4.97; P = 0.018) and GT + TT (OR<sub>adj</sub>:2.30; CI:1.12-4.74; P = 0.023) in male subpopulation were significantly higher in severe cases compared to lower grades. **Conclusions:** NOS3-c.894G/T may be associated with asthma risk and its severer grades, with greater effects in men.

**Keywords:** Lung; asthma; endothelial nitric oxide synthase; genetic association; rs1799983.

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. 2023 Mar 27;22(1):28.

doi: 10.1186/s12940-023-00984-x.

# Adult asthma associated with roadway density and housing in rural Appalachia: the Mountain Air Project (MAP)

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- PMCID: [PMC10041800](#)
- DOI: [10.1186/s12940-023-00984-x](#)

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## Abstract

**Background:** Appalachian Kentucky is a rural area with a high prevalence of asthma among adults. The relative contribution of environmental exposures in the etiology of adult asthma in these populations has been understudied.

**Objective:** This manuscript describes the aims, study design, methods, and characteristics of participants for the Mountain Air Project (MAP), and focuses on associations between small area environmental exposures, including roadways and mining operations, and lifetime and current asthma in adults.

**Methods:** A cohort of residents, aged 21 and older, in two Kentucky counties, was enrolled in a community-based, cross-sectional study. Stratified cluster sampling was used to select small geographic areas denoted as 14-digit USGS hydrologic units (HUCs). Households were enumerated within selected HUCs. Community health workers collected in-person interviews. The proximity of nearby active and inactive coal mining operations, density of oil and gas operations, and density of roadways were characterized for all HUCs. Poisson regression analyses were used to estimate adjusted prevalence ratios.

**Results:** From 1,459 eligible households contacted, 1,190 individuals were recruited, and 972 persons completed the interviews. The prevalence of lifetime asthma was 22.8%; current asthma was 16.3%. Adjusting for covariates, roadway density was positively associated with current asthma in the second (aPR = 1.61; 95% CI 1.04-2.48) and third tertiles (aPR = 2.00; 95% CI 1.32-3.03). Increased risk of current asthma was associated with residence in public, multi-unit housing (aPR = 2.01; 95% CI 1.27-3.18) compared to a residence in a single-family home. There were no notable associations between proximity to coal mining and oil and gas operations and asthma prevalence.

**Conclusions:** This study suggests that residents in rural areas with higher roadway density and those residing in public housing units may be at increased risk for current asthma after accounting for other known risk factors. Confirming the role of traffic-related particulates in producing high asthma risk among adults in this study contributes to the understanding of the multiple environmental exposures that influence respiratory health in the Appalachia region.

**Keywords:** Adult; Appalachia; Asthma; Epidemiology; Mining.

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## Conflict of interest statement

The authors declare that they have no competing interests.

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

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. 2023 Apr;72(2):207-226.

doi: 10.1016/j.alit.2023.02.006. Epub 2023 Mar 22.

## [Executive summary: Japanese guidelines for adult asthma \(JGL\) 2021](#)

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- DOI: [10.1016/j.alit.2023.02.006](https://doi.org/10.1016/j.alit.2023.02.006)

**Free article**

### Abstract

Asthma is characterized by chronic airway inflammation, variable airway narrowing, and sensory nerve irritation, which manifest as wheezing, dyspnea, chest tightness, and cough. Longstanding asthma may result in airway remodeling and become intractable. Despite the increased prevalence of asthma in adults, asthma-associated deaths have decreased in Japan (0.94 per 100,000 people in 2020). The goals of asthma treatment include the control of symptoms and reduction of future risks. A functional partnership between physicians and patients is indispensable for achieving these goals. Long-term management with medications and the elimination of triggers and risk factors are fundamental to asthma treatment. Asthma is managed via four steps of pharmacotherapy ("controllers"), ranging from mild to intensive treatments, depending on disease severity; each step involves daily

administration of an inhaled corticosteroid, which varies from low to high dosage. Long-acting  $\beta_2$  agonists, leukotriene receptor antagonists, sustained-release theophylline, and long-acting muscarinic antagonists are recommended as add-on drugs. Allergen immunotherapy is a new option that is employed as a controller treatment. Further, as of 2021, anti-IgE antibody, anti-IL-5 and anti-IL-5 receptor  $\alpha$ -chain antibodies, and anti-IL-4 receptor  $\alpha$ -chain antibodies are available for the treatment of severe asthma. Bronchial thermoplasty can be performed for asthma treatment, and its long-term efficacy has been reported. Algorithms for their usage have been revised. Comorbidities, such as allergic rhinitis, chronic rhinosinusitis, chronic obstructive pulmonary disease, and aspirin-exacerbated respiratory disease, should also be considered during the treatment of chronic asthma. Depending on the severity of episodes, inhaled short-acting  $\beta_2$  agonists, systemic corticosteroids, short-acting muscarinic antagonists, oxygen therapy, and other approaches are used as needed ("relievers") during exacerbation.

**Keywords:** Asthma; Exacerbation; Long-term management; Risk factors; Stepwise treatment.

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. 2023 Apr;71(4):256-263.

doi: 10.1007/s00106-023-01273-2. Epub 2023 Mar 20.



# [Treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) with monoclonal antibodies (biologics): S2k guideline of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (DGHNO-KHC), and the German College of General Practitioners and Family Physicians (DEGAM)]

[Article in German]

[Oliver Pfaar](#)<sup>1</sup>, [Achim Georg Beule](#)<sup>2,3</sup>, [Martin Laudien](#)<sup>4</sup>, [Boris A Stuck](#)<sup>5</sup>; [erweiterte Leitliniengruppe ‚Biologika bei CRSwNP‘](#)

Collaborators, Affiliations [expand](#)

- PMID: 36941387
- PMCID: [PMC10066152](#)
- DOI: [10.1007/s00106-023-01273-2](#)

**Free PMC article**

## Abstract

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

Monoclonal antibodies (so-called biologics) can be prescribed for chronic rhinosinusitis with nasal polyps (CRSwNP) within the scope of their market authorization. However, their prescription is limited to severe CRSwNP without disease control, whereby certain requirements must be met. Dupilumab, omalizumab, and mepolizumab have currently gained market authorization, with adequate evidence for their efficacy and safety available in the literature. It can be assumed that other biologics will be approved for this indication

in the future. The severity of disease and the efficacy of treatment should be assessed objectively and subjectively before treatment initiation and after an appropriate duration, respectively. The documentation sheet proposed in this guideline chapter can be used for the assessments. In the presence of relative contraindications, a treatment should only be initiated after differentiated consideration by an experienced physician in the sense of a case-by-case decision. In summary, this guideline chapter aims to contribute to high-quality care of adult patients with these therapies in view of the increasing evidence for treatment with these substances and the increasing number of market authorizations of different biologics.

**Keywords:** Asthma; Nasal polyps; Sinunasal diseases; Sinusitis.

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

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J Asthma

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. 2023 Mar 27;1-7.

doi: 10.1080/02770903.2023.2189947. Online ahead of print.

## [Redefining biomarkers in pediatric asthma: a commentary](#)

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- PMID: 36894331

- DOI: [10.1080/02770903.2023.2189947](https://doi.org/10.1080/02770903.2023.2189947)

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. 2023 Mar 8;32(167):220202.

doi: 10.1183/16000617.0202-2022. Print 2023 Mar 31.

# [Strength of association between comorbidities and asthma: a meta-analysis](#)

[Paola Rogliani](#)<sup>1</sup>, [Rossella Laitano](#)<sup>2</sup>, [Josuel Ora](#)<sup>2</sup>, [Richard Beasley](#)<sup>3</sup>, [Luigino Calzetta](#)<sup>4</sup>

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- PMCID: [PMC10032614](#)
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**Free PMC article**

# Abstract

**Background:** The strength of association between comorbidities and asthma has never been ranked in relation to the prevalence of the comorbidity in the nonasthma population. We investigated the strength of association between comorbidities and asthma.

**Methods:** A comprehensive literature search was performed for observational studies reporting data on comorbidities in asthma and nonasthma populations. A pairwise meta-analysis was performed and the strength of association calculated by anchoring odds ratios and 95% confidence intervals with the rate of comorbidities in nonasthma populations *via* Cohen's *d* method. Cohen's *d*=0.2, 0.5 and 0.8 were cut-off values for small, medium and large effect sizes, respectively; very large effect size resulted for Cohen's *d* >0.8. The review was registered in the PROSPERO database; identifier number CRD42022295657.

**Results:** Data from 5 493 776 subjects were analysed. Allergic rhinitis (OR 4.24, 95% CI 3.82-4.71), allergic conjunctivitis (OR 2.63, 95% CI 2.22-3.11), bronchiectasis (OR 4.89, 95% CI 4.48-5.34), hypertensive cardiomyopathy (OR 4.24, 95% CI 2.06-8.90) and nasal congestion (OR 3.30, 95% CI 2.96-3.67) were strongly associated with asthma (Cohen's *d* >0.5 and ≤0.8); COPD (OR 6.23, 95% CI 4.43-8.77) and other chronic respiratory diseases (OR 12.85, 95% CI 10.14-16.29) were very strongly associated with asthma (Cohen's *d* >0.8). Stronger associations were detected between comorbidities and severe asthma. No bias resulted according to funnel plots and Egger's test.

**Conclusion:** This meta-analysis supports the relevance of individualised strategies for disease management that look beyond asthma. A multidimensional approach should be used to assess whether poor symptom control is related to uncontrolled asthma or to uncontrolled underlying comorbidities.

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## Conflict of interest statement

Conflict of interest: P. Rogliani participated as a lecturer and advisor in scientific meetings and courses under the sponsorship of Almirall, AstraZeneca, Biofutura, Boehringer Ingelheim, Chiesi Farmaceutici, GlaxoSmithKline, Menarini Group, Mundipharma, and Novartis, and her department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici Novartis, and Zambon, outside the submitted work. Conflict of interest: R. Laitano has nothing to disclose. Conflict of interest: J. Ora has nothing to disclose. Conflict of interest: R. Beasley reports grants and personal fees from AstraZeneca, grants from GlaxoSmithKline and Genentech, personal fees from Avillion and Theravance, outside the submitted work. Conflict of interest: L. Calzetta has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis; received nonfinancial support from AstraZeneca; a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; is or has been a consultant to

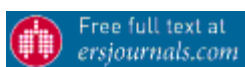
ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; and his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon, outside the submitted work.

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

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. 2023 Apr;13(4):293-859.

doi: 10.1002/alr.23090. Epub 2023 Mar 6.

## International consensus statement on allergy and rhinology: Allergic rhinitis – 2023

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Affiliations expand

- PMID: 36878860
- DOI: [10.1002/alr.23090](https://doi.org/10.1002/alr.23090)

## Abstract

**Background:** In the 5 years that have passed since the publication of the 2018 International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis (ICAR-Allergic Rhinitis 2018), the literature has expanded substantially. The ICAR-Allergic Rhinitis 2023 update presents 144 individual topics on allergic rhinitis (AR), expanded by over 40 topics from the 2018 document. Originally presented topics from 2018 have also been reviewed and updated. The executive summary highlights key evidence-based findings and recommendation from the full document.

**Methods:** ICAR-Allergic Rhinitis 2023 employed established evidence-based review with recommendation (EBRR) methodology to individually evaluate each topic. Stepwise iterative peer review and consensus was performed for each topic. The final document was then collated and includes the results of this work.

**Results:** ICAR-Allergic Rhinitis 2023 includes 10 major content areas and 144 individual topics related to AR. For a substantial proportion of topics included, an aggregate grade of evidence is presented, which is determined by collating the levels of evidence for each available study identified in the literature. For topics in which a diagnostic or therapeutic intervention is considered, a recommendation summary is presented, which considers the aggregate grade of evidence, benefit, harm, and cost.

**Conclusion:** The ICAR-Allergic Rhinitis 2023 update provides a comprehensive evaluation of AR and the currently available evidence. It is this evidence that contributes to our current knowledge base and recommendations for patient evaluation and treatment.

**Keywords:** IgE; allergen extract; allergen immunotherapy; allergic rhinitis; allergy; antihistamine; asthma; atopic dermatitis; avoidance; biologic; cockroach; conjunctivitis; consensus; corticosteroid; cough; cromolyn; decongestant; environment; eosinophilic esophagitis; epicutaneous; epidemiology; evidence-based medicine; food allergy; house dust mite; immunoglobulin E; immunotherapy; inhalant allergy; leukotriene; microbiome; occupational rhinitis; omalizumab; pediatric; perennial; pet dander; pollen; probiotic; rhinitis; rhinosinusitis; saline; seasonal; sensitization; sinusitis; socioeconomic; specific IgE; subcutaneous immunotherapy; sublingual immunotherapy; systematic review; total IgE; transcutaneous immunotherapy; validated survey.

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. 2023 Apr;5(4):e177-e178.

doi: 10.1016/S2589-7500(23)00042-0. Epub 2023 Mar 3.

## Could an electronic tool to assess asthma control with a 1-day timeframe be useful for clinical management?

[Montse Ferrer](#)<sup>1</sup>, [Catalina Lizano-Barrantes](#)<sup>2</sup>

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- PMID: 36872190
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### Conflict of interest statement

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SUPPLEMENTARY INFO

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. 2023 Apr;5(4):e227-e238.

doi: 10.1016/S2589-7500(23)00020-1. Epub 2023 Mar 3.

# [Development and validation of an electronic daily control score for asthma \(e-DASTHMA\): a real-world direct patient data study](#)

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Affiliations expand

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# Abstract

**Background:** Validated questionnaires are used to assess asthma control over the past 1-4 weeks from reporting. However, they do not adequately capture asthma control in patients with fluctuating symptoms. Using the Mobile Airways Sentinel Network for airway diseases (MASK-air) app, we developed and validated an electronic daily asthma control score (e-DASTHMA).

**Methods:** We used MASK-air data (freely available to users in 27 countries) to develop and assess different daily control scores for asthma. Data-driven control scores were developed based on asthma symptoms reported by a visual analogue scale (VAS) and self-reported asthma medication use. We included the daily monitoring data from all MASK-air users aged 16-90 years (or older than 13 years to 90 years in countries with a lower age of digital consent) who had used the app in at least 3 different calendar months and had reported at least 1 day of asthma medication use. For each score, we assessed construct validity, test-retest reliability, responsiveness, and accuracy. We used VASs on dyspnoea and work disturbance, EQ-5D-VAS, Control of Allergic Rhinitis and Asthma Test (CARAT), CARAT asthma, and Work Productivity and Activity Impairment: Allergy Specific (WPAI:AS) questionnaires as comparators. We performed an internal validation using MASK-air data from Jan 1 to Oct 12, 2022, and an external validation using a cohort of patients with

physician-diagnosed asthma (the INSPIRERS cohort) who had had their diagnosis and control (Global Initiative for Asthma [GINA] classification) of asthma ascertained by a physician.

**Findings:** We studied 135 635 days of MASK-air data from 1662 users from May 21, 2015, to Dec 31, 2021. The scores were strongly correlated with VAS dyspnoea (Spearman correlation coefficient range 0.68-0.82) and moderately correlated with work comparators and quality-of-life-related comparators (for WPAI:AS work, we observed Spearman correlation coefficients of 0.59-0.68). They also displayed high test-retest reliability (intraclass correlation coefficients range 0.79-0.95) and moderate-to-high responsiveness (correlation coefficient range 0.69-0.79; effect size measures range 0.57-0.99 in the comparison with VAS dyspnoea). The best-performing score displayed a strong correlation with the effect of asthma on work and school activities in the INSPIRERS cohort (Spearman correlation coefficients 0.70; 95% CI 0.61-0.78) and good accuracy for the identification of patients with uncontrolled or partly controlled asthma according to GINA (area under the receiver operating curve 0.73; 95% CI 0.68-0.78).

**Interpretation:** e-DASTHMA is a good tool for the daily assessment of asthma control. This tool can be used as an endpoint in clinical trials as well as in clinical practice to assess fluctuations in asthma control and guide treatment optimisation.

**Funding:** None.

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## Conflict of interest statement

Declaration of interests IA is an associate editor for Allergy and Clinical and Translational Allergy journals. RAI reports personal fees from operation POCI-01-0145-36 FEDER-029130 (titled “mINSPIRE-mHealth to measure and improve adherence to medication in chronic respiratory diseases—generalisation and evaluation of gamification, peer support and advanced image processing technologies”), co-funded by European Regional Development Fund, Programa Operacional Competitividade e Internacionalização, Portugal 2020, and by Portuguese Funds through Fundação para a Ciência e a Tecnologia, outside the submitted work. SB-A reports grants from TEVA, and personal fees from Teva, AstraZeneca, Boehringer Ingelheim, GSK, Sanofi, and Mylan, outside the submitted work. L-PB reports grants from Amgen, AstraZeneca, GlaxoSmithKline, Merck, Novartis, and Sanofi-Regeneron; personal fees from AstraZeneca, Novartis, GlaxoSmithKline, Merck, Sanofi-Regeneron, Covis, and Sanofi, outside the submitted work; and is a member of the Chair of Global Initiative for Asthma (GINA) Board of Directors, President of the Global Asthma Organisation (Interasma), and is a member of the Canadian Thoracic Society Respiratory Guidelines Committee and Laval University Chair on Knowledge Transfer, and Prevention and Education in Respiratory and Cardiovascular Health. JB reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Purina, Sanofi-Aventis,

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. 2023 Mar 28;42(3):112208.

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# LMAN1 is a receptor for house dust mite allergens

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Affiliations [expand](#)

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## Abstract

Development of therapies with the potential to change the allergic asthmatic disease course will require the discovery of targets that play a central role during the initiation of an allergic response, such as those involved in the process of allergen recognition. We use a receptor glyco-capture technique to screen for house dust mite (HDM) receptors and identify LMAN1 as a candidate. We verify the ability of LMAN1 to directly bind HDM allergens and demonstrate that LMAN1 is expressed on the surface of dendritic cells (DCs) and airway epithelial cells (AECs) in vivo. Overexpression of LMAN1 downregulates NF- $\kappa$ B signaling in response to inflammatory cytokines or HDM. HDM promotes binding of LMAN1 to the FcR $\gamma$  and recruitment of SHP1. Last, peripheral DCs of asthmatic individuals show a significant reduction in the expression of LMAN1 compared with healthy controls. These findings have potential implications for the development of therapeutic interventions for atopic disease.

**Keywords:** CP; Immunology; ERGIC-53; LMAN1; allergen receptors; allergens; asthma; house dust mite.

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## Conflict of interest statement

Declaration of interests The authors declare no competing interests.

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Respir Med

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doi: 10.1016/j.rmed.2023.107170. Epub 2023 Feb 24.

# Patient characteristics and eligibility for biologics in severe asthma: Results from the Greek cohort of the RECOGNISE "real world" study

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## Abstract

**Background:** Some patients with severe asthma do not achieve sufficient symptom control despite guideline-based treatment, and therefore receive oral (OCS) and systemic corticosteroids (SCS) on regular basis. The side effects of corticosteroid use negatively impact patients' health-related quality of life (HRQoL) and increase the disease burden. Biologics have shown promise in asthma therapy; however, identifying patients who might benefit from biologic therapy is complex due to the heterogeneous pathophysiology of the disease.

**Methods:** The European, non-interventional, multicentre RECOGNISE study ([NCT03629782](https://clinicaltrials.gov/ct2/show/study/NCT03629782)) assessed patient characteristics, asthma medication and control, HRQoL as assessed by St. George's Respiratory Questionnaire (SGRQ), and health care resource use in patients with severe asthma, as well as their eligibility for biologic treatment. Here, data from the Greek cohort (N = 97) are reported.

**Results:** In Greece, patients with severe asthma were more often female (71%) and never smokers (68%). 87% of patients were assessed as eligible for biologic treatment by investigator's judgement (per label criteria: 76%). Most patients had been previously treated with SCS (82% eligible vs 85% non-eligible), with OCS use being more common in non-eligible patients (23.1% vs 11.9%). More eligible patients had poorly controlled asthma (76% vs 54%), and more impaired HRQoL (mean total SGRQ score: 46% vs 39%); symptom burden was significantly higher (mean symptom score: 60% vs. 44%,  $p = 0.0389$ ).

**Conclusions:** A high proportion of Greek patients with severe asthma are eligible for biologic therapy; however, individual risk factors and differences between asthma types must be considered before the introduction of targeted therapy.

**Keywords:** Asthma control; Eligibility for biologics; Greece; Health-related quality of life; RECOGNISE study; Severe asthma.

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## Conflict of interest statement

Declaration of competing interest BP reports honoraria for presentations, participation fees in advisory boards and support for attending meetings from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GSK, MSD, Novartis and Specialty. Therapeutics. TS reports honoraria for presentations, participation fees in advisory boards from AstraZeneca, Chiesi, Elpen and Menarini. PA has nothing to disclose. NM is an employee of AstraZeneca Greece, Athens, Greece. PG is an employee of AstraZeneca Greece, Athens, Greece.

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Curr Opin Allergy Clin Immunol

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. 2023 Apr 1;23(2):137-143.

doi: 10.1097/ACI.0000000000000891.

# E-cigarettes and asthma in adolescents

[Folashade Afolabi](#)<sup>1,2,3</sup>, [Devika R Rao](#)<sup>1,2,3</sup>

Affiliations expand

- PMID: 36821483
- DOI: [10.1097/ACI.0000000000000891](https://doi.org/10.1097/ACI.0000000000000891)

## Abstract

**Purpose of review:** E-cigarettes have been long purported to be a mechanism of harm reduction in current smokers. However, market expansion to adolescents has been aggressive, despite government interventions. Research examining the adverse effects of e-cigarettes in teens with asthma has been limited. We discuss the most recent data on the pulmonary manifestations of e-cigarettes use and exposure in adolescents with asthma.

**Recent findings:** Adolescents with asthma are more likely to be e-cigarette users than those without asthma and more likely to have asthma exacerbations. Increased pulmonary inflammatory cytokines have been seen in e-cigarette users and mouse models. Yet, providers are not confident in e-cigarette screening and counselling despite acknowledging adolescents are using e-cigarettes regularly.



**Summary:** Since the introduction of e-cigarettes into the United States market in 2007, adolescents use of these products has risen, even after a brief decline during the height of the COVID-19 pandemic. This review will describe the most recent studies on e-cigarette use trends, cytotoxicity of e-cigarette aerosol and associations with the diagnosis and symptoms of asthma. Knowledge gaps, advocacy efforts, evidence on e-cigarette cessation will be highlighted.

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. 2023 Apr 1;23(2):98-99.

doi: 10.1097/ACI.0000000000000896.

## [Pediatric asthma and development of atopy 2023](#)

[Mattia Giovannini](#)<sup>1,2</sup>, [Wanda Phipatanakul](#)<sup>3</sup>

Affiliations expand

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- DOI: [10.1097/ACI.0000000000000896](https://doi.org/10.1097/ACI.0000000000000896)

*No abstract available*

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Meta-Analysis

Curr Opin Allergy Clin Immunol

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. 2023 Apr 1;23(2):76-84.

doi: 10.1097/ACI.0000000000000882. Epub 2023 Feb 6.

## Wood dust and asthma

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Affiliations expand

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- PMCID: PMC9977320 (available on 2024-04-01)
- DOI: [10.1097/ACI.0000000000000882](https://doi.org/10.1097/ACI.0000000000000882)

## Abstract

**Purpose of the review:** Review recent developments on asthma associated with wood dust, given the increasing scale of wood handling and processing activities globally.

**Recent findings:** Work in wood industries is associated with a significantly increased risk of respiratory symptoms, rhinitis and asthma. This can be attributed to traditional processing techniques and newer technologies producing complex bioaerosol exposures, which may include chemicals. Meta-analysis studies indicate strong evidence for wood dusts as occupational sensitizers for asthma, but the underlying mechanisms remain poorly understood. The global prevalence of asthma in wood workers ranges between 6-18% and for rhinitis 16-33%. Exposure estimates show wide variation. Risk factors include atopy and exposure to certain wood species, elevated current and cumulative particulate exposures.

**Summary:** Future studies should focus on better characterization of wood dust allergens and other bioaerosol components, specific immunoglobulin E responses to different wood species, pathophysiological mechanisms underlying asthma, and modelling dose-response relationships using refined exposure metrics for dust particulate and other bioaerosol components. There is a need for improved health-based international exposure standards and effective workplace control measures to reduce exposures to wood dust particulate (hard and soft woods), endotoxin and  $\beta$ -glucan, to reduce the risks of asthma in wood workers.

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## Conflict of interest statement

Conflicts of interest

None

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Respirology

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. 2023 Apr;28(4):406-408.

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# Lessons from a failed randomized controlled trial of speech pathology intervention in vocal cord dysfunction

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**Keywords:** asthma; inducible laryngeal obstruction; speech pathology; vocal cord dysfunction.

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Lancet Respir Med

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. 2023 Apr;11(4):e31-e32.

doi: 10.1016/S2213-2600(23)00042-5. Epub 2023 Feb 15.

# Sedative medications: an avoidable cause of asthma and COPD exacerbations?

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Affiliations expand

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## **Conflict of interest statement**

We declare no competing interests. CVC had full access to all the study data and takes full responsibility for the integrity of the data and the accuracy of the data analysis. CVC and DES had final responsibility for the decision to submit for publication.

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Respir Med

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. 2023 Apr;209:107154.

doi: 10.1016/j.rmed.2023.107154. Epub 2023 Feb 14.

# Small airway dysfunction in asthmatic patients treated with as-needed SABA monotherapy: A perfect storm

[Marcello Cottini](#)<sup>1</sup>, [Carlo Lombardi](#)<sup>2</sup>, [Pasquale Comberiati](#)<sup>3</sup>, [Massimo Landi](#)<sup>4</sup>, [Alvise Berti](#)<sup>5</sup>, [Laura Ventura](#)<sup>6</sup>

Affiliations expand

- PMID: 36796546
- DOI: [10.1016/j.rmed.2023.107154](https://doi.org/10.1016/j.rmed.2023.107154)

## Abstract

**Background:** Short-acting beta agonist (SABA)-only treatment is associated with poor asthma control and adverse clinical outcomes. The importance of small airway dysfunction (SAD) is increasingly recognized in asthma, but less is known in patients using SABA-only therapy. We aimed to investigate the impact of SAD on asthma control in an unselected cohort of 60 adults with physician-diagnosed intermittent asthma treated with as-needed SABA monotherapy.

**Methods:** All patients underwent standard spirometry and impulse oscillometry (IOS) at the first visit and were stratified by the presence of SAD defined by IOS (fall in resistance 5-20 Hz [R5-R20]>0.07 kPa × s\*L<sup>-1</sup>). Univariable and multivariable analyses were used to analyze cross-sectional relationships between clinical variables and SAD.

**Results:** SAD was present in 73% of the cohort. Compared with patients without SAD, adults with SAD had a higher number of severe exacerbations (65.9% versus 25.0%,  $p < 0.05$ ), higher use of annual SABA canisters (median (IQR), 3 (1.75-3) versus 1 (1-2),  $p < 0.001$ ), and significantly less well-controlled asthma (11.7% versus 75.0%,  $p < 0.001$ ). Spirometry parameters were similar between patients with IOS-defined SAD and those without SAD. The multivariable logistic regression analysis showed that exercise-induced bronchoconstriction symptoms (EIB, odds ratio [OR] 31.18; 95%CI:4.85-365.00) and night awakenings due to asthma (OR 30.30; 95%CI:2.61-1141.00) were independent predictors of SAD, with a high predictive power of the model incorporating these baseline predictors (AUC 0.92).

**Conclusions:** EIB and nocturnal symptoms are strong predictors of SAD in asthmatic patients using as-needed SABA-monotherapy, helping to distinguish subjects with SAD among patients with asthma when IOS cannot be performed.

**Keywords:** Asthma; Impulse oscillometry; Short-acting beta agonist; Small airways.

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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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. 2023 Apr;50(2):63.

doi: 10.1111/iji.12615. Epub 2023 Feb 13.

## Interleukin 17A and 17F polymorphisms and asthma susceptibility: Correspondence

[Amnuay Kleebayoon](#)<sup>1</sup>, [Viroj Wiwanitkit](#)<sup>2</sup>

Affiliations expand

- PMID: 36779706

- DOI: [10.1111/iji.12615](https://doi.org/10.1111/iji.12615)

*No abstract available*

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Meta-Analysis

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. 2023 Apr;50(2):64.

doi: 10.1111/iji.12616. Epub 2023 Feb 13.

# IL-17A and IL-17F polymorphisms and asthma risk: A meta-analysis

[Young Ho Lee](#)<sup>1</sup>

Affiliations expand

- PMID: 36779703
- DOI: [10.1111/iji.12616](https://doi.org/10.1111/iji.12616)

*No abstract available*

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. 2023 Apr;209:107148.

doi: 10.1016/j.rmed.2023.107148. Epub 2023 Feb 6.

# Oscillometry to support clinical assessment in asthmatic preschoolers: Real-life impact

[Bennet Desormeau](#)<sup>1</sup>, [Anna Smyrnova](#)<sup>2</sup>, [Olivier Drouin](#)<sup>3</sup>, [Francine Monique Ducharme](#)<sup>3</sup>

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- PMID: 36754219
- DOI: [10.1016/j.rmed.2023.107148](https://doi.org/10.1016/j.rmed.2023.107148)

## Free article

## Abstract

In preschoolers, asthma control is assessed clinically using history and physical examination. In certain centres, oscillometry is used to support clinical assessment; yet its clinical utility for asthma management remains to be quantified. The objectives were to determine if oscillometry, as adjunct to clinical assessment, influences asthma assessment, management and control, compared to clinical assessment alone in preschoolers. We conducted a cross-sectional study in children aged 3-5 years with a confirmed asthma diagnosis. Oscillometry-tested preschoolers were matched by propensity score to untested children. The co-primary outcomes, the likelihood of a persistent asthma phenotype and a maintenance therapy prescription at the index visit, were examined by multivariable logistic regression. Asthma control over the next year was examined by cumulative logistic regression in the nested retrospective cohort with available drug claim data. The cohort comprised 726 (249 oscillometry-tested; 477 untested) children with 57.4% male (median age: 4.6 years). Propensity score matching resulted in comparable groups. Compared to controls, oscillometry-tested children were more frequently labelled with a persistent phenotype (67% vs. 50%; adjusted OR [95% CI]: 2.34 [1.66-3.34]) with no significant difference in maintenance therapy prescription (65% vs. 58%; 1.37 [0.98-1.92]); but experienced a lower likelihood of poor control over the next year (adjusted OR [95% CI]:

0.24 [0.08-0.74]). The association between the addition of oscillometry to clinical assessment with more persistent phenotype labelling and better asthma control supports its clinical utility; no significant impact on maintenance therapy prescription was observed at the index visit.

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## Conflict of interest statement

Declaration of competing interest Bennet Desormeau and Anna Smyrnova declare no conflicts of interest. Francine Monique Ducharme has received unrestricted research funds from Astra Zeneca, Covis Pharma, GlaxoSmithKline, Merck Canada, Novartis, Teva, Trudell Medical; research funds from Covis Pharma, GlaxoSmithKline, and MEDteq in partnership with Thorasys Inc.; honorarium for consultancy work from Astra Zeneca, Covis Pharma, Teva, and Thorasys Inc.; and honorarium as an invited speaker from Covis Pharma, Jean Jean-Coutu Pharmacy and Brunet Pharmacy. Olivier Drouin has received funding from Fonds de la Recherche du Québec en Santé and research funds from Covis Pharma.

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. 2023 Apr;209:107147.

doi: 10.1016/j.rmed.2023.107147. Epub 2023 Feb 6.

# Association of rest-activity circadian rhythm with chronic respiratory diseases, a cross-section survey from NHANES 2011-2014

[Wenbo Gu](#)<sup>1</sup>, [Zhen Tian](#)<sup>1</sup>, [Wei Tian](#)<sup>2</sup>, [Yuhua Song](#)<sup>1</sup>, [Guolian Qi](#)<sup>1</sup>, [Jiayue Qi](#)<sup>3</sup>, [Changhao Sun](#)<sup>4</sup>

Affiliations expand

- PMID: 36754218
- DOI: [10.1016/j.rmed.2023.107147](https://doi.org/10.1016/j.rmed.2023.107147)

## Abstract

**Objective:** A growing number of studies have examined the 24-h rest-activity characteristics in relation to health outcomes. Up to now, few studies have paid attention to the role of rest-activity circadian rhythm in chronic respiratory diseases (CRDs); therefore, to fill this gap, our study innovatively explored the association of rest-activity circadian rhythm indices with CRDs.

**Methods:** A total of 7412 participants from the National Health and Nutrition Examination Survey (NHANES) 2011–2014 were included in this study. The rest-activity circadian rhythm indices were calculated using accelerometer data and were divided into quartiles to perform logistic regression.

**Results:** Participants in the highest quartile of Relative amplitude (RA) had a lower prevalence of emphysema, chronic bronchitis and asthma, compared to those in the lowest quartile. Participants in the highest quartile of Intradaily variability (IV) was associated with a higher prevalence of emphysema relative to those in the lowest quartile. Compared to those in the lowest quartile, participants in the highest quartile of the average activity of the most active continuous 10-h period (M10) had a lower prevalence of emphysema. Additionally, compared to those in the lowest quartile of the average activity of the least active continuous 5-h period (L5) and L5 start time, participants in the highest quartile had a higher prevalence of asthma.

**Conclusions:** This study demonstrated that in general US adult population, disrupted rest-activity circadian rhythm was associated with a higher prevalence of CRDs.

**Keywords:** Asthma; Chronic bronchitis; Chronic respiratory diseases; Emphysema; Rest-activity circadian rhythm.

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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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. 2023 Apr;209:107149.

doi: 10.1016/j.rmed.2023.107149. Epub 2023 Feb 6.

# [Are BMI and adipokines associated with asthma, atopy and lung function in young adults previously hospitalized for bronchiolitis?](#)

[Karen Galta Sørensen](#)<sup>1</sup>, [Knut Øymar](#)<sup>2</sup>, [Grete Jonsson](#)<sup>3</sup>, [Ingvild Dalen](#)<sup>4</sup>, [Thomas Halvorsen](#)<sup>5</sup>, [Ingvild Bruun Mikalsen](#)<sup>2</sup>

Affiliations expand

- PMID: 36754217
- DOI: [10.1016/j.rmed.2023.107149](https://doi.org/10.1016/j.rmed.2023.107149)

## Abstract

**Background:** Children hospitalized for bronchiolitis have increased risk of asthma and low lung function persisting into adulthood, but the underlying mechanisms are poorly understood. Body mass index (BMI) and adipokines are associated with respiratory morbidity. We aimed to investigate if associations between BMI and adipokines and the

outcomes asthma, atopy, and lung function differed between young adults previously hospitalized for bronchiolitis and control subjects.

**Methods:** This sub study of a historical cohort enrolled 185 young adults previously hospitalized for bronchiolitis and 146 matched control subjects. Exposures (BMI and the adipokines: adiponectin, leptin, resistin, and ghrelin) and outcomes (asthma, atopy, and lung function) were measured cross-sectionally at 17-20 years of age. Associations were tested in regression models, and differences between the post-bronchiolitis- and control group were tested by including interaction terms.

**Results:** BMI was associated with asthma and lung function, but we did not find that the associations differed between the post-bronchiolitis- and control group. We also found some associations between adipokines and outcomes, but only associations between adiponectin and forced vital capacity (FVC) and between resistin and current asthma differed between the groups (p-value interaction term 0.027 and 0.040 respectively). Adiponectin tended to be positively associated with FVC in the post-bronchiolitis group, with an opposite tendency in the control group. Resistin was positively associated with current asthma only in the control group.

**Conclusion:** The increased prevalence of asthma and impaired lung function observed in young adults previously hospitalized for bronchiolitis do not seem to be related to growth and fat metabolism.

**Keywords:** Adipokines; Asthma; Atopy; BMI; Bronchiolitis; Lung function.

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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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. 2023 Apr 1;23(2):193-198.

doi: 10.1097/ACI.0000000000000893. Epub 2023 Jan 20.

# Coronavirus disease 2019 and severe asthma

[Alida Benfante](#)<sup>1</sup>, [Giuseppe Pirrello](#), [Francesca Sala](#), [Gabriele Seminara](#), [Nicola Scichilone](#)

Affiliations expand

- PMID: 36752375
- DOI: [10.1097/ACI.0000000000000893](https://doi.org/10.1097/ACI.0000000000000893)

## Abstract

**Purpose of review:** The relationship between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the most severe forms of asthma has been an object of discussion. Indeed, it is not clear whether asthma is among the risk factors for the occurrence of severe coronavirus disease 2019 (COVID-19) disease, or rather it plays a protective role against the worsening of the respiratory involvement in the SARS-CoV-2 infection. On the other hand, the extent to which coronavirus infection may trigger asthma attacks is still partly unknown. The current investigation aims at reviewing the available literature on the topic to address factors influencing this relationship.

**Recent findings:** Based on recent observations, it is likely that type 2 inflammation plays a protective role against SARS-CoV-2 infection and disease. In particular, asthmatics show different expression of angiotensin-converting enzyme2 (ACE2) and Transmembrane protease, serine 2 (TMPRSS2) that are responsible for a reduced risk of infection as well as lower risk of hospitalization. Interestingly, studies showed a safe profile of inhaled corticosteroids and biological drugs in SARS-CoV-2 infection. In addition, inhaled corticosteroid could play a protective role against worsening of asthma.

**Summary:** The current findings suggest that current treatment for asthma should be maintained to avoid severe exacerbations. Severe asthmatics under biological treatment should continue their medications, and be encouraged to receive COVID-19 vaccines.

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. 2023 Apr 1;23(2):111-118.

doi: 10.1097/ACI.0000000000000880. Epub 2022 Nov 24.

## [Biologics and severe asthma in children](#)

[Shikha Saxena](#)<sup>1</sup>, [Christian Rosas-Salazar](#)<sup>1</sup>, [Anne Fitzpatrick](#)<sup>2,3</sup>, [Leonard B Bacharier](#)<sup>1</sup>

Affiliations expand

- PMID: 36730217

- DOI: [10.1097/ACI.0000000000000880](https://doi.org/10.1097/ACI.0000000000000880)

### Abstract

**Purpose of review:** Severe asthma can carry significant morbidity and mortality for patients, and it places a burden on families and the healthcare system. Biologic agents have revolutionized the care of patients with severe asthma in recent years. Evidence surrounding some of these therapies is limited in the pediatric population, but recent studies show that they significantly improve asthma care when used appropriately. In this

review, we discuss the biologic therapies currently approved to treat severe asthma in school-age children and adolescents.

**Recent findings:** Randomized controlled trials have been published in support of biologics in children and/or adolescents. These therapies have been shown to reduce the annual rate of severe asthma exacerbations by at least 40-50%, and some up to about 70%. Improvements in asthma control, lung function, oral corticosteroid use, and quality of life have also been demonstrated, although these vary by agent. Furthermore, these therapies have reassuring safety profiles in pediatric patients.

**Summary:** With three biologic agents approved for children ages 6-11 years and five approved for adolescents ages >12 years, it can be challenging to select one. The therapy should be chosen after careful consideration of the patient's asthma phenotype and biomarkers. Additional pediatric-specific clinical trials would be helpful in developing evidence-based guidelines on biologic therapies in this population.

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. 2023 Apr 1;23(2):119-131.

doi: 10.1097/ACI.0000000000000883. Epub 2022 Nov 24.

## [Updates in school-based asthma management](#)



[Ashley A Lowe](#)<sup>1,2</sup>, [Ina St Onge](#)<sup>3</sup>, [Michelle Trivedi](#)<sup>3,4,5</sup>

Affiliations expand

- PMID: 36730215
- PMCID: PMC9974735 (available on 2024-04-01)
- DOI: [10.1097/ACI.0000000000000883](https://doi.org/10.1097/ACI.0000000000000883)

## Abstract

**Purpose of review:** School-based asthma management is an important component of pediatric asthma care that has the potential to provide more universal evidence-based asthma care to children and mitigate asthma-related health inequities. The purpose of this review is to highlight relevant developments in school-based asthma management over the past 2 years.

**Recent findings:** There have been considerable recent scientific advances in school-based asthma management including robust clinical trials of environmental interventions in the classroom setting, school-nurse led interventions, stock albuterol policy changes, school-based telemedicine approaches and innovative methods to engage community stakeholders in research that have pushed the frontiers of school-based asthma care.

**Summary:** Recent scientific work in school-based asthma management demonstrates the potential power of schools in providing access to guideline-based asthma care for all children with asthma and in improving their health outcomes. Future work should focus on the evaluation of methods to promote the adoption of school-based asthma management strategies in real-world practice and support evidence-based policy change and strategic partnerships to improve asthma health outcomes and produce meaningful public health impact for diverse children and families.

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## Conflict of interest statement

CONFLICT OF INTEREST: NA

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. 2023 Apr 1;23(2):100-110.

doi: 10.1097/ACI.0000000000000881. Epub 2022 Nov 24.

# [Air pollution and childhood asthma](#)

[Lana Mukharesh](#)<sup>1,2</sup>, [Wanda Phipatanakul](#)<sup>2,3</sup>, [Jonathan M Gaffin](#)<sup>1,2</sup>

Affiliations [expand](#)

- PMID: 36730122
- DOI: [10.1097/ACI.0000000000000881](https://doi.org/10.1097/ACI.0000000000000881)

## Abstract

**Purpose of review:** Asthma is the most common chronic disease of childhood. Environmental exposures, such as allergens and pollutants, are ubiquitous factors associated with asthma development and asthma morbidity. In this review, we highlight the most recent studies relevant to childhood asthma risk, onset, and exacerbation related to air pollution exposure.

**Recent findings:** In this article, we review current research that has been published between 2021 and 2022, demonstrating the effects of early-life exposure to key air pollutants (e.g., particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>) and ground-level ozone (O<sub>3</sub>), environmental tobacco smoke, radon, and volatile organic compounds (VOC) on respiratory health.

**Summary:** Air pollution continues to be a global burden with serious consequences related to respiratory health. Interventions aimed at reducing air pollution in the environment must be achieved in an effort to improve asthma outcomes and pediatric health.

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- [55 references](#)

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. 2023 Apr 1;23(2):63-69.

doi: 10.1097/ACI.0000000000000884. Epub 2022 Dec 2.

## [Update on irritant-induced occupational asthma](#)

[Steven Ronsmans](#)<sup>1</sup>, [Nicole Le Moual](#)<sup>2</sup>, [Orianne Dumas](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 36729951

- DOI: [10.1097/ACI.0000000000000884](https://doi.org/10.1097/ACI.0000000000000884)

## Abstract

**Purpose of review:** In this narrative review, we aim to highlight novel research findings on both acute/subacute irritant-induced asthma (IIA) and chronic exposure IIA (also called 'low dose' IIA).

**Recent findings:** Novel case series showed that acute and subacute IIA cases had similar causal agents (e.g., acid or base aerosols/fumes, dusts, mixtures) but had occurred in different circumstances (accidents vs. regular work). Acute and subacute IIA cases had similar clinical characteristics but poorer short-term outcomes than sensitizer-induced occupational asthma patients. Novel large epidemiological studies reported associations between chronic occupational exposure to irritants and current adult-onset asthma and poor asthma control, and with a specific asthma endotype characterized by neutrophilic inflammation and oxidative stress. Recent studies reconfirmed the association of the use of disinfectants and cleaning products (especially sprays) with IIA. A role for genetic susceptibility has been suggested.

**Summary:** Recent literature provided further understanding of both acute/subacute and chronic exposure IIA, in terms of causes, possible mechanisms, and consequences such as poor asthma control. Research is needed to clarify several aspects of IIA, including its frequency (still likely underestimated), modulating factors, and mechanisms. Research aiming at improving irritant exposure assessment, including intensity/duration, and determining relevant exposure windows would be welcome.

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. 2023 Apr 1;23(2):144-150.

doi: 10.1097/ACI.0000000000000872. Epub 2022 Dec 27.

# Social determinants of health and asthma

[Andre E Espallat](#)<sup>1</sup>, [Michelle L Hernandez](#)<sup>2,3</sup>, [Allison J Burbank](#)<sup>2,3</sup>

Affiliations expand

- PMID: 36728768
- PMCID: PMC9974568 (available on 2024-04-01)
- DOI: [10.1097/ACI.0000000000000872](https://doi.org/10.1097/ACI.0000000000000872)

## Abstract

**Purpose of review:** Social determinants of health play a major role in healthcare utilization and outcomes in patients with asthma. Continuing to understand how these complex and interwoven relationships interact to impact patient care will be crucial to creating innovative programmes that address these disparities.

**Recent findings:** The current literature continues to support the association of substandard housing, urban and rural neighbourhoods, and race/ethnicity with poor asthma outcomes. Targeted interventions with community health workers (CHWs), telemedicine and local environmental rectifications can help improve outcomes.

**Summary:** The link between social determinants and poor asthma outcomes continues to be supported by recent literature. These factors are both nonmodifiable and consequences of institutionalized racist policies that require innovative ideas, technologic equity and funding for groups most at risk for poorer outcomes.

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## Conflict of interest statement

Conflicts of Interest: The authors have nothing to disclose.

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. 2023 Apr 1;23(2):179-184.

doi: 10.1097/ACI.0000000000000890. Epub 2023 Jan 12.

# Environment and the development of severe asthma in inner city population

[Julia X Lee](#)<sup>1</sup>, [Wanda Phipatanakul](#)<sup>2,3</sup>, [Jonathan M Gaffin](#)<sup>1,3</sup>

Affiliations expand

- PMID: 36728241
- PMID: PMC9974609 (available on 2024-04-01)
- DOI: [10.1097/ACI.0000000000000890](https://doi.org/10.1097/ACI.0000000000000890)

## Abstract

**Purpose of review:** Higher asthma prevalence and morbidity are seen in inner-city areas, disproportionately affecting low-income families living in substandard housing. Children within these families experience more frequent asthma exacerbations, acute care and emergency department visits, and hospitalizations, thus characterizing severe asthma. In this review, we assess recent published literature focused on indoor and outdoor exposures that contribute to the development and morbidity of asthma.

**Recent findings:** Many urban environmental exposures contribute to asthma burden, including tobacco/e-cigarette smoke, pest allergens, molds, and possibly synthetic chemicals such as phthalates and bisphenol A, radon, and volatile organic compounds. Individuals living in inner-city areas also experience higher levels of air pollutants and ambient heat, further perpetuating asthma incidence and severity.

**Summary:** This article summarizes the latest advances and provides direction for future research on risk factors, interventions, and public policy to help alleviate the burden of asthma due to urban environment exposures.

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## Conflict of interest statement

Conflict of Interest: Jonathan Gaffin receives research support from NIEHS/NIH, Vertex pharmaceuticals; consulting fees from Syneos Health and AiCME. Wanda Phipatanakul reports grant and clinical trial support from NIH, Genentech, Novartis, Astra Zeneca, Regeneron, GSK, Merck, Sanofi, and consulting fees from Genentech, Novartis, Astra Zeneca, Regeneron, GSK, Merck, Sanofi, and Teva.

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Allergy

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. 2023 Apr;78(4):940-956.

doi: 10.1111/all.15666. Epub 2023 Feb 15.

# Decoding the genetic and epigenetic basis of asthma

[Bernard S Stikker](#)<sup>1</sup>, [Rudi W Hendriks](#)<sup>1</sup>, [Ralph Stadhouders](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36727912
- DOI: [10.1111/all.15666](https://doi.org/10.1111/all.15666)

## Abstract

Asthma is a complex and heterogeneous chronic inflammatory disease of the airways. Alongside environmental factors, asthma susceptibility is strongly influenced by genetics. Given its high prevalence and our incomplete understanding of the mechanisms underlying disease susceptibility, asthma is frequently studied in genome-wide association studies (GWAS), which have identified thousands of genetic variants associated with asthma development. Virtually all these genetic variants reside in non-coding genomic regions, which has obscured the functional impact of asthma-associated variants and their translation into disease-relevant mechanisms. Recent advances in genomics technology and epigenetics now offer methods to link genetic variants to gene regulatory elements embedded within non-coding regions, which have started to unravel the molecular mechanisms underlying the complex (epi)genetics of asthma. Here, we provide an integrated overview of (epi)genetic variants associated with asthma, focusing on efforts to link these disease associations to biological insight into asthma pathophysiology using state-of-the-art genomics methodology. Finally, we provide a perspective as to how decoding the genetic and epigenetic basis of asthma has the potential to transform clinical management of asthma and to predict the risk of asthma development.

**Keywords:** EWAS; GWAS; PRS; asthma; epigenetics.

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Pediatr Blood Cancer



. 2023 Apr;70(4):e30231.

doi: 10.1002/pbc.30231. Epub 2023 Feb 1.

# The relationship between childhood leukaemia and childhood asthma: A pharmacoepidemiological study from the Netherlands

[Elias Atmaj](#)<sup>1</sup>, [Catharina C M Schuiling-Veninga](#)<sup>1</sup>, [Eline L van Tuinen](#)<sup>1</sup>, [Jens H J Bos](#)<sup>1</sup>, [Tjalling W de Vries](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 36726028
- DOI: [10.1002/pbc.30231](https://doi.org/10.1002/pbc.30231)

## Abstract

**Background:** It has been suggested that childhood asthma lowers the risk of childhood leukaemia. Studies have found an inverse association between these conditions. However, most studies on this relationship are based on questionnaires and telephone interviews, introducing recall bias. Therefore, we conducted a matched case-control study based on drug prescription data to assess the relationship between both conditions.

**Methods:** In a large database, covering more than one million individuals, we identified cases of children who had been prescribed 6-mercaptopurine (6-MP). This drug is used in the outpatient maintenance therapy of childhood leukaemia. We matched every child with leukaemia on sex and age ( $\pm 6$  months) to children without leukaemia (controls). The variable of having had asthma was defined as receiving at least two prescriptions for an inhaled corticosteroid within 12 months.

**Results:** We identified 59 children aged 2-18 who had been prescribed 6-MP (cases), and they were matched to 21,918 controls. Of the children with childhood leukaemia, three (5%) had childhood asthma, whereas in the control group 4889 (22%) had childhood asthma (odds ratio [OR] 0.19; 95% confidence interval 0.06-0.60).

**Conclusion:** In this study on the relationship between childhood asthma and childhood leukaemia, we found a strong inverse association.

**Keywords:** asthma; atopy; childhood leukaemia; pharmacoepidemiology.

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- [10 references](#)

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. 2023 Apr;78(4):928-939.

doi: 10.1111/all.15662. Epub 2023 Feb 7.

# [Understanding the increased susceptibility to asthma development in preterm infants](#)

[Jeremy Anderson](#)<sup>1,2</sup>, [Lien Anh Ha Do](#)<sup>1,2</sup>, [Danielle Wurzel](#)<sup>1,3,4</sup>, [Paul V Licciardi](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36719074
- DOI: [10.1111/all.15662](https://doi.org/10.1111/all.15662)

## Abstract

Preterm birth is associated with aberrant pulmonary development and increased susceptibility to a range of chronic lung diseases. Even in healthy preterms, the prevalence of physician-diagnosed asthma is far higher than in infants born at term. While physiological, environmental, and genetic factors have been studied extensively, few studies have investigated the immunological factors underpinning this increased susceptibility. Lower rates of atopy and allergic sensitization in preterm compared to term infants suggests non-allergic mechanisms may be driving asthma development in preterms. Preterm infants are more likely to develop severe RSV and HRV disease and have altered microbiomes compared to term infants. Therefore, investigating the differences in immunological interactions (e.g., response to viral infections, microbiome) between children born preterm and term will aid in understanding the immunological basis for their increased susceptibility to asthma development. This is critical to inform the development of interventions to reduce the burden of asthma in this highly vulnerable demographic.

**Keywords:** RSV; allergy; asthma; microbiome; preterm infant.

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. 2023 Apr;57(8):481-489.

doi: 10.1136/bjsports-2022-106059. Epub 2023 Jan 30.

# Diagnostic approach to lower airway dysfunction in athletes: a systematic review and meta-analysis by a subgroup of the IOC consensus on 'acute respiratory illness in the athlete'

[Tonje Reier-Nilsen](#)<sup>1,2</sup>, [Nicola Sewry](#)<sup>3,4</sup>, [Bruno Chenuel](#)<sup>5,6</sup>, [Vibeke Backer](#)<sup>7,8</sup>, [Kjell Larsson](#)<sup>9</sup>, [Oliver J Price](#)<sup>10,11</sup>, [Lars Pedersen](#)<sup>12</sup>, [Valerie Bougault](#)<sup>13</sup>, [Martin Schwellnus](#)<sup>3,4</sup>, [James H Hull](#)<sup>14,15</sup>

Affiliations expand

- PMID: 36717213
- DOI: [10.1136/bjsports-2022-106059](https://doi.org/10.1136/bjsports-2022-106059)

## Abstract

**Objectives:** To compare the performance of various diagnostic bronchoprovocation tests (BPT) in the assessment of lower airway dysfunction (LAD) in athletes and inform best clinical practice.

**Design:** Systematic review with sensitivity and specificity meta-analyses.

**Data sources:** PubMed, EBSCOhost and Web of Science (1 January 1990-31 December 2021).

**Eligibility criteria:** Original full-text studies, including athletes/physically active individuals (15-65 years) who underwent assessment for LAD by symptom-based questionnaires/history and/or direct and/or indirect BPTs.

**Results:** In 26 studies containing data for quantitative meta-analyses on BPT diagnostic performance (n=2624 participants; 33% female); 22% had physician diagnosed asthma and 51% reported LAD symptoms. In athletes with symptoms of LAD, eucapnic voluntary hyperpnoea (EVH) and exercise challenge tests (ECTs) confirmed the diagnosis with a 46% sensitivity and 74% specificity, and 51% sensitivity and 84% specificity, respectively, while

methacholine BPTs were 55% sensitive and 56% specific. If EVH was the reference standard, the presence of LAD symptoms was 78% sensitive and 45% specific for a positive EVH, while ECTs were 42% sensitive and 82% specific. If ECTs were the reference standard, the presence of LAD symptoms was 80% sensitive and 56% specific for a positive ECT, while EVH demonstrated 65% sensitivity and 65% specificity for a positive ECT.

**Conclusion:** In the assessment of LAD in athletes, EVH and field-based ECTs offer similar and moderate diagnostic test performance. In contrast, methacholine BPTs have lower overall test performance.

**Prospero registration number:** CRD42020170915.

**Keywords:** Asthma; Athletes; Diagnosis; Exercise Test; Respiratory System.

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## Conflict of interest statement

Competing interests: None declared.

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Can J Physiol Pharmacol

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. 2023 Apr 1;101(4):200-213.

doi: 10.1139/cjpp-2022-0334. Epub 2023 Jan 30.

## [Female-biased association of NOS2-c.1823C>T \(rs2297518\) with co-susceptibility to metabolic syndrome and asthma](#)

[Younes Aftabi](#)<sup>1,2</sup>, [Neda Gilani](#)<sup>3</sup>, [Atefeh Ansarin](#)<sup>1</sup>, [Amir Amiri-Sadeghan](#)<sup>1</sup>, [Nasim Bakhtiyari](#)<sup>1</sup>, [Maryam Seyyedi](#)<sup>1</sup>, [Elnaz Faramarzi](#)<sup>4</sup>, [Akbar Sharifi](#)<sup>1</sup>, [Khalil Ansarin](#)<sup>1,2</sup>, [Ensiyeh Seyedrezazadeh](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36716438
- DOI: [10.1139/cjpp-2022-0334](https://doi.org/10.1139/cjpp-2022-0334)

## Abstract

The nitric oxide (NO) pathway contributes to the pathogenesis of metabolic syndrome (MetS) and asthma. *NOS2* encodes inducible-NO synthase, which is an important enzyme of the pathway, and its variations could affect the risk of asthma and MetS and thereby co-susceptibility to them. This study aims to estimate the association of *NOS2*-c.1823C>T with risk of asthma, MetS, and asthma with MetS condition (ASMetS), and with asthma stages: intermittent, mild, moderate, and severe asthma. The study included asthmatics ( $n = 555$ ), MetS ( $n = 334$ ), and ASMetS cases ( $n = 232$ ) and 351 controls, which were genotyped by the PCR-RFLP method. The T allele was significantly associated with an increased risk of asthma and MetS in the sample population and females. CT genotype and CT+TT model were significantly associated with increased risk of ASMetS in females. A significant association between CT genotype and increased risk of ASMetS in the sample population and females was found in ASMetS versus MetS. In the sample population and among females, the T allele was significantly associated with severe asthma. The rs2297518 single nucleotide polymorphism of *NOS2* contributes to the risk of MetS, asthma, and co-susceptibility to them, and this contribution may be stronger in females compared to males.

**Keywords:** SNP; iNOS; lung; metabolic disorder; nitric oxide pathway; p.Ser608Leu.

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Respir Med

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. 2023 Apr-May;210:107125.

doi: 10.1016/j.rmed.2023.107125. Epub 2023 Jan 24.

# Allergen immunotherapy for allergic asthma: The future seems bright

[Zuzana Diamant](#)<sup>1</sup>, [Maurits van Maaren](#)<sup>2</sup>, [Antonella Muraro](#)<sup>3</sup>, [Milos Jesenak](#)<sup>4</sup>, [Ilja Striz](#)<sup>5</sup>

Affiliations expand

- PMID: 36702170
- DOI: [10.1016/j.rmed.2023.107125](https://doi.org/10.1016/j.rmed.2023.107125)

## Abstract

Allergen specific immunotherapy (AIT) is the only causal therapeutic option for allergic airway diseases including asthma and allergic rhinitis. AIT has been shown to restore the allergen immune tolerance, can modify both the early and late-onset allergen-specific airway hyperreactivity, helps to achieve disease control/remission and prevents new sensitisations. Recent real life data on long-term effectiveness of house dust mite (HDM) AIT in a large group of patients with HDM-driven asthma further underscored its unique therapeutic potential as well as confirmed previous data with pollen AIT. More widespread use of this causal treatment in select patient populations should further move this promising therapeutic field. In this mini-review, we discuss updates on new insights based on real world patient data.

**Keywords:** Allergen immunotherapy; Asthma; Clinical effectiveness; Disease modification; Disease remission; Mechanisms; Prevention.

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Eur Respir Rev

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. 2023 Jan 25;32(167):220144.

doi: 10.1183/16000617.0144-2022. Print 2023 Mar 31.

# Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD

[Ariel A Calderon](#)<sup>1</sup>, [Colin Dimond](#)<sup>1</sup>, [David F Choy](#)<sup>1</sup>, [Rajita Pappu](#)<sup>1</sup>, [Michele A Grimbaldston](#)<sup>1</sup>, [Divya Mohan](#)<sup>2</sup>, [Kian Fan Chung](#)<sup>3</sup>

Affiliations expand

- PMID: 36697211
- PMID: [PMC9879340](#)
- DOI: [10.1183/16000617.0144-2022](#)

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## Abstract

Interleukin-33 (IL-33) and thymic stromal lymphopoietin (TSLP) are alarmins that are released upon airway epithelial injury from insults such as viruses and cigarette smoke, and play critical roles in the activation of immune cell populations such as mast cells, eosinophils and group 2 innate lymphoid cells. Both cytokines were previously understood to primarily drive type 2 (T2) inflammation, but there is emerging evidence for a role for



these alarmins to additionally mediate non-T2 inflammation, with recent clinical trial data in asthma and COPD cohorts with non-T2 inflammation providing support. Currently available treatments for both COPD and asthma provide symptomatic relief with disease control, improving lung function and reducing exacerbation rates; however, there still remains an unmet need for further improving lung function and reducing exacerbations, particularly for those not responsive to currently available treatments. The epithelial cytokines/alarmins are involved in exacerbations; biologics targeting TSLP and IL-33 have been shown to reduce exacerbations in moderate-to-severe asthma, either in a broad population or in specific subgroups, respectively. For COPD, while there is clinical evidence for IL-33 blockade impacting exacerbations in COPD, clinical data from anti-TSLP therapies is awaited. Clinical data to date support an acceptable safety profile for patients with airway diseases for both anti-IL-33 and anti-TSLP antibodies in development. We examine the roles of IL-33 and TSLP, their potential use as drug targets, and the evidence for target patient populations for COPD and asthma, together with ongoing and future trials focused on these targets.

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## Conflict of interest statement

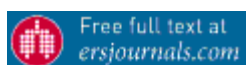
Conflict of interest: A.A. Calderon has nothing to declare. C. Dimond, D.F. Choy, R. Pappu, M.A. Grimaldeston and D. Mohan are employees of Genentech, Inc., a member of the Roche group, and are Roche stockholders. D.F. Choy and M.A. Grimaldeston are co-inventors on patents that have been filed or are pending relating to the diagnosis and treatment of chronic respiratory diseases for Genentech, Inc. D. Mohan was previously an employee and shareholder of GSK. K.F. Chung received personal payments for service on an advisory board for Roche, Merck, Rickett-Beckinson and Shinogi, data safety monitoring board for Nocrion, and for speaking engagements from Novartis and AstraZeneca; and received the MRC, EPSRC, and GSK grants for his institution.

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. 2023 Jan 25;32(167):220109.

doi: 10.1183/16000617.0109-2022. Print 2023 Mar 31.

# Physical activity promotion interventions in chronic airways disease: a systematic review and meta-analysis

[Caroline Reilly](#)<sup>1</sup>, [Joe Sails](#)<sup>1</sup>, [Antonios Stavropoulos-Kalinoglou](#)<sup>1</sup>, [Rebecca J Birch](#)<sup>2</sup>, [Jim McKenna](#)<sup>1</sup>, [Ian J Clifton](#)<sup>2,3</sup>, [Daniel Peckham](#)<sup>2,3</sup>, [Karen M Birch](#)<sup>4</sup>, [Oliver J Price](#)<sup>5,3,4</sup>

Affiliations expand

- PMID: 36697208
- PMCID: [PMC9879326](#)
- DOI: [10.1183/16000617.0109-2022](#)

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## Abstract

Physical inactivity is common in people with chronic airways disease (pwCAD) and associated with worse clinical outcomes and impaired quality of life. We conducted a systematic review and meta-analysis to characterise and evaluate the effectiveness of interventions promoting step-based physical activity (PA) in pwCAD. We searched for studies that included a form of PA promotion and step-count outcome measure. A random-effects model was used to determine the overall effect size using post-intervention values. 38 studies (n=32 COPD; n=5 asthma; n=1 bronchiectasis; study population: n=3777) were included. Overall, implementing a form of PA promotion

resulted in a significant increase in step-count: median (IQR) 705 (183-1210) when compared with usual standard care: -64 (-597-229), standardised mean difference (SMD) 0.24 (95% CI: 0.12-0.36),  $p < 0.01$ . To explore the impact of specific interventions, studies were stratified into subgroups: PA promotion+wearable activity monitor-based interventions ( $n=17$ ) (SMD 0.37,  $p < 0.01$ ); PA promotion+step-count as an outcome measure ( $n=9$ ) (SMD 0.18,  $p=0.09$ ); technology-based interventions ( $n=12$ ) (SMD 0.16,  $p=0.01$ ). Interventions promoting PA, particularly those that incorporate wearable activity monitors, result in a significant and clinically meaningful improvement in daily step-count in pwCAD.

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## Conflict of interest statement

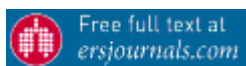
Conflict of interest: I.J. Clifton reports personal fees from GlaxoSmithKline, outside the submitted work. The remaining authors have no conflicts to declare.

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- [4 figures](#)

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Pediatr Pulmonol

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. 2023 Apr;58(4):1229-1236.

doi: 10.1002/ppul.26327. Epub 2023 Feb 2.

# Effect of lockdowns on the epidemiology of pediatric respiratory disease–A retrospective analysis of the 2021 summer epidemic

[Matthijs D Kruizinga](#)<sup>1</sup>, [Jeroen G Noordzij](#)<sup>2</sup>, [Marlies A van Houten](#)<sup>3</sup>, [Jantien Wieringa](#)<sup>4</sup>, [Gerdien A Tramper-Stranders](#)<sup>5</sup>, [Vishal Hira](#)<sup>6</sup>, [Jolita Bekhof](#)<sup>7</sup>, [Nienke J Vet](#)<sup>8</sup>, [Gertjan J A Driessen](#)<sup>9</sup>, [Mirjam van Veen](#)<sup>1</sup>

Affiliations expand

- PMID: 36695757
- DOI: [10.1002/ppul.26327](https://doi.org/10.1002/ppul.26327)

## Abstract

**Background:** The imposition of lockdowns during the severe acute respiratory syndrome coronavirus-2 pandemic led to a significant decrease in pediatric care utilization in 2020. After restrictions were loosened, a surge in pediatric respiratory disease was observed in pediatric wards. The aim of this study was to quantify the effect of the lockdown(s) on the incidence of pediatric respiratory disease.

**Methods:** For this multicenter retrospective study, emergency department (ED) visit and admission data between January 2017 and September 2021 was collected from eight general hospitals in the Netherlands. Clinical diagnoses were extracted and categorized in groups ("communicable infectious disease," "all respiratory infections," "upper respiratory tract infection," "lower respiratory tract infection," and "asthma/preschool wheezing"). The incidence of admissions and ED visits during 2020 and 2021 was compared to the incidence in 2017-2019.

**Results:** Successive lockdowns resulted in a maximum decrease of 61% and 57% in ED visits and admissions, respectively. After loosening restrictions during the summer of 2021, a 48% overall increase in ED visits and 31% overall increase in admission numbers was observed in July compared to the average July in 2017-2019. This was explained by a 381% increase in ED visits and a 528% increase in ward admissions due to overall respiratory infections, mainly due to lower respiratory tract infections.

**Conclusions:** Successive lockdowns in the spring and winter of 2020 and 2021 led to a decreased incidence of communicable infections, especially respiratory tract infections. The

resulting lack of pediatric immunity resulted in an off-season surge in care utilization at an unexpected moment.

**Keywords:** COVID-19; ED visits; SARS-CoV-2; admissions; asthma; bronchiolitis; corona; lockdown; pediatrics; pneumonia; wheezing.

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- [20 references](#)

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Int J Immunogenet

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. 2023 Apr;50(2):53-62.

doi: 10.1111/iji.12611. Epub 2023 Jan 19.

## [Associations between interleukin 17A and 17F polymorphisms and asthma susceptibility: A meta-analysis](#)

[Young Ho Lee](#)<sup>1</sup>, [Gwan Gyu Song](#)<sup>1</sup>

Affiliations expand

- PMID: 36658661

- DOI: [10.1111/iji.12611](https://doi.org/10.1111/iji.12611)

## Abstract

Owing to their role in inflammatory reactions and immunological responses as well as their chromosomal location, interleukin (IL) 17A and 17F are regarded as candidate causal genes associated with asthma. The aim of this study was to determine whether IL17 polymorphisms are associated with susceptibility to asthma. We used the PubMed/Medline and Embase databases to search for studies reporting IL17 polymorphisms in patients with asthma and healthy controls. Meta-analyses were conducted to determine the associations between IL17A rs8193036 (-737C/T), rs2275913 (-197G/A), rs3819024 (A/G), rs3748067 (C/T), and rs4711998 (A/G) and IL17F rs763780 (7488A/G), rs2397084 (T/C), rs1889570 (C/T), rs11465553 (G/A), and rs1266828 (T/C) polymorphisms and asthma susceptibility. A total of 20 studies were included in this meta-analysis. Our results revealed the IL17A rs8193036 CC genotype was associated with asthma susceptibility (odds ratio [OR] = 1.490, 95% confidence interval [CI] = 1.027-2.161,  $p = .036$ ). However, stratification by ethnicity indicated no association between this polymorphism and asthma in European and Asian subjects. Furthermore, no association was found between this polymorphism and asthma using the allele contrast, dominant or homozygous contrast models. No evidence of an association was found between any of the other IL17A and IL17F polymorphisms and asthma susceptibility in this meta-analysis. This meta-analysis showed that, among the studied polymorphisms, only the CC genotype of IL17A rs8193036 is associated with asthma susceptibility.

**Keywords:** asthma; interleukin 17; meta-analysis; polymorphism.

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- [55 references](#)

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. 2023 Apr;32(4):1053-1067.

doi: 10.1007/s11136-022-03322-9. Epub 2023 Jan 13.

# Patient-reported outcome (PRO) measurements in chronic and malignant diseases: ten years' experience with PRO-algorithm-based patient-clinician interaction (telePRO) in AmbuFlex

[Niels Henrik I Hjollund](#)<sup>1,2,3</sup>, [Louise Pape Larsen](#)<sup>4</sup>, [Annette Ladefoged de Thurah](#)<sup>5</sup>, [Birgith Engelst Grove](#)<sup>4</sup>, [Halla Skuladottir](#)<sup>6</sup>, [Hanne Linnet](#)<sup>6</sup>, [Rasmus Blechingberg Friis](#)<sup>6</sup>, [Søren Paaske Johnsen](#)<sup>7</sup>, [Ole May](#)<sup>8</sup>, [Annesofie Lunde Jensen](#)<sup>9</sup>, [Troels Krarup Hansen](#)<sup>9</sup>, [Gry Assam Taarnhøj](#)<sup>10</sup>, [Lærke Kjær Tolstrup](#)<sup>10</sup>, [Helle Pappot](#)<sup>10</sup>, [Per Ivarsen](#)<sup>11,12</sup>, [Liv Dørflinger](#)<sup>13</sup>, [Anne Jessen](#)<sup>4</sup>, [Nanna Toxvig Sørensen](#)<sup>4</sup>, [Liv Marit Valen Schougaard](#)<sup>4</sup>, [The AmbuFlex Team](#)<sup>4</sup>

Affiliations expand

- PMID: 36639598
- PMCID: [PMC10063508](#)
- DOI: [10.1007/s11136-022-03322-9](#)

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## Abstract

**Background:** Patient-reported Outcome (PRO) measures may be used as the basis for out-patient follow-up instead of fixed appointments. The patients attend follow-up from home by filling in questionnaires developed for that specific aim and patient group (telePRO). The questionnaires are handled in real time by a specific algorithm, which assigns an outcome color reflecting clinical need. The specific questionnaires and algorithms (named solutions) are constructed in a consensus process with clinicians. We aimed to describe

AmbuFlex' telePRO solutions and the algorithm outcomes and variation between patient groups, and to discuss possible applications and challenges.

**Methods:** TelePRO solutions with more than 100 processed questionnaires were included in the analysis. Data were retrieved together with data from national registers. Characteristics of patients, questionnaires and outcomes were tabulated for each solution. Graphs were constructed depicting the overall and within-patient distribution of algorithm outcomes for each solution.

**Results:** From 2011 to 2021, 29 specific telePRO solutions were implemented within 24 different ICD-10 groups. A total of 42,015 patients were referred and answered 171,268 questionnaires. An existing applicable instrument with cut-off values was available for four solutions, whereas items were selected or developed ad hoc for the other solutions. Mean age ranged from 10.7 (Pain in children) to 73.3 years (chronic kidney disease). Mortality among referred patients varied between 0 (obesity, asthma, endometriosis and pain in children) and 528 per 1000 patient years (Lung cancer). There was substantial variation in algorithm outcome across patient groups while different solutions within the same patient group varied little.

**Discussion:** TelePRO can be applied in diseases where PRO can reflect clinical status and needs. Questionnaires and algorithms should be adapted for the specific patient groups and clinical aims. When PRO is used as replacement for clinical contact, special carefulness should be observed with respect to patient safety.

**Keywords:** Algorithm; Chronic disease; Decision support systems; Malignant diseases; Outpatient follow-up; Patient-reported outcome measures; Questionnaires.

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## Conflict of interest statement

The authors have no relevant financial or non-financial interests to disclose.

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

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. 2023 Apr 1;23(2):132-136.

doi: 10.1097/ACI.0000000000000892. Epub 2023 Jan 12.

# Applying the new guidelines to asthma management in children

[Riccardo Castagnoli](#)<sup>1,2</sup>, [Ilaria Brambilla](#)<sup>1,2</sup>, [Michele Miraglia Del Giudice](#)<sup>3</sup>, [Gian Luigi Marseglia](#)<sup>1,2</sup>, [Amelia Licari](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36637070
- DOI: [10.1097/ACI.0000000000000892](https://doi.org/10.1097/ACI.0000000000000892)

## Abstract

**Purpose of review:** This review aims to provide paediatricians with novel concepts from scientific evidence applicable to treating children with asthma. The latest guideline updates on paediatric asthma are discussed here, with a focus on the 2022 update of the GINA document.

**Recent findings:** Mild asthma remains to be an important challenge for the paediatrician, and the introduction of new evidence-based treatment strategies, particularly those symptom-driven, could have a significant impact on the paediatric population. The identification of predictive biomarkers, the definition of biological treatment response, the possible duration of these therapies in this age group, as well as their potential action on airway remodelling are desirable in the short term. As the number of available biological treatment options expands, paediatricians should be supported by further evidence in decision-making.

**Summary:** There is an urgent need to implement at multiple levels the latest therapeutic strategies proposed for asthma at all severities.

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. 2023 Apr;112(4):820-829.

doi: 10.1111/apa.16666. Epub 2023 Jan 20.

# Blood eosinophils during bronchiolitis: Associations with atopy, asthma and lung function in young adults

[Karen Galta Sørensen](#)<sup>1,2</sup>, [Knut Øymar](#)<sup>1,2</sup>, [Ingvild Dalen](#)<sup>3</sup>, [Thomas Halvorsen](#)<sup>2,4</sup>, [Ingvild Bruun Mikalsen](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36627486
- DOI: [10.1111/apa.16666](https://doi.org/10.1111/apa.16666)

## Abstract

**Aim:** To study if blood eosinophils during bronchiolitis were associated with atopy, asthma and lung function in young adults and if these associations differed between respiratory syncytial virus (RSV) bronchiolitis and non-RSV bronchiolitis.

**Methods:** This historical cohort enrolled 225 subjects. Blood eosinophils were measured during bronchiolitis in infancy, and the subjects were invited to a follow-up at 17-20 years of age including questionnaires for asthma and examinations of lung function and atopy.

**Results:** The level of eosinophils was positively associated with subsequent atopy in the unadjusted analysis, but not in the adjusted analysis, and not with asthma. There was a negative association between the level of eosinophils and forced vital capacity (FVC) (-0.11; -0.19, -0.02) and forced expiratory volume in first second (FEV<sub>1</sub>) (-0.12; -0.21, -0.03) (regression coefficient; 95% confidence interval). The non-RSV group had higher levels of eosinophils during bronchiolitis, but there was no interaction between the level of eosinophils and RSV status for any outcome.

**Conclusions:** The level of eosinophils during bronchiolitis was negatively associated with lung function in young adult age, but we found no associations with atopy or asthma. These associations were not different after RSV bronchiolitis compared to non-RSV bronchiolitis.

**Keywords:** asthma; atopy; bronchiolitis; eosinophils; lung function.

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- [30 references](#)

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MeSH terms, Grant supportexpand

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Curr Opin Allergy Clin Immunol

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. 2023 Apr 1;23(2):151-157.

doi: 10.1097/ACI.0000000000000887. Epub 2023 Jan 3.

## Regulatory T-cells in asthma

[Hani Harb](#)<sup>1</sup>, [Talal A Chatila](#)<sup>2</sup>

Affiliations expand

- PMID: 36602889
- PMCID: PMC9974575 (available on 2024-04-01)
- DOI: [10.1097/ACI.0000000000000887](https://doi.org/10.1097/ACI.0000000000000887)

## Abstract

**Purpose of review:** This review addresses recent progress in our understanding of the role of regulatory T (Treg) cells in enforcing immune tolerance and tissue homeostasis in the lung at steady state and in directing the immune response in asthmatic lung inflammation.

**Recent findings:** Regulatory T cells regulate the innate and adaptive immune responses at steady state to enforce immune tolerance in lung tissues at steady state and their control of the allergic inflammatory responses induced by allergens. This regulatory function can break down in the context of chronic asthmatic airway inflammation such that the lung tissue Treg cells become skewed towards a pathogenic phenotype that aggravates and perpetuates disease. Subversion of lung tissue Treg cell function involves their upregulation of Notch4 expression, which in turn acts to amplify T helper type 2 and type 17 and innate lymphoid cell type 2 responses in the airways.

**Summary:** A dual role for Treg cells has emerged both as immune regulators but also a potential disease effectors in asthma, with implications for disease therapy.

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## Conflict of interest statement

Conflict of Interest

T.A.C., H.H., and A.M. are inventors on published US patent application No. WO2019178488A1 submitted by The Children's Medical Center Corporation, titled "Method for treating asthma or allergic disease". T.A.C. and H.H. are scientific co-founders of and hold equity in Alcea Therapeutics.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Thorax

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. 2023 Apr;78(4):335-343.

doi: 10.1136/thorax-2021-217736. Epub 2022 Dec 7.

# Th2 high and mast cell gene signatures are associated with corticosteroid sensitivity in COPD

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- PMID: 36598042
- DOI: [10.1136/thorax-2021-217736](https://doi.org/10.1136/thorax-2021-217736)

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## Abstract

**Rationale:** Severe asthma and chronic obstructive pulmonary disease (COPD) share common pathophysiological traits such as relative corticosteroid insensitivity. We recently published three transcriptome-associated clusters (TACs) using hierarchical analysis of the sputum transcriptome in asthmatics from the Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes (U-BIOPRED) cohort comprising one Th2-high inflammatory signature (TAC1) and two Th2-low signatures (TAC2 and TAC3).

**Objective:** We examined whether gene expression signatures obtained in asthma can be used to identify the subgroup of patients with COPD with steroid sensitivity.

**Methods:** Using gene set variation analysis, we examined the distribution and enrichment scores (ES) of the 3 TACs in the transcriptome of bronchial biopsies from 46 patients who participated in the Groningen Leiden Universities Corticosteroids in Obstructive Lung Disease COPD study that received 30 months of treatment with inhaled corticosteroids (ICS) with and without an added long-acting  $\beta$ -agonist (LABA). The identified signatures were then associated with longitudinal clinical variables after treatment. Differential gene expression and cellular convolution were used to define key regulated genes and cell types.

**Measurements and main results:** Bronchial biopsies in patients with COPD at baseline showed a wide range of expression of the 3 TAC signatures. After ICS $\pm$ LABA treatment, the ES of TAC1 was significantly reduced at 30 months, but those of TAC2 and TAC3 were unaffected. A corticosteroid-sensitive TAC1 signature was developed from the TAC1 ICS-responsive genes. This signature consisted of mast cell-specific genes identified by single-cell RNA-sequencing and positively correlated with bronchial biopsy mast cell numbers following ICS $\pm$ LABA. Baseline levels of gene transcription correlated with the change in RV/TLC %predicted following 30-month ICS $\pm$ LABA.

**Conclusion:** Sputum-derived transcriptomic signatures from an asthma cohort can be recapitulated in bronchial biopsies of patients with COPD and identified a signature of airway mast cells as a predictor of corticosteroid responsiveness.

**Keywords:** COPD pathology; airway epithelium; oxidative stress.

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## Conflict of interest statement

Competing interests: None declared.

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. 2023 Apr;58(4):1127-1135.

doi: 10.1002/ppul.26303. Epub 2023 Jan 9.

# Primary ciliary dyskinesia: A multicenter survey on clinical practice and patient management in Italy

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- PMID: 36588099

- DOI: [10.1002/ppul.26303](https://doi.org/10.1002/ppul.26303)

## Abstract

**Introduction:** There are no recent data on primary ciliary dyskinesia (PCD) distribution, diagnosis and treatment in Italy.

**Methods:** A descriptive study based on a survey questionnaire. It consisted of three sections (patients, diagnosis, and treatment), and sent to all the Italian PCD Centers.

**Results:** Questionnaires obtained from 20/22 centers in 12/20 regions showed that the total number of PCD patients treated at the participating centers was of 416. Out of all centers, 55% follow <20 patients, two centers have >40 patients, and 75% follow both pediatric and adults. Age at diagnosis was between 4 and 8 years in 45% of the centers, <3 years in three centers. Nasal nitric oxide, transmission electron microscopy and ciliary high-speed video microscopy are performed in 75%, 90%, and 40% of centers, respectively. Immunofluorescence is available in five centers. Genetic analysis is offered in 55% of the centers, and in seven centers >50% of the patients have a known genetic profile. Patients treated at all centers receive inhaled saline solutions, corticosteroids and chest

physiotherapy. Prophylactic antibiotics and mucolytics are prescribed in 95% and 50% of the centers, respectively. Pseudomonas infection is treated with oral or inhaled antibiotics.

**Conclusions:** Many Italian centers care for a small number of pediatric and adult patients, and diagnosis is often delayed. We found a great variability in the available diagnostic procedures, as well in the prescribed therapies. Our study will help to uniform diagnostic algorithm and share treatments protocols for PCD in Italy and allowed to set specific national goals.

**Keywords:** children; diagnosis; management; primary ciliary dyskinesia; treatment.

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. 2023 Apr;72(2):194-200.

doi: 10.1016/j.alit.2022.12.001. Epub 2022 Dec 29.

## [Group 2 innate lymphoid cells in human asthma](#)

[Arifumi Iwata](#)<sup>1</sup>, [Yosuke Toda](#)<sup>1</sup>, [Hiroki Furuya](#)<sup>1</sup>, [Hiroshi Nakajima](#)<sup>2</sup>

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- PMID: 36585333



- DOI: [10.1016/j.alit.2022.12.001](https://doi.org/10.1016/j.alit.2022.12.001)

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# Abstract

Asthma is characterized by increased airway hyperresponsiveness, reversible airflow limitation, and remodeling due to allergic airway inflammation. Asthma has been proposed to be classified into various phenotypes by cluster analyses integrating clinical information and laboratory data. Recently, asthma has been classified into two major endotypes, Type 2-high and Type 2-low asthma, and various subtypes based on the underlying molecular mechanisms. In Type 2-high asthma, Th2 cells, together with group 2 innate lymphoid cells (ILC2s), produce type 2 cytokines such as IL-4, IL-5, IL-9, and IL-13, which play crucial roles in causing airway inflammation. The roles of ILC2s in asthma pathogenesis have been analyzed primarily in murine models, demonstrating their importance not only in IL-33- or papain-induced innate asthma models but also in house dust mite (HDM)- or ovalbumin (OVA)-induced acquired asthma models evoked in an antigen-specific manner. Recently, evidence regarding the roles of ILC2s in human asthma is also accumulating. This minireview summarizes the roles of ILC2s in asthma, emphasizing human studies.

**Keywords:** Asthma; Epithelial cytokines; Humans; ILC2s; Type 2-high.

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. 2023 Apr;58(4):1068-1073.

# Pediatric pulmonology 2021 year in review: Asthma

[Nicole Stephenson](#)<sup>1</sup>, [Ceila E Loughlin](#)<sup>1</sup>

Affiliations expand

- PMID: 36573469
- DOI: [10.1002/ppul.26295](https://doi.org/10.1002/ppul.26295)

## Abstract

Asthma is the most common chronic disease in children, affecting an estimated 6.1 million children in the United States. SARS-CoV2 had a significant impact on asthma exacerbations and healthcare utilization of patients with asthma in 2021. Additionally, studies in 2021 influenced the field of asthma with improvements in diagnostic testing and monitoring, treatment of severe exacerbations, social determinants of health, and evaluation of medical costs. This article is part of our 2021 "Year in Review" series, in which we summarize publications in major pulmonary topics, in the context of selected literature from other journals relevant to our discipline.

**Keywords:** 2021; YIR; asthma; childhood; pediatric.

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. 2023 Apr;58(4):996-1003.

doi: 10.1002/ppul.26284. Epub 2022 Dec 28.

# Exercise-induced bronchoconstriction is associated with air humidity and particulate matter concentration in preschool children

[Anna P Tikkakoski](#)<sup>1</sup>, [Antti Tikkakoski](#)<sup>2</sup>, [Kalle Sipilä](#)<sup>2</sup>, [Juho E Kivistö](#)<sup>1,3</sup>, [Heini Huhtala](#)<sup>4</sup>, [Mika Kähönen](#)<sup>1,2</sup>, [Jussi Karjalainen](#)<sup>1,3</sup>, [Lauri Lehtimäki](#)<sup>1,3</sup>

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- PMID: 36530015
- DOI: [10.1002/ppul.26284](https://doi.org/10.1002/ppul.26284)

## Abstract

**Background:** Long-term exposure to air pollution is connected to asthma morbidity in children. Exercise-induced bronchoconstriction (EIB) is common in asthma, and the free running test outdoors is an important method for diagnosing asthma in children. It is not known whether momentary air pollution exposure affects the results of outdoor exercise tests in children.

**Methods:** We analyzed all reliable exercise challenge tests with impulse oscillometry in children (n = 868) performed between January 2012 and April 2015 at Tampere University Hospital. Pollutant concentrations (PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>) at the time of the exercise test were collected from public registers. We compared the pollutant concentrations with the proportion and severity of EIB and adjusted the analyses for air humidity and pollen counts.

**Results:** Pollution levels were rarely high (median PM<sub>2.5</sub> 6.0 µg/m<sup>3</sup>, NO<sub>2</sub> 12.0 µg/m<sup>3</sup>, and O<sub>3</sub> 47.0 µg/m<sup>3</sup>). The relative change in resistance at 5 Hz after exercise did not correlate with O<sub>3</sub>, NO<sub>2</sub> or PM<sub>2.5</sub> concentrations (p values 0.065-0.884). In multivariate logistic regression, we compared the effects of PM<sub>2.5</sub> over 10 µg/m<sup>3</sup>, absolute humidity (AH) over

10 g/m<sup>3</sup> and alder or birch pollen concentration over 10 grains/m<sup>3</sup>. High (over 10 g/m<sup>3</sup>) AH was associated with decreased incidence (OR 0.31, p value 0.004), and PM<sub>2.5</sub> over 10 µg/m<sup>3</sup> was associated with increased incidence (OR 1.69, p value 0.036) of EIB.

**Conclusions:** Even low PM<sub>2.5</sub> levels may have an effect on EIB in children. Of the other properties of air, only AH was associated with the incidence of EIB.

**Keywords:** air pollution; air quality; asthma; exercise test; exercise-induced bronchoconstriction; impulse oscillometry; particulate matter; pulmonary Function Tests.

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. 2023 Apr;72(4):623-628.

doi: 10.1016/j.jadohealth.2022.10.034. Epub 2022 Dec 15.

## Adolescent Knowledge of When to Use Inhaled Asthma Medications: Implications for Management

[Sean M Frey<sup>1</sup>](#), [Maria Fagnano<sup>2</sup>](#), [Jill S Halterman<sup>2</sup>](#)

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- PMID: 36528520
- PMCID: PMC10033387 (available on 2024-04-01)
- DOI: [10.1016/j.jadohealth.2022.10.034](https://doi.org/10.1016/j.jadohealth.2022.10.034)

## Abstract

**Purpose:** It is unclear how often adolescents with persistent asthma know when to use different inhaled medications (as-needed rescue vs. daily controller; 'accurate use'), or whether this knowledge is associated with clinical asthma outcomes. This study aimed to characterize adolescent knowledge of accurate use; examine whether accurate use is associated with controller medication adherence, asthma symptoms, or exacerbations requiring acute health care services; and determine whether knowledge of accurate use improves following regular exposure to controller medications with school-based directly observed therapy (DOT).

**Methods:** We analyzed baseline and 7-month data from the School-Based Asthma Care for Teens trial. Adolescents (12-16 years) identified inhaled medications on a chart and stated when each is used. We compared accurate use with adolescent-reported adherence, recent symptoms, and asthma-related acute health care visits; and exposure to DOT. Analyses were limited to subjects with controller medication.

**Results:** Of 430 participants, 252 had controller medication at baseline. Knowledge of accurate use was described by 62%, and associated with adherence (odds ratio [OR]: 2.06, 95% confidence interval [CI]: 1.12-3.83). By 7 months, 313 adolescents had controller medication; 75% described accurate use, which was associated with adherence (OR: 3.46, 95% CI: 1.83-6.54), health care (OR: 0.39, 95% CI: 0.20-0.79), and DOT exposure (OR: 1.83, 95% CI: 1.10-3.32). Associations with adherence and health care at 7 months persisted in adjusted analyses.

**Discussion:** Adolescent knowledge of accurate medication use was linked with greater adherence (baseline, 7 months), less acute health care (7 months), and exposure to in-school DOT. Interventions to support adolescents with persistent asthma should consider school-based care strategies and facilitate adolescent understanding of when to use different medications.

**Keywords:** Adherence; Adolescent; Asthma; Identification; Management; Medication; Respiratory; Treatment.

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## Conflict of interest statement

Conflicts of interest: None of the authors have any conflicts of interest to disclose.

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. 2023 Apr;133(4):863-865.

doi: 10.1002/lary.30527. Epub 2022 Dec 16.

# [Benralizumab as an Adjuvant Therapy for Recurrent Laryngeal Papillomatosis](#)

[Kayla J Krause](#)<sup>1</sup>, [David Goldrich](#)<sup>1</sup>, [John Gniady](#)<sup>1</sup>

Affiliations expand

- PMID: 36524437

- DOI: [10.1002/lary.30527](https://doi.org/10.1002/lary.30527)

## Abstract

Recurrent respiratory (RRP) or laryngeal papillomatosis is the result of human papillomavirus-mediated benign tumor growth on the larynx and is challenging to manage. Benralizumab is a monoclonal antibody targeted against the alpha subunit of the IL-5 receptor on eosinophils. A 61-year-old male patient presented with refractory RRP following multiple surgical excisions. His disease course improved substantially when benralizumab was added to his asthma regimen. There is no clear mechanistic role suggested for benralizumab directly treating RRP. This case may represent a novel application of benralizumab as an adjuvant treatment for patients with RRP and comorbid asthma. *Laryngoscope*, 133:863-865, 2023.

**Keywords:** benralizumab; eosinophilic asthma; fasenra; immunotherapy; laryngeal papillomatosis; laryngology; recurrent respiratory papillomatosis.

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. 2023 Mar 30;61(3):2200558.

doi: 10.1183/13993003.00558-2022. Print 2023 Mar.

## [Development of a tool to detect small airways dysfunction in asthma clinical practice](#)

[Janwillem Kocks](#)<sup>1,2,3,4</sup>, [Thys van der Molen](#)<sup>1,2</sup>, [Jaco Voorham](#)<sup>5</sup>, [Simonetta Baldi](#)<sup>6</sup>, [Maarten van den Berge](#)<sup>2,4</sup>, [Chris Brightling](#)<sup>6</sup>, [Leonardo M Fabbri](#)<sup>7</sup>, [Monica Kraft](#)<sup>8</sup>, [Gabriele](#)

[Nicolini](#)<sup>9</sup>, [Alberto Papi](#)<sup>7</sup>, [Klaus F Rabe](#)<sup>10</sup>, [Salman Siddiqui](#)<sup>11</sup>, [Dave Singh](#)<sup>12</sup>, [Judith Vonk](#)<sup>2,13</sup>, [Marika Leving](#)<sup>1</sup>, [Bertine Flokstra-de Blok](#)<sup>14,2,15</sup>

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- PMID: 36517179
- PMCID: [PMC10060661](#)
- DOI: [10.1183/13993003.00558-2022](#)

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## Abstract

**Background:** Small airways dysfunction (SAD) in asthma is difficult to measure and a gold standard is lacking. The aim of this study was to develop a simple tool including items of the Small Airways Dysfunction Tool (SADT) questionnaire, basic patient characteristics and respiratory tests available depending on the clinical setting to predict SAD in asthma.

**Methods:** This study was based on the data of the multinational ATLANTIS (Assessment of Small Airways Involvement in Asthma) study including the earlier developed SADT questionnaire. Key SADT items together with clinical information were now used to build logistic regression models to predict SAD group (less likely or more likely to have SAD). Diagnostic ability of the models was expressed as area under the receiver operating characteristic curve (AUC) and positive likelihood ratio (LR+).

**Results:** SADT item 8, "I sometimes wheeze when I am sitting or lying quietly", and the patient characteristics age, age at asthma diagnosis and body mass index could reasonably well detect SAD (AUC 0.74, LR+ 2.3). The diagnostic ability increased by adding spirometry (percentage predicted forced expiratory volume in 1 s: AUC 0.87, LR+ 5.0) and oscillometry (resistance difference between 5 and 20 Hz and reactance area: AUC 0.96, LR+ 12.8).

**Conclusions:** If access to respiratory tests is limited (e.g. primary care in many countries), patients with SAD could reasonably well be identified by asking about wheezing at rest and a few patient characteristics. In (advanced) hospital settings patients with SAD could be identified with considerably higher accuracy using spirometry and oscillometry.

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**Conflict of interest statement**



Conflict of interest: J. Kocks reports grants, personal fees and nonfinancial support from AstraZeneca, Boehringer Ingelheim and GlaxoSmithKline, grants and personal fees from Chiesi and Teva, nonfinancial support from Mundi Pharma, personal fees from MSD and COVIS Pharma, grants from Valneva, outside the submitted work; holds <5% shares of Lothar Medtec GmbH and 72.5% of shares in the General Practitioners Research Institute. T. van der Molen reports personal fees and nonfinancial support from Chiesi, GlaxoSmithKline and AstraZeneca. J. Voorham reports no conflict of interest. S. Baldi reports no conflict of interest. M. van den Berge reports research grants paid to institution from Chiesi, Novartis, Genentech, Roche, AstraZeneca and GlaxoSmithKline. C. Brightling reports support for the present manuscript from Chiesi and NIHR BRC; grants and consulting fees from AstraZeneca, GlaxoSmithKline, Chiesi, Sanofi, Roche, Genentech, Mologic and 4DPharma, outside the submitted work. L.M. Fabbri reports grants, personal fees, and nonfinancial support from AstraZeneca, Chiesi, GlaxoSmithKline, Alfasigma, Lusofarma and Novartis. M. Kraft reports grants (paid to institution) for research from the National Institutes of Health, American Lung Association and Chiesi (for support of this study), AstraZeneca and Sanofi Regeneron; personal fees for consultancies from Chiesi, Genentech (Roche), GlaxoSmithKline, Sanofi Regeneron and AstraZeneca, speaker fees from Chiesi; personal fees from participation on data safety and monitoring boards from AstraZeneca and ALung; and leadership of the American Thoracic Society. G. Nicolini is an employee of Chiesi, the company who sponsored the ATLANTIS study generating the data analysed in the current manuscript. A. Papi reports grants from Chiesi, AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Teva and Sanofi; consulting fees, honoraria for lectures or advisory boards from Chiesi, AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Novartis, Sanofi, IQVIA, Avillon, Elpen Pharmaceuticals, Menarini, Zambon and Mundipharma. K.F. Rabe reports grants, personal fees and nonfinancial support from AstraZeneca, Boehringer Ingelheim, Chiesi, DevPro and Sanofi Regeneron. Klaus F. Rabe is co-founder of ratics and receives federal grants from the BMBF, Germany for the German Center for Lung Research. S. Siddiqui reports grants, personal fees and nonfinancial support from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Boehringer Ingelheim, Novartis, ERT Medical, Knopp Biosciences and Thorasys Ltd. D. Singh has received personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Synairgen, Teva, Theravance and Verona. J. Vonk reports no conflict of interest. M. Leving and B. Flokstra-de Blok were employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past 3 years (2019–2021), GPRI conducted investigator- and sponsor-initiated research funded by noncommercial organisations, academic institutes, and pharmaceutical companies (including AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Novartis and Teva).

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Noble PB, Donovan GM. Eur Respir J. 2023 Mar 30;61(3):2202307. doi: 10.1183/13993003.02307-2022. Print 2023 Mar. PMID: 36997235 No abstract available.

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. 2023 Apr;72(2):262-270.

doi: 10.1016/j.alit.2022.10.007. Epub 2022 Nov 17.

## Differential role of mucus plugs in asthma: Effects of smoking and association with airway inflammation

[Akira Oguma](#)<sup>1</sup>, [Kaoruko Shimizu](#)<sup>2</sup>, [Hirokazu Kimura](#)<sup>1</sup>, [Naoya Tanabe](#)<sup>3</sup>, [Susumu Sato](#)<sup>3</sup>, [Isao Yokota](#)<sup>4</sup>, [Michiko Takimoto-Sato](#)<sup>1</sup>, [Machiko Matsumoto-Sasaki](#)<sup>1</sup>, [Yuki Abe](#)<sup>1</sup>, [Nozomu Takei](#)<sup>1</sup>, [Houman Goudarzi](#)<sup>1</sup>, [Masaru Suzuki](#)<sup>1</sup>, [Hironi Makita](#)<sup>5</sup>, [Toyohiro Hirai](#)<sup>3</sup>, [Masaharu Nishimura](#)<sup>5</sup>, [Satoshi Konno](#)<sup>1</sup>; [Hi-CARAT investigators](#)

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- PMID: 36402674
- DOI: [10.1016/j.alit.2022.10.007](https://doi.org/10.1016/j.alit.2022.10.007)

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## Abstract

**Background:** The physiological importance of mucus plugs in computed tomography (CT) imaging is being increasingly recognized. However, whether airway inflammation and smoking affect the association between mucus plugs and clinical-physiological outcomes in asthma remains to be elucidated. The objective of this study is to examine how airway inflammation and/or smoking affect the correlation of CT-based mucus plug scores with exacerbation frequency and airflow limitation indices in asthma.

**Methods:** A total of 168 patients with asthma who underwent chest CT and sputum evaluation were enrolled and classified in eosinophilic asthma (EA; n = 103) and non-eosinophilic asthma (NEA; n = 65) groups based on sputum eosinophil percentage (cut-off: 3%). The mucus plug score was defined as the number of lung segments with mucus plugs seen on CT.

**Results:** More mucus plugs were detected on CT scans in the EA group than in the NEA group, regardless of smoking status. Mucus plug score and exacerbation frequency during one year after enrollment were significantly associated in the EA group but not in the NEA group after adjusting for demographics, blood eosinophil count, and fractional exhaled nitric oxide. Mucus plug score was associated with percentage of predicted forced expiratory volume in 1 s in non-smoking individuals in the EA and NEA group and in smoking individuals in the EA group but not in the NEA group after adjusting for demographics.

**Conclusions:** The association of mucus plug score with exacerbation frequency and reduced lung function may vary due to airway inflammatory profile and smoking status in asthma.

**Keywords:** Airflow limitation; Eosinophilic asthma; Exacerbation; Mucus plug; Smoking.

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. 2023 Apr;72(2):252-261.

# Frailty and muscle weakness in elderly patients with asthma and their association with cumulative lifetime oral corticosteroid exposure

[Kai Ryu](#)<sup>1</sup>, [Yuma Fukutomi](#)<sup>2</sup>, [Eiji Nakatani](#)<sup>3</sup>, [Maki Iwata](#)<sup>4</sup>, [Kisako Nagayama](#)<sup>4</sup>, [Koichi Yano](#)<sup>4</sup>, [Yuto Nakamura](#)<sup>4</sup>, [Yuto Hamada](#)<sup>4</sup>, [Kentaro Watai](#)<sup>5</sup>, [Yosuke Kamide](#)<sup>4</sup>, [Kiyoshi Sekiya](#)<sup>4</sup>, [Jun Araya](#)<sup>6</sup>, [Kazuyoshi Kuwano](#)<sup>6</sup>, [Masami Taniguchi](#)<sup>7</sup>

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- PMID: 36371246
- DOI: [10.1016/j.alit.2022.10.005](https://doi.org/10.1016/j.alit.2022.10.005)

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## Abstract

**Background:** Frailty is a geriatric syndrome of age-related physiological decline, which is associated with higher mortality and decreased healthy life expectancy, and muscle weakness is one of the presentations of frailty. We investigated an association between lifetime oral corticosteroid (OCS) exposure with frailty and muscle weakness among elderly patients with asthma.

**Methods:** We studied 203 consecutive elderly outpatients with asthma aged  $\geq 60$  years old. They were classified into three groups according to their cumulative lifetime OCS dose (lifetime non-users, lower-dose users, and higher-dose users), which was retrospectively estimated from the response to a structured questionnaire. The prevalence of frailty determined by the Kihon Checklist was compared between the three groups. Hand-grip strength, and lean mass index were also measured as markers of muscle strength.

**Results:** Thirty-seven percent of the patients studied were considered frail. Higher cumulative lifetime OCS exposure was associated with a significantly higher prevalence of frailty (33% in lifetime non-users, 59% in lower-dose users, and 68% in higher-dose users;  $P$  for trend  $< 0.005$ ). This was also associated with lower hand-grip strength in both sexes ( $P$  for trend; 0.012 in men, and 0.020 in women), and lower lean mass index in men ( $P$  for trend 0.002). However, current doses of OCS were not significantly associated with these outcomes.

**Conclusions:** Cumulative lifetime OCS exposure was associated with a higher prevalence of frailty and muscle weakness. These findings emphasize the importance of minimizing lifetime OCS exposure for the prolongation of healthy life expectancy in patients with asthma.

**Keywords:** Asthma; Elderly; Frailty; Healthy life expectancy; Oral corticosteroids.

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. 2023 Apr;28(4):350-356.

doi: 10.1111/resp.14400. Epub 2022 Nov 6.

## [Contribution of obesity to breathlessness in a large nationally representative sample of Australian adults](#)

[Yue Leon Guo](#)<sup>1,2,3,4</sup>, [Maria R Ampon](#)<sup>1,2</sup>, [Leanne M Poulos](#)<sup>1,2</sup>, [Sharon R Davis](#)<sup>1,2</sup>, [Brett G Toelle](#)<sup>1,2,5</sup>, [Guy B Marks](#)<sup>1,2,6</sup>, [Helen K Reddel](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36336647
- DOI: [10.1111/resp.14400](https://doi.org/10.1111/resp.14400)

# Abstract

**Background and objective:** Breathlessness is prevalent and associated with medical consequences. Obesity is related to breathlessness. However, the magnitude of its contribution has not been clearly documented. This investigation aimed to determine the contribution of obesity to breathlessness by estimating the population attributable fraction (PAF) in a representative sample of Australian adults.

**Methods:** A cross-sectional, nationally representative survey of Australian residents aged  $\geq 18$  years was conducted in October 2019. Breathlessness was defined as modified Medical Research Council (mMRC) dyspnoea scale grade  $\geq 2$ . BMI was calculated from self-reported height and weight. Adjusted relative risks (aRRs) were estimated using a generalized linear model with Poisson distribution, adjusted for age group and/or participant-reported diagnosed illnesses. Adjusted PAFs were estimated using aRR and obesity prevalence in Australian adults.

**Results:** Among those who completed the National Breathlessness Survey, 9769 participants (51.4% female) were included in the analysis; 28.1% of participants were obese. The prevalence of breathlessness was 9.54%. The aRR of obesity for breathlessness was 2.04, adjusted for age. Adjusting for various co-morbid conditions, the aRR was slightly attenuated to around 1.85–1.98. The PAF, adjusted only for age, was 24.6% (95% CI 20.1–29.1) and after further adjustment for co-morbid conditions, the PAF ranged from 21.1% to 23.6%. Obesity accounted for a higher proportion of breathlessness in women than in men.

**Conclusion:** Our results demonstrate that obesity accounts for around a quarter of breathlessness symptoms in Australian adults. This has important implications for health policy in light of the global trend in increasing obesity.

**Keywords:** COPD; asthma; breathlessness; chronic obstructive pulmonary disease; dyspnoea; obesity; population attributable fraction.

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- [33 references](#)

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Allergy

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. 2023 Apr;78(4):957-967.

doi: 10.1111/all.15566. Epub 2022 Nov 16.

# Biomarkers of asthma relapse and lung function decline in adults with spontaneous asthma remission: A population-based cohort study

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Affiliations expand

- PMID: 36301194

- DOI: [10.1111/all.15566](https://doi.org/10.1111/all.15566)

## Abstract

**Background:** The extent to which biomarkers of asthma activity persist in spontaneous asthma remission and whether such markers are associated with future respiratory outcomes remained unclear. We investigated the association between sub-clinical inflammation in adults with spontaneous asthma remission and future asthma relapse and lung function decline.

**Methods:** The Tasmanian Longitudinal Health Study is a population-based cohort (n = 8583). Biomarkers of systemic inflammation were measured on participants at age 45, and latent profile analysis was used to identify cytokine profiles. Bronchial hyperresponsiveness (BHR) and nitric oxide products in exhaled breath condensate (EBC NOx) were measured at age 50. Participants with spontaneous asthma remission at ages 45 (n = 466) and 50 (n =

318) were re-evaluated at age 53, and associations between baseline inflammatory biomarkers and subsequent asthma relapse and lung function decline were assessed.

**Results:** We identified three cytokine profiles in adults with spontaneous asthma remission: average (34%), Th2-high (42%) and Th2-low (24%). Compared to the average profile, a Th2-high profile was associated with accelerated decline in post-BD FEV<sub>1</sub> /FVC (MD -0.18% predicted per-year; 95% CI -0.33, -0.02), while a Th2-low profile was associated with accelerated decline in both post-BD FEV<sub>1</sub> (-0.41%; -0.75, -0.06) and post-BD FVC (-0.31%; -0.62, 0.01). BHR and high TNF- $\alpha$  during spontaneous remission were associated with an increased risk of asthma relapse. In contrast, we found no evidence of association between EBC NO<sub>x</sub> and either asthma relapse or lung function decline.

**Conclusion:** BHR and serum inflammatory cytokines have prognostic value in adults with spontaneous asthma remission. At-risk individuals with BHR, Th2-high or Th2-low cytokine profiles may benefit from closer monitoring and on-going follow-up.

**Keywords:** asthma; biomarkers; endotypes; precision medicine.

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- [49 references](#)

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. 2023 Apr;78(4):1116-1119.

doi: 10.1111/all.15564. Epub 2022 Nov 5.



# Incidence of adverse events prompting switching between biologics among adults with asthma: A retrospective cohort study

[Ayobami Akenroye](#)<sup>1,2,3</sup>, [Guohai Zhou](#)<sup>4</sup>, [John W Jackson](#)<sup>3,5,6,7</sup>, [Jodi Segal](#)<sup>3,5,8</sup>, [G Caleb Alexander](#)<sup>3,5,8</sup>, [Sonal Singh](#)<sup>9</sup>

Affiliations expand

- PMID: 36286487
- PMCID: [PMC10066822](#)
- DOI: [10.1111/all.15564](#)

## Free PMC article

*No abstract available*

## Conflict of interest statement

### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest in relation to this work. Dr. Alexander is past Chair and a current member of FDA's Peripheral and Central Nervous System Advisory Committee; is a co-founding Principal and equity holder in Monument Analytics, a health care consultancy whose clients include the life sciences industry as well as plaintiffs in opioid litigation, for whom he has served as a paid expert witness; and is a past member of OptumRx's National P&T Committee. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict-of-interest policies.

### SUPPLEMENTARY INFO

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. 2023 Apr;280(4):1775-1784.

doi: 10.1007/s00405-022-07704-0. Epub 2022 Oct 22.

# Nasal eosinophilia as a preliminary discriminative biomarker of non-allergic rhinitis in every day clinical pediatric practice

[Athina Papadopoulou](#)<sup>1,2</sup>, [Stavroula Lambidi](#)<sup>3</sup>, [Theano Lagousi](#)<sup>4</sup>, [Maria Syrrou](#)<sup>5</sup>, [Fani Giannoula](#)<sup>4</sup>, [Efstathia Staikou](#)<sup>5</sup>, [Stavroula Kostaridou](#)<sup>6</sup>, [Despoina-Zoe T Mermiri](#)<sup>4</sup>

Affiliations expand

- PMID: 36271956
- DOI: [10.1007/s00405-022-07704-0](https://doi.org/10.1007/s00405-022-07704-0)

## Abstract

**Background:** Non-allergic rhinitis (NAR) in children, named local allergic rhinitis (LAR) and non-allergic rhinitis with eosinophilia syndrome (NARES), are recently termed entities in childhood characterized by symptoms suggestive of allergic rhinitis in the absence of systemic atopy. Nasal eosinophils (nEo) are the principal cells involved in the allergy inflammation and nasal allergen provocation test is the gold standard method for the diagnosis, albeit with several limitations. The aim of this study was to validate the presence of nEo in combination with the therapeutic response to nasal steroids, as a preliminary discriminator of NAR in real life data.

**Methods:** In a prospective cohort study, 128 children (63.3% male, aged  $72 \pm 42$  m) with history of NAR were enrolled and followed up for  $52 \pm 32$  m. Nasal cytology was performed and nasal steroids trial was recommended initially in all and repeatedly in relapsing cases. Response to therapy was clinically evaluated using 10-VAS.

**Results:** Significant nEo was found in 59.3% of the cases and was related to reported dyspnea episodes. 23.4% had no response to therapy, whereas 51.5% were constantly good responders. Response to therapy was related to nEo and a cutoff point of 20% was defined as the most reliable biological marker with 94% sensitivity and 77% specificity.

**Conclusions:** In children with symptoms of NAR, the presence of nEo > 20% constantly responding to nasal steroid therapy, is a clear indicator of atopy. In an everyday clinical setting, it emerged as an easy, preliminary, cell biomarker suggestive of further investigation such as NAPT, to discriminate LAR from NARES.

**Keywords:** Biomarker; Children; Nasal eosinophils; Nasal steroids; Non-allergic rhinitis.

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. 2023 Apr;78(4):1113-1116.

doi: 10.1111/all.15550. Epub 2022 Oct 21.

**Patient-reported outcome measures in birch pollen allergic patients treated with sublingual immunotherapy reflect real life**

[Farah Bahbah](#)<sup>1</sup>, [Catherine Gentil](#)<sup>2</sup>, [Bernardo Sousa-Pinto](#)<sup>3,4</sup>, [G Walter Canonica](#)<sup>5,6</sup>, [Philippe Devillier](#)<sup>7</sup>, [Oliver Pfaar](#)<sup>8</sup>, [Jean Bousquet](#)<sup>9,10,11</sup>

Affiliations expand

- PMID: 36226843
- DOI: [10.1111/all.15550](https://doi.org/10.1111/all.15550)

*No abstract available*

- [6 references](#)

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. 2023 Apr;72(2):316-323.

doi: 10.1016/j.alit.2022.08.008. Epub 2022 Sep 29.

## [A diagnostic score for eosinophilic granulomatosis with polyangiitis among eosinophilic disorders](#)

[Hideyuki Takahashi](#)<sup>1</sup>, [Toshihiko Komai](#)<sup>2</sup>, [Keigo Setoguchi](#)<sup>3</sup>, [Hirofumi Shoda](#)<sup>1</sup>, [Keishi Fujio](#)<sup>1</sup>

Affiliations expand

- PMID: 36184347

- DOI: [10.1016/j.alit.2022.08.008](https://doi.org/10.1016/j.alit.2022.08.008)

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# Abstract

**Background:** Eosinophilic granulomatosis with polyangiitis (EGPA) is a form of systemic vasculitis with eosinophilic inflammation. However, existing classification criteria are all designed to classify EGPA among vasculitis and there is no established method distinguishing EGPA from other eosinophilic disorders. The aim of the present study was to propose a scoring system to differentiate EGPA among eosinophilic disorders.

**Methods:** Non-supervised hierarchical clustering using Ward's method and principal component analysis (PCA) were performed for 19 clinical parameters of 58 patients with eosinophilia-related diseases at a tertiary university hospital. The newly proposed scoring system was externally validated in 40 patients at another tertiary institution.

**Results:** Two distinct clusters were identified, and clinical features including peripheral neuropathy, asthma, skin involvement, lung involvement, rheumatoid factor (RF) positivity, myeloperoxidase (MPO)-anti-neutrophil cytoplasmic antibody (ANCA) positivity, IgE elevation, C-reactive protein (CRP) elevation, and vasculitis pathological findings were predominantly observed in one of these clusters ( $p < 0.05$ ). Ten features defining the cluster with a high rate of vasculitis were weighted by PCA to create the E-CASE (EGPA classification among systemic eosinophilia) scoring system, on a 16-point scale. Based on the distribution of scores in the primary cohort, we defined an E-CASE score  $\geq 12$  as positive,  $\leq 8$  as negative, and 9-11 as undeterminable. The sensitivity and specificity of the E-CASE score in the validation cohort were 93.3% and 100%, respectively.

**Conclusions:** We developed and verified a novel scoring system for differentiating EGPA from other types of eosinophilic disorders.

**Keywords:** Classification criteria; Diagnosis; Diagnostic score; Eosinophilia; Eosinophilic granulomatosis with polyangiitis.

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. 2023 Apr;60(4):824-834.

doi: 10.1080/02770903.2022.2102037. Epub 2022 Aug 2.

# Physical activity levels in asthma: relationship with disease severity, body mass index and novel accelerometer-derived metrics

[Helen Clare Ricketts](#)<sup>1</sup>, [Duncan S Buchan](#)<sup>2</sup>, [Femke Steffensen](#)<sup>3</sup>, [Rekha Chaudhuri](#)<sup>4</sup>, [Julien S Baker](#)<sup>5</sup>, [Douglas C Cowan](#)<sup>6</sup>

Affiliations expand

- PMID: 35876843
- DOI: [10.1080/02770903.2022.2102037](https://doi.org/10.1080/02770903.2022.2102037)

## Abstract

**Objectives:** Patients with asthma may feel limited in physical activity (PA). Reduced PA has been demonstrated in asthmatics versus healthy controls, and increasing PA associated with improved asthma outcomes. Obesity is commonly found with difficult-to-control asthma and worsens outcomes. We compared PA levels in participants with difficult-to-control asthma and elevated body mass index (BMI) (DOW group) and two mild-moderate asthma groups: one with BMI <25 kg/m<sup>2</sup> (MHW) and one with BMI ≥25 (MOW).

**Methods:** This cross-sectional study used 7-day recordings from wrist-worn accelerometers to compare PA between groups. Inactive time, light (LPA), moderate-vigorous PA (MVPA) were measured, along with two novel metrics: intensity gradient (IG) reflecting PA intensity, and average acceleration (AA) reflecting PA volume. PA parameters were compared using ANOVA or Kruskal-Wallis testing. Correlation and linear regression analyses explored associations between PA parameters and asthma outcomes. As AA was the PA parameter correlated most closely with asthma-related outcomes, an exploratory analysis compared outcomes in highest and lowest AA quartiles.

**Results:** 75 participants were recruited; 57 accelerometer readings were valid and included in analysis. Inactive time was significantly higher ( $p < 0.001$ ), and LPA ( $p < 0.007$ ), MVPA ( $p < 0.001$ ), IG ( $p < 0.001$ ) and AA ( $p < 0.001$ ) all significantly lower in DOW versus MHW and MOW groups, even after adjusting for age and BMI. Quartiles based on AA had significantly different asthma profiles.

**Conclusions:** Overweight/obese participants with difficult-to-control asthma performed less PA, and activity of reduced intensity and volume. Increased AA is associated with improvement in several asthma-related outcomes. Increased PA should be recommended to relevant patients.

**Keywords:** Accelerometer; asthma; difficult-to-control asthma; obesity; physical activity.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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. 2023 Apr;60(4):811-823.

doi: 10.1080/02770903.2022.2102036. Epub 2022 Jul 21.

## [Impact of mepolizumab in patients with high-burden severe asthma within a managed care population](#)

[Njira L Lugogo](#)<sup>1</sup>, [Michael Bogart](#)<sup>2</sup>, [Thomas Corbridge](#)<sup>2</sup>, [Elizabeth R Packnett](#)<sup>3</sup>, [Joanne Wu](#)<sup>3</sup>, [Beth Hahn](#)<sup>2</sup>

Affiliations expand

- PMID: 35853158

- DOI: [10.1080/02770903.2022.2102036](https://doi.org/10.1080/02770903.2022.2102036)

## Abstract

**Objective:** To evaluate the real-world impact of mepolizumab on the incidence of asthma exacerbations, oral corticosteroid (OCS) use and asthma exacerbation-related costs in patients with high-burden severe asthma.

**Methods:** This was a retrospective study of the MarketScan Commercial and Medicare Databases in patients with high-burden severe asthma ( $\geq 80$ th percentile of total healthcare expenditure and/or significant comorbidity burden). Patients were  $\geq 12$  years of age upon mepolizumab initiation (index date November 1, 2015–December 31, 2018) and had  $\geq 2$  mepolizumab administrations during the 6 months post-index. Asthma exacerbation frequency (primary outcome), use of OCS (secondary outcome), and asthma exacerbation-related costs (exploratory outcome) were assessed during the 12 months pre-index (baseline) and post-index (follow-up).

**Results:** In total, 281 patients were analyzed. Mepolizumab significantly reduced the proportion of patients with any asthma exacerbation ( $P < 0.001$ ) or exacerbations requiring hospitalization ( $P = 0.004$ ) in the follow-up versus baseline period. The mean number of exacerbations decreased from 2.5 to 1.5 events/patient/year (relative reduction: 40.0%;  $P < 0.001$ ). The proportion of patients with  $\geq 1$  OCS claim also decreased significantly from 94.0% to 81.9% (relative reduction: 12.9%;  $P < 0.001$ ), corresponding to a decrease from 6.6 to 4.7 claims/person/year ( $P < 0.001$ ). Of the 264 patients with  $\geq 1$  OCS claim during baseline, 191 (72.3%) showed a decrease in mean daily OCS use by  $\geq 50\%$  in 117 patients (61.3%). Total asthma exacerbation-related costs were significantly lower after mepolizumab was initiated ( $P < 0.001$ ).

**Conclusions:** Mepolizumab reduced exacerbation frequency, OCS use and asthma exacerbation-related costs in patients with high-cost severe asthma. Mepolizumab provides real-world benefits to patients, healthcare systems and payers.

**Keywords:** Costs; corticosteroid use; exacerbations; hospitalization; real-world; retrospective study.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Observational Study

J Asthma

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. 2023 Apr;60(4):727-736.

doi: 10.1080/02770903.2022.2093217. Epub 2022 Jul 18.

# Regional variation in prevalence of difficult-to-treat asthma and oral corticosteroid use for patients in Australia: heat map analysis

[Peter A B Wark](#)<sup>1</sup>, [Mark Hew](#)<sup>2,3</sup>, [Yang Xu](#)<sup>4</sup>, [Clare Ghisla](#)<sup>5</sup>, [Tra-My Nguyen](#)<sup>6</sup>, [Bora Erdemli](#)<sup>7</sup>, [Aditya Samant](#)<sup>7</sup>, [Cassandra Nan](#)<sup>8</sup>

Affiliations expand

- PMID: 35844195
- DOI: [10.1080/02770903.2022.2093217](https://doi.org/10.1080/02770903.2022.2093217)

## Abstract

**Background:** In Australia, the regional prevalence of difficult-to-treat asthma is unknown. We aimed to describe regional variation in difficult-to-treat asthma prevalence and oral corticosteroid (OCS) use.

**Methods:** In this retrospective, observational, longitudinal study using data from March 2018-February 2019 in the NostraData longitudinal database, prescriptions dispensed for obstructive airway disease were processed through a high-level algorithm to identify patients with asthma. Difficult-to-treat asthma was defined by  $\geq 2$  high-dosage inhaled corticosteroids plus long-acting beta-agonist prescriptions over 6 months. Patients who additionally received OCS prescriptions sufficient to treat  $\geq 2$  exacerbations over 6 months

were classified as having uncontrolled difficult-to-treat asthma. Patient-level data were analyzed across 340 geographic areas in Australia to determine regional prevalence of difficult-to-treat asthma, uncontrolled difficult-to-treat asthma, and OCS use.

**Results:** Of 1 851 129 people defined as having asthma, 440 800 (24%) were classified as having difficult-to-treat disease. Of those difficult-to-treat asthma patients, 96 338 (22%) were considered to have uncontrolled disease. Between 29% and 48% of patients had difficult-to-treat asthma in 49 geographic areas, most frequently located in Western Australia. Between 26% and 67% of patients had uncontrolled difficult-to-treat asthma in 29 geographic areas (mostly in Eastern Australia). Overall, a wide variability of asthma severity and control was observed among regions.

**Conclusions:** Despite global and national guidelines, regional differences in the prevalence of difficult-to-treat asthma and uncontrolled difficult-to-treat asthma and OCS use exist in Australia. Understanding these regional variations should inform policy and target management in the areas with the greatest unmet need.

**Keywords:** Oral corticosteroids; difficult-to-treat asthma; epidemiology; uncontrolled asthma.

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. 2023 Apr;60(4):737-743.

doi: 10.1080/02770903.2022.2093218. Epub 2022 Jul 15.

## [The usefulness of YouTube videos as a source of information in asthma](#)

[Caroline Skovsgaard Diers](#)<sup>1</sup>, [Celine Remvig](#)<sup>1</sup>, [Hanieh Meteran](#)<sup>2</sup>, [Simon Francis Thomsen](#)<sup>3,4</sup>, [Torben Sigsgaard](#)<sup>5</sup>, [Simon Høj](#)<sup>6</sup>, [Howraman Meteran](#)<sup>5,7,8,9</sup>

Affiliations expand

- PMID: 35837808
- DOI: [10.1080/02770903.2022.2093218](https://doi.org/10.1080/02770903.2022.2093218)

## Abstract

**Background:** Patient education is a key element in the management of asthma.

**Aims:** This study aimed to evaluate the popularity and usefulness of YouTube videos on asthma.

**Methods:** Two authors screened and evaluated the 200 most popular videos. Data on likes, dislikes, views, comment, source of uploader, days since upload, and usefulness were recorded and included for analyses. The usefulness of the videos was categorized as follows: *useful*, *misleading*, or *neutral*. Misleading videos provided at least one scientifically incorrect detail, whereas useful videos contained scientifically correct information.

**Results:** A total of 130 videos were included, and the total number of views was 100,290,242 with a total duration of 29 h and 8 min. While 26.6% of videos were uploaded by TV shows and YouTube channels, only 7.7% were uploaded by lung specialists. 65.4% of the videos contained scientifically correct information, whereas 18.5% contained misleading information. Although videos from medical professionals had a higher quality than videos from YouTube channels and TV shows, the latter were more popular. Misleading videos had numerically, but not statistically significant higher views compared with useful videos.

**Conclusions:** YouTube videos on asthma are popular in terms of viewer interaction, and the popularity is not restricted to videos uploaded by professional sources. Although more than half of the videos were found to be useful, a non-negligible proportion of videos were assessed as misleading. The usefulness of YouTube videos on asthma is variable and initiatives should be taken to increase the potential of YouTube as an useful source in patient education.

**Keywords:** YouTube; allergy; asthma; digital health; patient education.

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Mol Aspects Med

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. 2023 Apr;90:101104.

doi: 10.1016/j.mam.2022.101104. Epub 2022 Jul 11.

## Siglecs in allergy and asthma

[Bruce S Bochner](#)<sup>1</sup>, [Jeremy A O'Sullivan](#)<sup>2</sup>, [Alan T Chang](#)<sup>3</sup>, [Bradford A Youngblood](#)<sup>1,3</sup>

Affiliations expand

- PMID: 35835621

- DOI: [10.1016/j.mam.2022.101104](https://doi.org/10.1016/j.mam.2022.101104)

### Abstract

The term "allergic diseases" encompasses several common, IgE-mediated conditions that range from being annoying to those that are life-threatening. Available treatments include active avoidance of the instigating allergen and the use of a variety of oral, inhaled, intranasal, intraocular and injected agents. While most individuals with allergies do well with existing therapies, there are still unmet therapeutic needs. Siglecs (sialic acid-binding, immunoglobulin-like lectins) are a family of single-pass transmembrane I-type lectins found on various subsets of cells, especially those of the immune system. All Siglecs have extracellular domains recognizing sialoside ligands, and most contain cytoplasmic domains with inhibitory signaling activity. This review focuses on Siglecs that likely play a role in regulating allergic and asthmatic responses, and how specific Siglecs, expressed on cells such as eosinophils and mast cells, are being targeted for therapeutic benefit.

## Conflict of interest statement

Declaration of competing interest B.S.B. receives remuneration for serving on the scientific advisory board of Allakos, Inc. and owns stock in Allakos. He receives publication-related royalty payments from Elsevier and UpToDate. He is a co-inventor on existing Siglec-8-related patents and thus may be entitled to a share of royalties received by Johns Hopkins University during development and potential sales of such products. B.S.B. is also a co-founder of Allakos, Inc. which makes him subject to certain restrictions under University policy. The terms of this arrangement are being managed by Johns Hopkins University and Northwestern University in accordance with their conflict of interest policies. J.A.O. has nothing to disclose. A.T.C and B.A.Y. are current employees of and/or own stock and/or stock options from Allakos, Inc.

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. 2023 Apr;60(4):802-810.

doi: 10.1080/02770903.2022.2097919. Epub 2022 Jul 13.

# [Potential for repurposing oral hypertension/diabetes drugs to decrease asthma risk in obesity](#)

[Akshay Sood](#)<sup>1</sup>, [Clifford Qualls](#)<sup>2</sup>, [Allison Murata](#)<sup>2</sup>, [Phillip J Kroth](#)<sup>3</sup>, [Jenny Mao](#)<sup>1</sup>, [David S Schade](#)<sup>4</sup>, [Glen Murata](#)<sup>2</sup>

[Affiliations expand](#)

- PMID: 35796615
- DOI: [10.1080/02770903.2022.2097919](https://doi.org/10.1080/02770903.2022.2097919)

## Abstract

**Objective:** Risk for asthma in the overweight/obese may be mediated by adiponectin and peroxisome proliferator activated receptor pathways and may be reduced by the use of oral drugs impacting these pathways, such as angiotensin converting enzyme inhibitors (ACE-I), thiazolidinediones (TZD), and angiotensin receptor blockers (ARB). Our study objective was to determine whether ACE-I, TZD, and/or ARB use in overweight/obese adults with diabetes mellitus and/or hypertension is associated with a lower risk for incident asthma.

**Methods:** Using an existing cohort of American veterans, we performed a longitudinal data analysis over 15 years. Exposure was defined by the prescription pickup of ACE-I, TZD, and/or ARB for at least 4 weeks. The outcome, time until new-onset of clinician-diagnosed asthma, was studied using survival analysis. The propensity scoring method controlled for treatment selection bias.

**Results:** 2.83 million eligible veterans, including 77,278 with incident asthma, were studied. As compared to those unexposed, the use of ACE-I alone, TZD alone, or their combinations were each associated with decreased risk for incident asthma (hazard ratios of 0.88, 0.74, and 0.20, respectively;  $p < 0.001$  for all analyses in the fully adjusted statistical models). TZD lowered the risk among racial/ethnic minority subjects more than among White participants ( $p < 0.001$ ). On the other hand, ARB use alone or in combination with TZD was associated with a higher risk for incident asthma.

**Conclusions:** Use of ACE-I and/or TZD was associated with a lower risk for incident asthma in overweight/obese patients with diabetes mellitus and/or hypertension.

**Keywords:** Angiotensin converting enzyme inhibitor; adiponectin; angiotensin receptor blocker; incident asthma; peroxisome proliferator-activated receptor; thiazolidinediones.

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Publication types, MeSH terms, Substances, Grant support[expand](#)

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. 2023 Apr;60(4):769-783.

doi: 10.1080/02770903.2022.2094803. Epub 2022 Jul 10.

# Usefulness of simultaneous impulse oscillometry and spirometry with airway response to bronchodilator in the diagnosis of asthmatic cough

[Namiko Taniuchi](#)<sup>1,2</sup>, [Mitsunori Hino](#)<sup>1,2</sup>, [Akiko Yoshikawa](#)<sup>1,2</sup>, [Akihiko Miyanaga](#)<sup>1,2</sup>, [Yosuke Tanaka](#)<sup>2</sup>, [Masahiro Seike](#)<sup>2</sup>, [Akihiko Gemma](#)<sup>2</sup>

Affiliations [expand](#)

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- DOI: [10.1080/02770903.2022.2094803](https://doi.org/10.1080/02770903.2022.2094803)

## Abstract

**Objective:** Some of the most common causes of chronic cough include cough variant asthma (CVA), bronchial asthma (BA), and asthma-COPD overlap (ACO). Although there is some overlap in the etiology of these diseases, it is clinically important to attempt an early differential diagnosis due to treatment strategies and prognoses. **Methods:** Spirometry and impulse oscillometry (IOS) before and after bronchodilator inhalation were analyzed for clinically diagnosed CVA (cCVA,  $n = 203$ ), BA (cBA,  $n = 222$ ), and ACO (cACO,  $n = 61$ ). **Results:** A significant difference in  $\Delta FEV_1$  was observed between cBA and cCVA ( $\Delta FEV_1$  improvement of 122.5 mL/5.4% and 65.7 mL/2.2%, respectively), but no difference was observed in  $\Delta PEF$ ,  $\Delta V50$ , or  $\Delta V25$ . Except for R20 (resistance at 20 Hz), significant differences between the three groups were observed in IOS. In IOS, cCVA and cBA showed comparable peripheral airway response to bronchodilator which was thought to be commensurate with changes in V50 and V25. cACO improved  $\Delta FEV_1$  improvement of 81.0

mL/6.2% and was distinguished by a downward respiratory system reactance (Xrs) waveform with a limited bronchodilator response. FEV<sub>1</sub>/FVC, %FEV<sub>1</sub>, and %V25 had relatively strong correlations with the three IOS parameters, X5 (reactance at 5 Hz), resonant frequency (Fres), and low-frequency reactance area (ALX), in the correlation between IOS and spirometers. **Conclusion:** Changes in IOS parameters were more sensitive in this study than changes in FEV<sub>1</sub> or the flow-volume curve. Considering the benefits and relevance of the two different tests, simultaneous IOS and spirometry testing were useful in the diagnosis of asthmatic cough.

**Keywords:** IOS; Impulse oscillometry; asthma; chronic cough; spirometry.

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. 2023 Apr;60(4):784-793.

doi: 10.1080/02770903.2022.2094804. Epub 2022 Jul 7.

## [Trends in seasonal pollen and asthma-related morbidity among adults and children in a U.S. high-density urban center, 2001–2020](#)

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Affiliations expand

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- DOI: [10.1080/02770903.2022.2094804](https://doi.org/10.1080/02770903.2022.2094804)

## Abstract

**Objective:** To analyze the long-term trends in pollen counts and asthma-related emergency department visits (AREDV) in adult and pediatric populations in the Bronx.

**Methods:** Daily values of adult and pediatric AREDV were retrospectively obtained from three major Bronx hospitals using ICD-10 codes and pollen counts were obtained from the Armonk station from 2001-2020. Wilcoxon Ranked Sum was applied to compare median values, while Spearman correlation was employed to examine the association between these variables, for both decades and each season.

**Results:** The median value of pediatric AREDV increased by 200% from the 1st to 2nd decade ( $p < 0.001$ ) and AREDV peak shifted from predominantly the spring season in the 1st decade to the fall and winter seasons in the 2nd decade. Seasonal patterns were consistent over 20 years with summer AREDV lower than all other seasons (9 vs. 17 per day) ( $p < 0.001$ ). Spring tree pollen peaks were correlated with AREDV peaks ( $\rho = 0.34$ ) ( $p < 0.001$ ). Tree pollen exceeding 100 grains/m<sup>3</sup> corresponded to a median of 19.0 AREDVs while all other tree pollen (0 - 99 grains/m<sup>3</sup>) corresponded to a median of 15.0 AREDVs ( $p < 0.001$ ). AREDVs sharply declined in 2020, coinciding with the emergence of COVID-19.

**Conclusions:** Pollen and AREDVs peak earlier in the spring and are more strongly interconnected, while asthma rates among children are rapidly rising, particularly in the fall and winter. These findings can advise targeted awareness campaigns for better management of asthma related morbidity.

**Keywords:** Asthma; emergency department visits; epidemiology; pollen; surveillance; urban.

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Multicenter Study

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. 2023 Apr;60(4):708-717.

doi: 10.1080/02770903.2022.2089996. Epub 2022 Jun 24.

# Modifiable factors associated with pediatric asthma readmissions: a multi-center linked cohort study

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Affiliations expand

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## Abstract

**Objectives:** To (a) identify rates of hospital readmission and emergency department (ED) re-presentation for asthma within a 12-month period, (b) estimate the effects of modifiable hospital, general practitioner (GP) and home environmental factors on hospital readmission, ED re-presentations and rescue oral corticosteroid use.

**Methods:** We recruited 767 children aged 3-18 years who were admitted to 3 hospitals in Victoria, Australia between 2017 and 2018 with a validated diagnosis of asthma on chart review. Primary outcome was hospital readmission with asthma within 12 months of index admission. Secondary outcomes were ED re-presentation for asthma and rescue oral corticosteroid use. All outcomes were identified through linked administrative datasets. Their caregivers and 277 nominated GPs completed study surveys regarding the home environment and their usual asthma management practices respectively.

**Results:** Within 12 months of an index admission for asthma 263 (34.3%) participants were readmitted to a hospital for asthma, with participants between the ages of 3-5 years accounting for 69.2% of those readmitted. The estimated effect of GP reported guideline discordant care on the odds of readmission was OR 1.57, 95% CI 1.00-2.47,  $p = 0.05$ . None

of the hospital or home environmental factors appeared to be associated with hospital readmissions.

**Conclusions:** Hospital readmissions among Australian children with asthma are increasing, and linked datasets are important for objectively identifying the health services burden of asthma. They also confirm the important role of the GP in the management of pediatric asthma.

**Keywords:** Asthma; linkage; paediatrics; readmissions.

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Multicenter Study

Laryngoscope

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. 2023 Apr;133(4):970-976.

doi: 10.1002/lary.30256. Epub 2022 Jun 22.

## Multi-Institutional Study of Patient-Reported Outcomes of Paradoxical Vocal Fold Motion

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Affiliations expand

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- DOI: [10.1002/lary.30256](https://doi.org/10.1002/lary.30256)

## Abstract

**Objective:** To explore patient-reported outcome measures of pediatric paradoxical vocal fold motion through a multi-institutional study of geographically diverse United States medical facilities to assess long-term management and outcomes.

**Methods:** Eligible participants >8 years of age diagnosed with PVFM over a 10-year period from 7 tertiary pediatric hospitals were invited to complete a survey addressing study objectives.

**Results:** 65 participants completed the survey, of whom 80% were female, 75% reported a 3.5 grade point average or better, and 75% identified as competitive athletes or extremely athletic individuals. Participants rated their perceived efficacy of 13 specific treatments. Only five treatments were considered effective by a majority of the participants who tried them. The treatments that participants tried most often were breathing exercises (89.2%), bronchodilator treatments (45%), and allergy medications (35.4%). 78.8% of participants reported receiving more than one treatment and 25% reported receiving a combination of bronchodilators, anticholinergics, and steroids. At the time of PVFM diagnosis, 38% of participants had no idea when their symptoms would completely resolve. 23.3% of participants did not experience symptom resolution until greater than 1 year after diagnosis.

**Conclusions:** Traditional management tools such as breathing exercises and biofeedback treatments may not provide the long-term benefit that providers anticipate. In addition to these commonly used management strategies, highly efficacious techniques such as counseling and lifestyle management should be incorporated into the long-term management of patients whose symptoms are refractory to traditional care.

**Level of evidence:** 4 Laryngoscope, 133:970-976, 2023.

**Keywords:** PVFM; asthma; paradoxical vocal fold motion; vocal cord dysfunction.

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- [20 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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doi: 10.1080/02770903.2022.2093220. Epub 2022 Jun 30.

# The assessment of effectiveness, tolerance, and patient satisfaction with the use of a new fixed-dose combination product, containing salmeterol and fluticasone propionate, Salflumix Easyhaler® in the treatment of asthma in the daily clinical practice

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Affiliations [expand](#)

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## Abstract

**Background:** The effectiveness of a fix-dose salmeterol/fluticasone combination therapy in asthma was previously shown for the original product. The study aim was to evaluate the

clinical effectiveness and safety of a second entry DPI - dry powder inhaler (Salflumix Easyhaler) in patients with asthma in everyday clinical practice.

**Patients and methods:** This multicenter Investigator-Initiated Study that enrolled 2,037 adult outpatients with asthma treated with Salflumix Easyhaler, was conducted by 220 pulmonologists across Poland. Asthma control was assessed during 3 visits with  $6 \pm 2$  weeks intervals based on the Asthma Control Test (ACT). In addition, patient Satisfaction with Asthma Treatment Questionnaire (SATQ) and adherence and adverse events (AEs) were monitored.

**Results:** During the observation ( $86 \pm 30$  days) the percentage of patients with controlled asthma (ACT 20-25 pts) increased from 35.5% at the first visit to 86.5% at the third visit ( $p < 0.001$ ). In the subgroup analysis, there were more patients not obtaining asthma control among patients that switched from the treatment with other devices than in naïve ones. Global SATQ scores increased from  $5.8 \pm 0.7$  to  $6.2 \pm 0.6$  during the observation. Patients' satisfaction with the use of the Salflumix Easyhaler was high. Adherence exceeded 95%. Eight AEs were reported.

**Conclusions:** Salflumix Easyhaler is highly effective and well-tolerated by naïve patients with asthma and those switching from another device. In general, patients show good compliance with medical product and are satisfied with the use of this new device, and not reporting difficulties and errors related to its' use. Their physicians' overall perception of Salflumix Easyhaler use is very positive.

**Keywords:** asthma; fix-dose salmeterol/fluticasone combination therapy; patients satisfaction; real-life data.

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. 2023 Apr;60(4):635-646.

# Barriers and facilitators of electronic patient portal uptake for asthma management

[Ilana Radparvar](#)<sup>1</sup>, [Mindy K Ross](#)<sup>2</sup>

Affiliations expand

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- PMCID: PMC9763543 (available on 2024-04-01)
- DOI: [10.1080/02770903.2022.2087190](https://doi.org/10.1080/02770903.2022.2087190)

## Abstract

**Objective:** An active patient-practitioner partnership is a key aspect of asthma management and patient-reported data helps with shared decision making. Technological advances such as the electronic patient portal can facilitate partnership, with the goal of improved asthma outcomes. However, uptake of portals by end-users for asthma management has been low. We studied portal-based asthma interventions to understand barriers and facilitators to its use.

**Data sources:** We searched within the PubMed, Web of Science, Scopus, MEDLINE, and Google Scholar databases.

**Study selections:** We used the PRISMA extension for scoping reviews to guide our analysis of studies related to asthma and patient portals. We summarized relevant studies in terms of barriers and facilitators as well as study characteristics.

**Results:** Sixteen studies were included in our final analysis. Common barriers to patient portal use for asthma management were lack of perceived value by the end-user, low end-user technological literacy, and limited resources. Facilitators of portal use included ease of use, personalization, and adequate technical support. Patient portals in these studies were used for a variety of applications related to core asthma management concepts of assessment and monitoring, education for a partnership in asthma care, environmental factors, co-morbidities, and medications.

**Conclusions:** Patient portal use for asthma management can be encouraged by ensuring the portal is easy to access and navigate, demonstrates values, as well as has readily available technical support. Involving end-users closely in the design process and implementation may help address barriers. Special attention is needed for groups with technological resource limitations.

**Keywords:** Pediatrics; control/management; education.

## Conflict of interest statement

Declarations of Interests: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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. 2023 Apr;60(4):718-726.

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# [Asthma, chronic obstructive pulmonary disease, and asthma-COPD overlap among US working adults](#)

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Affiliations expand

- PMID: 35696621



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## Abstract

**Background:** Asthma-COPD overlap (ACO) is a respiratory condition with more severe respiratory symptoms, poorer quality of life, and increased hospital admissions compared with asthma or COPD alone.

**Objectives:** Estimate asthma, chronic obstructive pulmonary disease (COPD), and ACO prevalence among workers by industry and occupation and assess physical and mental health status, healthcare utilization, among workers with ACO.

**Methods:** The 2014-2018 National Health Interview Survey (NHIS) data for working adults aged  $\geq 18$  years employed (sample  $n = 99,424$ ) in the 12 months prior to the survey were analyzed. Age-adjusted ACO, COPD and asthma prevalence and prevalence ratios adjusted for age, sex, race and smoking status were estimated.

**Results:** During 2014-2018, of the estimated 166 million (annual average) US workers, age-adjusted asthma, COPD, and ACO prevalence was 6.9%, 4.0%, and 1.1%, respectively. ACO prevalence was highest among workers aged  $\geq 65$  years (2.0%), females (1.6%), current smokers (1.9%), those living below the federal poverty level (2.3%), and workers in the accommodation and food services (1.6%) industry and personal care and service (2.3%) occupations. Workers with ACO had more frequent ( $p < 0.05$ ) physician office visits, emergency department visits; and were more likely to be in poorer mental health, obese, have more lost workdays, more bed days, and comorbidities compared to workers with asthma alone and workers with COPD alone. **Conclusion:** Higher ACO prevalence among worker groups and increased healthcare utilization underscores the need for early identification of asthma and COPD, assessment of potential workplace exposures, and implementation of tailored interventions to reduce ACO among working adults.

**Keywords:** Asthma-COPD overlap; exposures; occupation; prevalence industry; workers; workplace.

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MeSH termsexpand

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# Evaluation of the factors affecting lung function in pediatric patients with asthma

[Tao Ai](#)<sup>1</sup>, [Ying Wu](#)<sup>1</sup>, [Lei Zhang](#)<sup>1</sup>, [Ronghua Luo](#)<sup>1</sup>, [Huling Liao](#)<sup>1</sup>, [Yinghong Fan](#)<sup>1</sup>, [Wanmin Xia](#)<sup>1</sup>, [Cheng Xie](#)<sup>1</sup>, [Libing Zhang](#)<sup>1</sup>

Affiliations expand

- PMID: 35674402
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## Abstract

**Purpose:** This study aimed to analyze the risk factors affecting lung function in children with asthma based on clinical data to advice on clinical treatment and prognosis.

**Methods:** This study included newly diagnosed patients with asthma admitted to the Respiratory Department of Chengdu Women's and Children's Central Hospital in Sichuan from July 2020 to June 2021. The factors associated with lung function were analyzed using univariate and multivariate linear regression with the forward method, while factors affecting lung ventilation function were analyzed using multivariate logistic regression.

**Results:** Sixty percent of the patients had normal lung function. Age was significantly negatively correlated with forced vital capacity (FVC)/FVC<sub>predicted</sub> ( $B = -1.385$ ,  $p = 0.001$ ), FEV<sub>1</sub>/FEV<sub>1predicted</sub> ( $B = -2.092$ ,  $p < 0.001$ ), and FEV<sub>1</sub>%/FEV<sub>1o</sub>predicted ( $B = -0.834$ ,  $p = 0.001$ ). Body mass index (BMI) for age Z score ( $B = 1.661$ ,  $p = 0.045$ ) and cesarean delivery ( $B = 4.471$ ,  $p = 0.013$ ) were significantly positively correlated with FVC/FVC<sub>predicted</sub>. Birth weight was significantly positively correlated with FEV<sub>1</sub>/FEV<sub>1predicted</sub> ( $B = 4.593$ ,  $p = 0.027$ ). Multivariate logistic regression analysis revealed that age  $\geq 6$  years and cough variant asthma (CVA) were risk factors for abnormal lung function.

**Conclusions:** Age, BMI for age Z score, mode of delivery, and birth weight were significantly correlated with lung function in children with asthma. Furthermore, children with asthma and normal lung function were more likely to be overlooked. More attention should be given to children with asthma and normal lung function, and CVA.

**Keywords:** Asthma; factors; lung function; pediatric.

- [Cited by 1 article](#)

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. 2023 Apr;60(4):843-844.

doi: 10.1080/02770903.2022.2087187. Epub 2022 Jun 10.

## [Factors associated with wheezing recurrence in clinical practice](#)

[Giorgio Ciprandi](#)<sup>1</sup>, [Luigi Cioffi](#)<sup>2</sup>, [Irene Schiavetti](#)<sup>3</sup>, [Michele Miraglia Del Giudice](#)<sup>4</sup>, [Maria Angela Tosca](#)<sup>5</sup>

Affiliations [expand](#)

- PMID: 35666209
- DOI: [10.1080/02770903.2022.2087187](https://doi.org/10.1080/02770903.2022.2087187)

*No abstract available*

- [Cited by 1 article](#)

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. 2023 Apr;60(4):647-654.

doi: 10.1080/02770903.2022.2083636. Epub 2022 Jun 6.

# Antibiotic use among admitted pediatric patients in the United States with status asthmaticus before and during the COVID-19 pandemic

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Affiliations expand

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- DOI: [10.1080/02770903.2022.2083636](https://doi.org/10.1080/02770903.2022.2083636)

## Abstract

Hospital admission trends of children with status asthmaticus diminished during the Coronavirus-19 (COVID-19) pandemic of 2020, possibly secondary to several factors such as school closures and use of face masks. What effect this had on antibiotic prescribing practices has yet to be described. The objective of our study was to evaluate the use of

antibiotics in hospitalized children with a diagnosis of status asthmaticus before and during the COVID pandemic. **Methods:** A retrospective cross-sectional analysis was conducted using the TriNetX® cloud-based program with a national and institutional database. Each database was queried for all inpatient pediatric encounters from 3 to 18 years old, admitted with a diagnosis of status asthmaticus in the spring seasons of 2017-2019. Admission data and antibiotic usage were queried during the COVID-19 pandemic year of 2020 from both databases and compared amongst all study years. **Results:** In 2020, there was an overall decrease in the number of admissions as compared to the average number from 2017-2019, by 76.9% in the national database ( $p < 0.05$ ) and 91.2% in the institutional database. The rates of antibiotic prescriptions significantly dropped among the national database ( $p < 0.001$ ,  $z = 3.39$ ) and remained non-significantly changed among the institutional database ( $p = 0.944$  and  $z = 0.073$ ). **Conclusions:** Our study demonstrates that the COVID-19 pandemic year of 2020 coincided with a significant decrease in hospital admissions and antibiotic prescribing prevalence among children with status asthmaticus on a national level. Nonetheless, our reported trends in antibiotic prescribing are still grossly similar to that of pre-pandemic times and may demonstrate a continued need for antimicrobial stewardship.

**Keywords:** Control/Management; epidemiology; therapy; treatment.

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[Observational Study](#)

Clin Rev Allergy Immunol

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doi: 10.1007/s12016-022-08938-w. Epub 2022 Apr 14.

# Real-Life Effectiveness of Benralizumab, Mepolizumab and Omalizumab in Severe Allergic Asthma Associated with Nasal Polyps

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Affiliations expand

- PMID: 35420388
- DOI: [10.1007/s12016-022-08938-w](https://doi.org/10.1007/s12016-022-08938-w)

## Abstract

Biological therapies are available for the treatment of the severe allergic asthma (SAA) with blood eosinophil count  $\geq 0.3 \times 10^9/L$ . Several of them also showed benefits on nasal polyps (NP), one of the most frequent comorbidities of the severe asthma, but comparative studies on their effectiveness in the association SAA-NP are currently lacking. The aim of this study is to compare the effectiveness of benralizumab, mepolizumab and omalizumab in patients with SAA-NP in real-life settings. A retrospective, observational, multicenter real-life study was realized including patients with SAA-NP treated by benralizumab, mepolizumab or omalizumab for 6 months. We analysed the nasal and respiratory symptoms, the number of asthma attacks and salbutamol use/week, acute sinusitis and severe exacerbation rates, the asthma control score, the lung function parameters, the NP endoscopic score, the sinus imaging and the blood eosinophil count 6 months before and after treatment. Seventy-two patients with SAA-NP were included: 16 treated by benralizumab, 21 by mepolizumab and 35 by omalizumab. After 6 months of treatment, almost all studied parameters were improved (except sinus imaging) with a greater effect of omalizumab on the nasal pruritus ( $p = 0.001$ ) and more benefits of benralizumab on exacerbations rate, asthma attacks per week and lung function (all  $p < 0.05$ ). Benralizumab and mepolizumab were more effective to improve the NP endoscopic score and the blood eosinophil count (both  $p < 0.001$ ). All three biological therapies showed effectiveness by improving asthma and nasal outcomes in patients with SAA-NP. Several differences have been found that should be confirmed by larger comparative studies.

**Keywords:** Biological therapies; Comparative analysis; Effectiveness; Nasal polyposis; Severe allergic asthma.

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. 2023 Apr;64(2):161-178.

doi: 10.1007/s12016-022-08928-y. Epub 2022 Mar 11.

# [The Airway Microbiome–IL–17 Axis: a Critical Regulator of Chronic Inflammatory Disease](#)

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- PMID: 35275333
- PMCID: [PMC10017631](#)

- DOI: [10.1007/s12016-022-08928-y](https://doi.org/10.1007/s12016-022-08928-y)

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## Abstract

The respiratory tract is home to a diverse microbial community whose influence on local and systemic immune responses is only beginning to be appreciated. Increasing reports have linked changes in this microbiome to a range of pulmonary and extrapulmonary disorders, including asthma, chronic obstructive pulmonary disease and rheumatoid arthritis. Central to many of these findings is the role of IL-17-type immunity as an important driver of inflammation. Despite the crucial role played by IL-17-mediated immune responses in protection against infection, overt Th17 cell responses have been implicated in the pathogenesis of several chronic inflammatory diseases. However, our knowledge of the influence of bacteria that commonly colonise the respiratory tract on IL-17-driven inflammatory responses remains sparse. In this article, we review the current knowledge on the role of specific members of the airway microbiota in the modulation of IL-17-type immunity and discuss how this line of research may support the testing of susceptible individuals and targeting of inflammation at its earliest stages in the hope of preventing the development of chronic disease.

**Keywords:** Airway microbiota; Chronic inflammatory disease; IL-17; Respiratory tract; Th17 cells.

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## Conflict of interest statement

The authors declare no competing interests.

- [Cited by 2 articles](#)
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. 2023 Apr 1;18(2):82-89.

doi: 10.1097/SIH.0000000000000649. Epub 2022 Mar 2.

# Adaptation of a Simulation Model and Checklist to Assess Pediatric Emergency Care Performance by Prehospital Teams

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Affiliations expand

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- PMCID: PMC9437138 (available on 2023-09-02)
- DOI: [10.1097/SIH.0000000000000649](https://doi.org/10.1097/SIH.0000000000000649)

## Abstract

**Introduction:** Simulation tools to assess prehospital team performance and identify patient safety events are lacking. We adapted a simulation model and checklist tool of individual paramedic performance to assess prehospital team performance and tested interrater reliability.

**Methods:** We used a modified Delphi process to adapt 3 simulation cases (cardiopulmonary arrest, seizure, asthma) and checklist to add remote physician direction,

target infants, and evaluate teams of 2 paramedics and 1 physician. Team performance was assessed with a checklist of steps scored as complete/incomplete by raters using direct observation or video review. The composite performance score was the percentage of completed steps. Interrater percent agreement was compared with the original tool. The tool was modified, and raters trained in iterative rounds until composite performance scoring agreement was 0.80 or greater (scale <0.20 = poor; 0.21-0.39 = fair, 0.40-0.59 = moderate; 0.60-0.79 = good; 0.80-1.00 = very good).

**Results:** We achieved very good interrater agreement for scoring composite performance in 2 rounds using 6 prehospital teams and 4 raters. The original 175 step tool was modified to 171 steps. Interrater percent agreement for the final modified tool approximated the original tool for the composite checklist (0.80 vs. 0.85), cardiopulmonary arrest (0.82 vs. 0.86), and asthma cases (0.80 vs. 0.77) but was lower for the seizure case (0.76 vs. 0.91). Most checklist items (137/171, 80%) had good-very good agreement. Among 34 items with fair-moderate agreement, 15 (44%) related to patient assessment, 9 (26%) equipment use, 6 (18%) medication delivery, and 4 (12%) cardiopulmonary resuscitation quality.

**Conclusions:** The modified checklist has very good agreement for assessing composite prehospital team performance and can be used to test effects of patient safety interventions.

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## Conflict of interest statement

The authors declare no conflict of interest.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Rev Environ Health

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. 2021 Dec 24;38(1):137-150.  
doi: 10.1515/reveh-2021-0135. Print 2023 Mar 28.

# Exposure to ambient gaseous air pollutants and adult lung function: a systematic review

[Kazhal Masroor](#)<sup>1</sup>, [Mansour Shamsipour](#)<sup>2,3</sup>, [Ramin Mehrdad](#)<sup>4,5</sup>, [Farzad Fanaei](#)<sup>6</sup>, [Mina Aghaei](#)<sup>1</sup>, [Masud Yunesian](#)<sup>1,2</sup>

Affiliations expand

- PMID: 34957731
- DOI: [10.1515/reveh-2021-0135](https://doi.org/10.1515/reveh-2021-0135)

## Abstract

Exposure to hazardous air pollutants is identified as most obvious premature mortality factors in the world. Numerous epidemiological studies have estimated exposure to air pollutants may cause pulmonary toxicity and the incidence of respiratory diseases including chronic obstructive pulmonary disease (COPD), chronic bronchitis and asthma. The currently research was performed to evaluation the association between gaseous pollutants and lung function in healthy adults. Articles related to this study were selected from researches of Scopus, PubMed, and Web of Science databases. A total of 2,644 articles were retrieved and 39 records were reviewed after removing duplicates and excluding irrelevant studies. The result of this systematic review indicated that there is some evidence on decreasing lung function with exposure to gaseous air pollutants (NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>) which can have negative effects on human health. Although according to the evidence changes in lung function are mostly linked to the exposure to environmental pollutants including CO, O<sub>3</sub>, NO<sub>2</sub> and SO<sub>2</sub>, the results should be interpreted with caution considering some following issues discussed in this review. Therefore, further studies are required considering well-designed studies in large scales to strengthen the evidence.

**Keywords:** ambient air pollution; lung function; systematic review.

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- [65 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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J Pharm Pract

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. 2023 Apr;36(2):370-382.

doi: 10.1177/08971900211038251. Epub 2021 Aug 12.

# Effectiveness and Safety Studies of Omalizumab in Children and Adolescents With Moderate-To-Severe Asthma

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Affiliations expand

- PMID: 34384308
- DOI: [10.1177/08971900211038251](https://doi.org/10.1177/08971900211038251)

## Abstract

**Background:** Omalizumab is currently approved for the treatment of moderate-to-severe allergic asthma in patients 6 years and older. **Objective:** To assess the effectiveness and safety of subcutaneous omalizumab as an add-on therapy option for moderate-severe allergic asthma in patients aged 6-20 years old. **Methods:** The studies published from July,

1970 to May, 2021 were searched from the electronic databases which followed keywords: ("anti-IgE" OR "anti-immunoglobulin E" OR "anti-IgE antibody" OR "omalizumab" OR "rhuMAb-E25" OR "Xolair") AND "asthma" AND ("child" OR "children" OR "adolescents" OR "youth" OR "teenager" OR "kids" OR "pediatric"). Thirteen studies were pooled to determine the effectiveness and safety of omalizumab. Efficacy endpoints were evaluated using a fixed-effects model or a random-effects model depending on heterogeneity. Safety endpoints were evaluated by odds ratio. **Results:** Thirteen studies were included. In this meta-analysis, our results showed that fractional exhaled nitric oxide and asthma control test scores were significantly improved with omalizumab treatment. Serum immunoglobulin E was also decreased in children with moderate-to-severe asthma after treatment with omalizumab. The analysis found that there was no significant difference between pre-and post-treatment in forced expiratory volume in one second/ forced vital capacity ratio, forced expiratory flow between 25 and 75% of vital capacity, or FEV1. Overall, more adverse events occurred with omalizumab compared to placebo. However, the degree was mild to moderate. **Conclusion:** This meta-analysis indicates that omalizumab is safe and effective to treat children and adolescents with moderate-to-severe asthma.

**Keywords:** asthma; children and adolescents; effectiveness; omalizumab; pediatrics.

SUPPLEMENTARY INFO

Publication typesexpand

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# RHINITIS

1

Review

Allergy

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. 2023 Apr 1.

doi: 10.1111/all.15731. Online ahead of print.

# Organ-specific allergen challenges in airway allergy: current utilities and future directions

[J L Fauquert](#)<sup>1</sup>, [C Alba-Linero](#)<sup>2,3,4</sup>, [A Gherasim](#)<sup>5</sup>, [A Testera-Montes](#)<sup>3,6</sup>, [G Bentabol-Ramos](#)<sup>3,7</sup>, [R Saenz de Santa Maria-Garcia](#)<sup>3,6</sup>, [M J Torres](#)<sup>3,4,6</sup>, [I Eguluz-Gracia](#)<sup>3,6</sup>, [C Rondon](#)<sup>3,6</sup>

Affiliations expand

- PMID: 37002709
- DOI: [10.1111/all.15731](https://doi.org/10.1111/all.15731)

## Abstract

Atopy has been long used as the screening method for airway allergy. Nevertheless, aeroallergens can trigger respiratory symptoms not only in atopic patients (atopic respiratory allergy, ARA), but also in non-atopic subjects (local respiratory allergy, LRA). Moreover, ARA and LRA can coexist in the same patient, and this clinical scenario has been called dual respiratory allergy (DRA). When the clinical history cannot determine the relevance of sensitizations in ARA patients, nasal, conjunctival or bronchial allergen challenges (NAC, CAC and BAC, respectively) should be conducted. Moreover, these tests are required to identify patients with LRA and DRA. The clarification of the allergic triggers of airway diseases has a profound impact on the management strategies the patients can be offered. Importantly, allergen immunotherapy (AIT) remains as the only disease-modifying intervention for ARA. Recent data indicate that AIT might have a similar effect on LRA patients. Nevertheless, AIT success relies largely on the correct phenotyping of allergic individuals, and NAC, CAC and BAC are very helpful tools in this regard. In this review, we will summarize the main indications and methodology of CAC, NAC and BAC. Importantly, the clinical implementation of these tests might translate into precision medicine approaches and better health outcomes for patients with airway allergy.

**Keywords:** allergic asthma; allergic rhinitis; bronchial allergen challenge; conjunctival allergen challenge; nasal allergen challenge.

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. 2023 Mar 31;13(1):5273.

doi: 10.1038/s41598-023-32507-6.

# Experimental observation of the effect of immunotherapy on CD4+ T cells and Th1/Th2 cytokines in mice with allergic rhinitis

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Affiliations [expand](#)

- PMID: 37002325
- DOI: [10.1038/s41598-023-32507-6](https://doi.org/10.1038/s41598-023-32507-6)

## Abstract

The present study aims to investigate the effect of immunotherapy in a mouse model of allergic rhinitis (AR) and to explore the possible molecular mechanisms of action. An animal model of AR was established by sensitization and challenge of BALB/c mice with house dust mite (HDM) extract. The mice were injected subcutaneously with HDM for immunotherapy. AR nasal symptoms were evaluated according to the frequencies of nose rubbing and sneezing and the degree of rhinorrhea. The nasal mucosa and lung tissue architecture and inflammatory status by histological analysis; the infiltration of eosinophils in nasal lavage fluid (NALF) of mice was observed by Diff-Quik stain; ELISA-based quantification of serum HDM-specific IgE and TH1/TH2 cytokine concentration; and flow cytometry detected the number of serum CD4+/CD8+ cells to evaluate the mechanism of immunotherapy. It was found that after immunotherapy, the AR symptom score was reduced, the number of eosinophils in NALF was reduced, and the infiltration of inflammatory cells and tissue damage in the nasal mucosa and lung tissue were alleviated. Immunotherapy can increase the number of CD4+ T cells in the peripheral blood, increase

the ratio of CD4+/CD8+ cells, increase the expression of Th1 cytokines such as IL-2 and IFN- $\gamma$ , reduce the expression of Th2 cytokines such as IL-4 and IL-5. The results showed that repeated intraperitoneal injection of crude extract of HDM for sensitization, followed by nasal drops can effectively construct a mouse model of AR, and subcutaneous injection of immunotherapy in mice can reduce allergic inflammation in model mice and improve the inflammatory infiltration of the nasal cavity in allergic rhinitis. Immunotherapy can reduce the expression of inflammatory factors in AR, improve Th1/Th2 balance, and may play a role in the treatment of AR by improving the function of immune cells.

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Ann Allergy Asthma Immunol

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. 2023 Mar 27;S1081-1206(23)00204-1.

doi: 10.1016/j.anai.2023.03.022. Online ahead of print.

## [Randomized Double Blind Pilot Study of Universal, Species Abundant, Multi-Allergen Subcutaneous Immunotherapy for Moderate–Severe Allergic Rhinitis](#)

[Jody Tversky](#)<sup>1</sup>, [Pooja Patel](#)<sup>2</sup>, [Mudiaga Sowho](#)<sup>3</sup>, [Rakesh Natarajan](#)<sup>4</sup>, [Tae Chung](#)<sup>5</sup>, [Andrew Whelton](#)<sup>6</sup>, [Antoine Azar](#)<sup>2</sup>

Affiliations expand

- PMID: 36990203
- DOI: [10.1016/j.anai.2023.03.022](https://doi.org/10.1016/j.anai.2023.03.022)

### Abstract



**Background:** Allergic rhinitis affects approximately 10-20% of people living in industrialized nations leading to significant morbidity and large health care expenditures. Individualized high-dose, single species allergen immunotherapy has been shown to be effective in treating allergic rhinitis but can be associated with significant risks including anaphylaxis. Few studies have examined the safety and efficacy of universal low-dose multi-allergen immunotherapy.

**Objective:** To determine the efficacy and safety of a universal, multi-allergen immunotherapy formula for the treatment of allergic rhinitis.

**Methods:** Patients with moderate-severe perennial and seasonal allergic rhinitis were randomized in a double-blind, placebo-controlled fashion to receive a novel, subcutaneous multi-allergen immunotherapy (MAIT) regimen containing a unique mixture of more than 150 aeroallergens, including several cross-reactive species. All patients received the exact same universal immunotherapy formula regardless of which specific skin tests were positive. Primary outcome measures at 8 and 12 weeks of therapy included validated clinical assessments; TNSS and mini-RQLQ, and the use of rescue medications.

**Results:** Thirty-one subjects (n=31) were randomized to receive multi-allergen immunotherapy (MAIT) versus placebo. By week twelve, MAIT resulted in a -4.6 (-58%) decrease in the combined TNSS and rescue medication score (DCS) compared to -1.5 (-20%) for placebo (P = 0.037). Likewise, MAIT resulted in a mini-RQLQ decrease of -34.9 (-68%) compared to -17 (-42%) for placebo (P = 0.039). Mild adverse events were uncommon and with similar frequency among the groups.

**Conclusion:** A novel and universal, high species abundance, multi-allergen immunotherapy formula was well-tolerated and resulted in significant improvement in symptoms of moderate-severe allergic rhinitis. The results of this pilot study should be considered preliminary, pending further randomized clinical trials.

**Keywords:** Multi-allergen; SCIT; allergic rhinitis; allergy; dust mite; immunotherapy; perennial; rhinoconjunctivitis; universal.

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Int Arch Allergy Immunol

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. 2023 Mar 29;1-9.

doi: 10.1159/000529275. Online ahead of print.

# Disease and Quality of Life Aspects of Cat Allergy in Non-Pet Owners with Allergic Rhinitis

[Nesibe Gül Yüksel Aslier](#)<sup>1,2</sup>, [Özlem Saatçi](#)<sup>2</sup>, [Mustafa Aslier](#)<sup>3,2</sup>

Affiliations expand

- PMID: 36990066

- DOI: [10.1159/000529275](https://doi.org/10.1159/000529275)

## Abstract

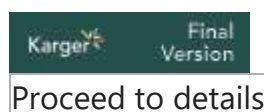
**Introduction:** The severity of cat allergy-related symptoms varies widely. The rising prevalence of cat owning makes it a significant human health problem. The aim of this study was to evaluate disease severity and quality of life (QoL) aspects of cat sensitization and allergy in non-pet owners with allergic rhinitis (AR).

**Methods:** In this study, 231 out of 596 patients with AR were enrolled. The disease severity and QoL measures of the non-pet owner patients were evaluated according to their demographics and allergen sensitizations. The data were re-gathered after cat exposure for cat-sensitized patients (n = 53).

**Results:** The median age of the patients (174 females, 57 males) was 33 (18-70). The overall frequency of cat sensitization was 12.6% (75/596). The frequency of cat allergy in this cohort was 13.9% (32/231). Family history of atopy and multi-allergen sensitization were more common in the cat-sensitized patients. Disease severity and QoL scores were higher in the cat allergy group after cat exposure. Cat allergy was the major independent risk factor for the severity of AR and QoL measures.

**Conclusion:** Due to the fact that indirect exposure to cat dander allergens can occur anywhere, even where cats are not present, cat-sensitized people should be aware of cat allergy. Cat allergy appears to be an independent risk factor for disease severity and QoL effects for non-pet owner patients with AR.

**Keywords:** Allergic rhinitis; Cat allergy; Nose; Pet; Quality of life.



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. 2023 Mar 29;44(1):17-26.

doi: 10.2478/prilozi-2023-0003. Print 2023 Mar 1.

# Comparison of Oxidative Stress Levels in Healthy Children and Children with Allergic Rhinitis

[Ivana Arnaudova Danevska<sup>1</sup>](#), [Tatjana Jakjovska<sup>1</sup>](#), [Dragica Zendelovska<sup>2</sup>](#), [Emilija Atanasovska<sup>2</sup>](#), [Pavlina Dzekova-Vidimliski<sup>3</sup>](#), [Marija Petrushevska<sup>2</sup>](#), [Katerina Boshkovska<sup>1</sup>](#), [Gorica Popova<sup>4</sup>](#), [Elena Gjinovska Tasevska<sup>4</sup>](#), [Trajan Balkanov<sup>2</sup>](#)

Affiliations expand

- PMID: 36987754
- DOI: [10.2478/prilozi-2023-0003](https://doi.org/10.2478/prilozi-2023-0003)

**Free article**

## Abstract

**Background/aim:** Allergic rhinitis (AR) is characterized by chronic inflammation of the nasal mucosa. Under the influence of exogenous factors - allergens, reactive oxygen species (ROS) are released during cellular metabolism. They induce a series of pathological changes in the mucosa. Oxidative stress is a result of an imbalance between the production of ROS and the ability to neutralize them. The aim of this study is to compare the levels of oxidative stress between healthy children and children with allergic rhinitis. **Material and**

**methods:** A total number of 60 children were included (30 healthy children and 30 children with AR). The oxidative stress index was determined by using the FRAS 5 (Free Radical Analytical System) Bravo system. Demographic characteristics, medical history, children's living conditions and eating habits were obtained from the questionnaire. Anthropometric measurements and the absolute number of eosinophils in the peripheral smear were performed on each child. **Results:** This study showed high oxidative stress index and a significantly higher value of the absolute number of eosinophils in the peripheral smear in children with AR in comparison to healthy children ( $p < 0.05$ ). The group of children with AR had more atopic characteristics and was more exposed to passive smoking than healthy children. **Conclusion:** Compared to healthy children, children with AR have a high index of oxidative stress, despite of the very high mean value of the concentration of water-soluble antioxidants in serum (PAT test) in the group of children with AR.

**Keywords:** OSI; PAT; allergic rhinitis; children; d-ROMs; oxidative stress.

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Allergy

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. 2023 Mar 28.

doi: 10.1111/all.15729. Online ahead of print.

# Immunomodulatory properties of mesenchymal stem cells: A potential therapeutic strategy for allergic rhinitis

[Ming Wang](#)<sup>1,2</sup>, [Ning Zhao](#)<sup>3</sup>, [Chengshuo Wang](#)<sup>1,2</sup>, [Zi-Bing Jin](#)<sup>3</sup>, [Luo Zhang](#)<sup>1,2,4</sup>

Affiliations expand

- PMID: 36975714

- DOI: [10.1111/all.15729](https://doi.org/10.1111/all.15729)

## Abstract

Allergic rhinitis is a highly prevalent chronic inflammatory disorder of the nasal mucosa that poses a significant burden on patients' health and quality of life. Current therapies for allergic rhinitis are unable to reinstate immune homeostasis or are restricted by specific allergens. Potential therapeutic strategies for allergic rhinitis are urgently needed. Mesenchymal stem cells (MSCs) are immune-privileged, have strong immunomodulatory effects, and can be easily isolated from various sources. Thus, MSC-based therapies demonstrate potential for treating inflammatory diseases. Recently, numerous studies have investigated the therapeutic effects of MSCs in animal models of allergic rhinitis. Here, we review the immunomodulatory effects and mechanisms of MSCs on allergic airway inflammation, especially allergic rhinitis, highlight the recent research regarding MSCs in the modulation of immune cells, and discuss the clinical potential of MSC-based therapy for allergic rhinitis.

**Keywords:** allergic rhinitis; extracellular vesicles; immunomodulation; mesenchymal stem cells.

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J Asthma

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. 2023 Mar 27;1-15.

doi: 10.1080/02770903.2023.2196567. Online ahead of print.

# Comparison of the clinical outcomes of patients with NSAID-exacerbated respiratory disease receiving aspirin or biologicals

[Gülseren Tuncay](#)<sup>1</sup>, [Ebru Damadoglu](#)<sup>1</sup>, [Melek Cihanbeylerden](#)<sup>1</sup>, [Ozge Can Bostan](#)<sup>1</sup>, [Hazal Kayıkcı](#)<sup>1</sup>, [Serdar Özer](#)<sup>2</sup>, [Gül Karakaya](#)<sup>1</sup>, [Ali Fuat Kalyoncu](#)<sup>1</sup>

Affiliations expand

- PMID: 36971076
- DOI: [10.1080/02770903.2023.2196567](https://doi.org/10.1080/02770903.2023.2196567)

## Abstract

**Objective:** NSAID-exacerbated respiratory disease (NERD) is characterized by exacerbation of respiratory symptoms after NSAID intake. While research for specific treatment options continues in patients who cannot tolerate or are unresponsive to aspirin treatment after aspirin desensitization (ATAD), biologicals have emerged as a new therapeutic option in NERD patients. The aim of this study was to compare the quality of life, and the sinonasal and respiratory outcomes of NERD patients treated with ATAD or biologicals.

**Methods:** Patients who have been followed up at a tertiary care allergy center and who have been receiving at least one of ATAD, mepolizumab or omalizumab for at least six months were included. Evaluations were made using sinonasal outcome test (SNOT-22), asthma control test (ACT), short form-36 (SF-36), blood eosinophil counts, need for

recurrent functional endoscopic sinus surgeries (FESS), and asthma or rhinitis exacerbations requiring oral corticosteroids (OCS).

**Results:** A total of 59 patients comprised of 35 (59%) females and 24 (41%) males with a mean age of 46.1 (min-max, 20-70) years were included. The baseline blood eosinophil count was higher, and a significant decrease in blood eosinophil counts was observed in the mepolizumab group compared to ATAD group ( $p = 0.001$ ,  $p < 0.001$ , respectively). At follow-up, the rate of recurrent FESS was lower in the group that received mepolizumab ( $p = 0.02$ ).

**Conclusions:** In NERD patients, mepolizumab significantly decreased blood eosinophil counts and recurrent FESS. There was no significant difference between the patients receiving ATAD or mepolizumab regarding other clinical parameters.

**Keywords:** NERD; NSAID intolerance; aspirin desensitization; mepolizumab; nasal polyp; omalizumab; severe asthma.

FULL TEXT LINKS



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Int J Pediatr Otorhinolaryngol

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. 2023 Apr;167:111511.

doi: 10.1016/j.ijporl.2023.111511. Epub 2023 Mar 13.

## [Are rhinitis and Eustachian tube dysfunction associated in United States adolescents?](#)

[Dara R Adams](#)<sup>1</sup>, [Nicholas R Rowan](#)<sup>2</sup>, [Sandra Y Lin](#)<sup>3</sup>, [Jayant M Pinto](#)<sup>4</sup>, [Christopher R Roxbury](#)<sup>5</sup>

Affiliations expand

- PMID: 36933343

- DOI: [10.1016/j.ijporl.2023.111511](https://doi.org/10.1016/j.ijporl.2023.111511)

## Abstract

**Objectives:** Despite longstanding clinical gestalt of a relationship between rhinitis and Eustachian tube dysfunction (ETD), population-level evidence supporting this connection is lacking, particularly among adolescents. We aimed to investigate the association between rhinitis and ETD in a nationally-representative sample of United States adolescents.

**Methods:** We performed cross-sectional analyses of 2005-2006 National Health and Nutrition Examination Survey data (n = 1955, ages 12-19). Rhinitis (self-reported hay fever and/or nasal symptoms in the past 12 months) was stratified as allergic (AR) or nonallergic rhinitis (NAR) based on serum IgE aeroallergen positivity. History of ear disease and procedures was recorded. Tympanometry was classified by type (A, B, C). Multivariable logistic regression was used to test the association of rhinitis and ETD.

**Results:** Among US adolescents, 29.4% reported rhinitis (NAR 38.9%, AR 61.1%), and 14.0% had abnormal tympanometry. Adolescents with rhinitis were more likely to report a history of  $\geq 3$  ear infections (NAR: OR 2.40, 95% CI: 1.72-3.34,  $p < 0.001$ ; AR: OR 1.89, 95% CI: 1.21-2.95,  $p = 0.008$ ) and tympanostomy tube placement (NAR: OR 3.53, 95% CI: 2.07-6.03,  $p < 0.001$ ; AR: OR 1.91, 95% CI: 1.24-2.94,  $p = 0.006$ ), compared to those without rhinitis. There was no association between rhinitis and abnormal tympanometry (NAR:  $p = 0.357$ ; AR:  $p = 0.625$ ).

**Conclusion:** NAR and AR are both associated with history of frequent ear infections and tympanostomy tube placement in US adolescents, supporting an association with ETD. This association is strongest for NAR, suggesting that specific inflammatory mechanisms may be involved in this condition and potentially explaining why traditional therapies for AR are largely ineffective for ETD.

**Keywords:** Allergic rhinitis; Epidemiology; Eustachian tube; Pediatric allergic rhinitis; Pediatric myringotomy tubes; Pediatric sinus.

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## Conflict of interest statement

Declaration of competing interest None.

SUPPLEMENTARY INFO

MeSH termsexpand

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Arch Argent Pediatr

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. 2023 Apr 1;121(2):e202202894.

doi: 10.5546/aap.2022-02894.

# [Allergic rhinitis in pediatrics: recommendations for diagnosis and treatment]

[Article in Spanish]

[Claudio A Agüero](#)<sup>1</sup>, [María P Sarraquigne](#)<sup>1</sup>, [Claudio A S Parisi](#)<sup>1</sup>, [Andrea I Mariño](#)<sup>1</sup>, [Karina López](#)<sup>1</sup>, [Betina Menéndez Porfirio](#)<sup>1</sup>, [Laura Sasia](#)<sup>1</sup>, [Alejandro Lozano](#)<sup>1</sup>, [María Del Pilar Bovina Martijena](#)<sup>1</sup>, [María E Gervasoni](#)<sup>1</sup>, [Martín Bózzola](#)<sup>1</sup>, [Mauricio Colella](#)<sup>1</sup>, [Ricardo Saranz](#)<sup>1</sup>, [Julio Orellana](#)<sup>1</sup>, [Jorge F Máspero](#)<sup>1</sup>, [Viviana Seisdedos](#)<sup>1</sup>, [Ilse Behrends](#)<sup>1</sup>, [Adolfo Blanco](#)<sup>1</sup>, [Patricia Dayán](#)<sup>1</sup>, [Mónica Matta Ruffolo](#)<sup>1</sup>, [Irene Aráoz](#)<sup>1</sup>, [Cristina Casaniti](#)<sup>1</sup>, [Jorge García](#)<sup>1</sup>, [Víctor Skrie](#)<sup>1</sup>, [Marcela García](#)<sup>1</sup>, [Juan M Suárez García](#)<sup>1</sup>, [Fabio Orellano](#)<sup>1</sup>, [Natalia Luconi](#)<sup>1</sup>, [Gloria Bandin](#)<sup>1</sup>

Affiliations expand

- PMID: 36924507
- DOI: [10.5546/aap.2022-02894](https://doi.org/10.5546/aap.2022-02894)

**Free article**

## Abstract

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

Allergic rhinitis (AR) is one of the most common chronic diseases in children. However, it remains underdiagnosed and undertreated. Its prevalence has increased in recent years

and varies from 2 to 25 %. Symptoms include sneezing, itching, runny nose, and nasal congestion. A correct diagnosis and treatment of AR and its comorbidities such as rhinosinusitis with or without nasal polyposis, conjunctivitis, otitis media, bronchial asthma and respiratory tract infections, are important to reduce the negative impact on the quality of life of the patient and their relatives, and in medical costs. Specific allergen immunotherapy, in correctly selected patients, prevents new sensitizations and reduces bronchial hyperreactivity associated with AR. Taking into account all these reasons, the National Allergy Committee of the Sociedad Argentina de Pediatría proposes current evidence based recommendations.

**Keywords:** allergic rhinitis; comorbidity; inflammation; pediatrics; sinusitis.

Sociedad Argentina de Pediatría.

SUPPLEMENTARY INFO

Publication types, MeSH terms expand

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Eur Respir Rev

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. 2023 Mar 8;32(167):220202.

doi: 10.1183/16000617.0202-2022. Print 2023 Mar 31.

## [Strength of association between comorbidities and asthma: a meta-analysis](#)

[Paola Rogliani](#)<sup>1</sup>, [Rossella Laitano](#)<sup>2</sup>, [Josuel Ora](#)<sup>2</sup>, [Richard Beasley](#)<sup>3</sup>, [Luigino Calzetta](#)<sup>4</sup>

Affiliations expand

- PMID: 36889783
- PMCID: [PMC10032614](#)
- DOI: [10.1183/16000617.0202-2022](#)

**Free PMC article**

## Abstract

**Background:** The strength of association between comorbidities and asthma has never been ranked in relation to the prevalence of the comorbidity in the nonasthma population. We investigated the strength of association between comorbidities and asthma.

**Methods:** A comprehensive literature search was performed for observational studies reporting data on comorbidities in asthma and nonasthma populations. A pairwise meta-analysis was performed and the strength of association calculated by anchoring odds ratios and 95% confidence intervals with the rate of comorbidities in nonasthma populations *via* Cohen's *d* method. Cohen's *d*=0.2, 0.5 and 0.8 were cut-off values for small, medium and large effect sizes, respectively; very large effect size resulted for Cohen's *d* >0.8. The review was registered in the PROSPERO database; identifier number CRD42022295657.

**Results:** Data from 5 493 776 subjects were analysed. Allergic rhinitis (OR 4.24, 95% CI 3.82-4.71), allergic conjunctivitis (OR 2.63, 95% CI 2.22-3.11), bronchiectasis (OR 4.89, 95% CI 4.48-5.34), hypertensive cardiomyopathy (OR 4.24, 95% CI 2.06-8.90) and nasal congestion (OR 3.30, 95% CI 2.96-3.67) were strongly associated with asthma (Cohen's *d* >0.5 and ≤0.8); COPD (OR 6.23, 95% CI 4.43-8.77) and other chronic respiratory diseases (OR 12.85, 95% CI 10.14-16.29) were very strongly associated with asthma (Cohen's *d* >0.8). Stronger associations were detected between comorbidities and severe asthma. No bias resulted according to funnel plots and Egger's test.

**Conclusion:** This meta-analysis supports the relevance of individualised strategies for disease management that look beyond asthma. A multidimensional approach should be used to assess whether poor symptom control is related to uncontrolled asthma or to uncontrolled underlying comorbidities.

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## Conflict of interest statement

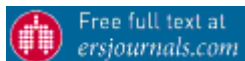
Conflict of interest: P. Rogliani participated as a lecturer and advisor in scientific meetings and courses under the sponsorship of Almirall, AstraZeneca, Biofutura, Boehringer Ingelheim, Chiesi Farmaceutici, GlaxoSmithKline, Menarini Group, Mundipharma, and Novartis, and her department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici Novartis, and Zambon, outside the submitted work. Conflict of interest: R. Laitano has nothing to disclose. Conflict of interest: J. Ora has nothing to disclose. Conflict of interest: R. Beasley reports grants and personal fees from AstraZeneca, grants from GlaxoSmithKline and Genentech, personal fees from Avillion and Theravance, outside the submitted work. Conflict of interest: L. Calzetta has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis; received nonfinancial support from AstraZeneca; a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; is or has been a consultant to ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; and his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon, outside the submitted work.

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# International consensus statement on allergy and rhinology: Allergic rhinitis – 2023

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## Abstract

**Background:** In the 5 years that have passed since the publication of the 2018 International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis (ICAR-Allergic Rhinitis 2018), the literature has expanded substantially. The ICAR-Allergic Rhinitis 2023 update presents 144 individual topics on allergic rhinitis (AR), expanded by over 40 topics from the 2018 document. Originally presented topics from 2018 have also been reviewed and updated. The executive summary highlights key evidence-based findings and recommendation from the full document.

**Methods:** ICAR-Allergic Rhinitis 2023 employed established evidence-based review with recommendation (EBRR) methodology to individually evaluate each topic. Stepwise iterative peer review and consensus was performed for each topic. The final document was then collated and includes the results of this work.

**Results:** ICAR-Allergic Rhinitis 2023 includes 10 major content areas and 144 individual topics related to AR. For a substantial proportion of topics included, an aggregate grade of evidence is presented, which is determined by collating the levels of evidence for each available study identified in the literature. For topics in which a diagnostic or therapeutic intervention is considered, a recommendation summary is presented, which considers the aggregate grade of evidence, benefit, harm, and cost.

**Conclusion:** The ICAR-Allergic Rhinitis 2023 update provides a comprehensive evaluation of AR and the currently available evidence. It is this evidence that contributes to our current knowledge base and recommendations for patient evaluation and treatment.

**Keywords:** IgE; allergen extract; allergen immunotherapy; allergic rhinitis; allergy; antihistamine; asthma; atopic dermatitis; avoidance; biologic; cockroach; conjunctivitis; consensus; corticosteroid; cough; cromolyn; decongestant; environment; eosinophilic esophagitis; epicutaneous; epidemiology; evidence-based medicine; food allergy; house dust mite; immunoglobulin E; immunotherapy; inhalant allergy; leukotriene; microbiome; occupational rhinitis; omalizumab; pediatric; perennial; pet dander; pollen; probiotic; rhinitis; rhinosinusitis; saline; seasonal; sensitization; sinusitis; socioeconomic; specific IgE; subcutaneous immunotherapy; sublingual immunotherapy; systematic review; total IgE; transcutaneous immunotherapy; validated survey.

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# Development and validation of an electronic daily control score for asthma (e-DASTHMA): a real-world direct patient data study

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## Abstract

**Background:** Validated questionnaires are used to assess asthma control over the past 1-4 weeks from reporting. However, they do not adequately capture asthma control in patients with fluctuating symptoms. Using the Mobile Airways Sentinel Network for airway diseases (MASK-air) app, we developed and validated an electronic daily asthma control score (e-DASTHMA).

**Methods:** We used MASK-air data (freely available to users in 27 countries) to develop and assess different daily control scores for asthma. Data-driven control scores were developed based on asthma symptoms reported by a visual analogue scale (VAS) and self-reported asthma medication use. We included the daily monitoring data from all MASK-air users aged 16-90 years (or older than 13 years to 90 years in countries with a lower age of digital consent) who had used the app in at least 3 different calendar months and had reported at least 1 day of asthma medication use. For each score, we assessed construct validity, test-retest reliability, responsiveness, and accuracy. We used VASs on dyspnoea and work disturbance, EQ-5D-VAS, Control of Allergic Rhinitis and Asthma Test (CARAT), CARAT asthma, and Work Productivity and Activity Impairment: Allergy Specific (WPAI:AS) questionnaires as comparators. We performed an internal validation using MASK-air data from Jan 1 to Oct 12, 2022, and an external validation using a cohort of patients with physician-diagnosed asthma (the INSPIRERS cohort) who had had their diagnosis and control (Global Initiative for Asthma [GINA] classification) of asthma ascertained by a physician.

**Findings:** We studied 135 635 days of MASK-air data from 1662 users from May 21, 2015, to Dec 31, 2021. The scores were strongly correlated with VAS dyspnoea (Spearman correlation coefficient range 0.68-0.82) and moderately correlated with work comparators and quality-of-life-related comparators (for WPAI:AS work, we observed Spearman correlation coefficients of 0.59-0.68). They also displayed high test-retest reliability (intraclass correlation coefficients range 0.79-0.95) and moderate-to-high responsiveness (correlation coefficient range 0.69-0.79; effect size measures range 0.57-0.99 in the comparison with VAS dyspnoea). The best-performing score displayed a strong correlation with the effect of asthma on work and school activities in the INSPIRERS cohort (Spearman correlation coefficients 0.70; 95% CI 0.61-0.78) and good accuracy for the identification of patients with uncontrolled or partly controlled asthma according to GINA (area under the receiver operating curve 0.73; 95% CI 0.68-0.78).

**Interpretation:** e-DASTHMA is a good tool for the daily assessment of asthma control. This tool can be used as an endpoint in clinical trials as well as in clinical practice to assess fluctuations in asthma control and guide treatment optimisation.

**Funding:** None.

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**Conflict of interest statement**



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## Brain response in allergic rhinitis: Profile and proposal

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Affiliations expand

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# Abstract

In addition to typical nasal symptoms, patients with allergic rhinitis (AR) will further lead to symptoms related to brain function such as hyposmia, anxiety, depression, cognitive impairment, memory loss, etc., which seriously affect the quality of life of patients and bring a heavy burden to the patient's family and society. Some scholars have speculated that there may be potential "nose-brain communication" mechanism in AR that rely on neuro-immunity. This mechanism plays an important role in AR-associated brain response process. However, no study has directly demonstrated which neural circuits will change in the connection between the nose and brain during the onset of AR, and the mechanism which underlines this question is also lack. Focusing on the topic of "nose-brain communication", this paper systematically summarizes the latest research progress between AR and related brain responses and discusses the mechanism of AR-related neurological phenotypes. Hope new diagnostic and therapeutic targets to ameliorate the brain function-related symptoms and improve the quality of life of AR patients will be developed.

**Keywords:** allergic rhinitis; inflammatory mediators; neuro-immune; neurological symptoms; nose-brain communication.

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# Occupational respiratory allergy to reactive dyes

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## Abstract

**Purpose of review:** Reactive dyes have been shown to cause respiratory sensitization in workers with occupational exposure. The present review analyzes the current knowledge of the role of reactive dyes in promoting occupational respiratory allergy. We discuss the current classification of reactive dyes as well as the potential development of occupational respiratory diseases after exposure to these substances.

**Recent findings:** Few descriptions of the role of reactive dyes in the development of occupational allergy have been published in recent years. Several reactive dyes are considered causes of occupational asthma (OA), mainly in workers in textile industries. Positive skin tests and the presence of specific serum IgE antibodies to reactive dyes suggest that respiratory symptoms provoked by reactive dyes may be immunoglobulin E (IgE)-mediated reactions. It was suggested that airborne dye molecules may act as haptens and induce IgE-mediated hypersensitivity reactions.

**Summary:** Reactive dyes are widely used in the textile industry, owing to their ability to produce strong covalent bonds to textile fibers. These substances have been identified as potential respiratory sensitizers causing OA and occupational rhinitis. The clinical presentation and phenotype of patients with OA due to reactive dyes is very similar to those presented by patients with OA to high molecular weight agents. The extensive use of reactive dyes in industry means that it is particularly important to describe their implications for health, which in fact are probably underestimated.

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. 2023 Apr;280(4):1523-1528.

doi: 10.1007/s00405-022-07748-2. Epub 2022 Nov 14.

# Biofilm in sino-nasal infectious diseases: the role nasal cytology in the diagnostic work up and therapeutic implications

[Matteo Gelardi](#)<sup>1</sup>, [Rossana Giancaspro](#)<sup>2</sup>, [Michele Cassano](#)<sup>1</sup>

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- PMID: 36376525
- DOI: [10.1007/s00405-022-07748-2](https://doi.org/10.1007/s00405-022-07748-2)

## Abstract

**Background:** Biofilm formation has been recently recognised as one of the most important etiopathological mechanisms underlying chronic rhinosinusitis (CRS) and its recalcitrance. In this context, nasal cytology (NC) has become an integral part of diagnostic work up of patients suffering from sino-nasal diseases, since it is an easy-to-apply, reproducible and non-invasive diagnostic tool that allows to assess both the nasal inflammatory infiltrate and the presence of biofilms on nasal mucosal surface, further orienting the therapeutic choices in case of infectious diseases for eradicating infections and biofilms. Nevertheless, biofilms are typically resistant to common antibiotic treatments and may trigger or

maintain chronic inflammation. Hence, the importance of correctly detecting the presence of biofilm and identifying new effective treatments.

**Purpose:** The aim of this brief review is to better clarify the role of biofilm in the pathogenesis and recurrence of sino-nasal disorders and to highlight the role of nasal cytology (NC) in the rhino-allergologic diagnostic path and in the evaluation of the effectiveness of new treatments.

**Keywords:** Antibiotic resistance; Biofilm; Infectious rhinopathies; Nasal cytology.

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- [41 references](#)

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. 2023 Apr;72(2):234-244.

doi: 10.1016/j.alit.2022.09.005. Epub 2022 Nov 1.

## [Biologics for allergy: therapeutic potential for ocular allergic diseases and adverse effects on the eye](#)

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- DOI: [10.1016/j.alit.2022.09.005](https://doi.org/10.1016/j.alit.2022.09.005)

## Free article

# Abstract

Biologics applying antibodies against IgE, IL-5, IL-5 receptor  $\alpha$ , IL-4 receptor  $\alpha$ , and IL-13 have dramatically improved recent treatment outcomes in allergic diseases including asthma, rhinitis, and atopic dermatitis. However, these drugs have not been approved for ocular allergic diseases such as allergic conjunctivitis, vernal keratoconjunctivitis, and atopic keratoconjunctivitis. Although the putative mechanisms suggest that these drugs should have beneficial effects in patients with ocular allergies and some studies have reported such beneficial effects, various adverse ocular symptoms have also been observed in clinical trials and off-label use studies. Since ocular allergic diseases have distinct pathogeneses, each biologic drug must be examined regarding specific effects on each ocular allergy. For example, IgE-mediated type 1 hypersensitivity plays a critical role in allergic conjunctivitis. By contrast, T cells and eosinophilic and non-IgE-mediated type 2 inflammation play important roles in vernal keratoconjunctivitis. Allergists must fully understand the effects of each drug on the eye. This review outlines both potential therapeutic and adverse effects of various biologics on allergic diseases of the eye.

**Keywords:** Allergic conjunctivitis; Atopic keratoconjunctivitis; Biologics; Cytokine; Vernal keratoconjunctivitis.

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Randomized Controlled Trial



# Posterior nasal nerve neurectomy for the treatment of chronic rhinosinusitis with nasal polyposis: a randomized controlled trial

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- PMID: 36331590
- DOI: [10.1007/s00405-022-07722-y](https://doi.org/10.1007/s00405-022-07722-y)

## Abstract

**Background:** Managing Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) is always challenging due to the chronicity of the disease and its intractable course. Posterior nasal neurectomy (PNN) can be effective in alleviating symptoms of CRSwNP.

**Materials and methods:** The study was conducted in a tertiary care referral hospital from August 2019 to April 2022. A total of 46 patients of CRSwNP were included (23 patients in the study and 23 in the control group). Patients in the study group underwent endoscopic sinus surgery (ESS) and PNN and patients in the control group with ESS. The symptoms and quality-of-life improvement were assessed at 1, 4, 12, and 24 weeks after the surgery.

**Results:** On intragroup analysis between the preoperative and postoperative scores (SNOT-22, RSDI and LK Score), we found a significant difference for each ( $p < 0.05$ ). When the improvement of outcome scores was compared between the two groups, a significant difference was obtained for SNOT-22 and RSDI scores at 1 week and 4 weeks ( $p < 0.05$ ). There was no significant difference found for the duration of surgery/complications between the two groups ( $p = 1.00$ ).

**Conclusion:** The PNN can be an effective add-on procedure in patients with CRSwNP in alleviating short-term control of the symptoms and the quality of life. A larger sample size with long-term follow-up may be required for a better understanding of the efficacy of the PNN in patients with CRSwNP.

**Keywords:** Chronic Rhinosinusitis with Nasal Polyposis; Outcomes; Posterior nasal neurectomy.

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. 2023 Apr;78(4):968-983.

doi: 10.1111/all.15574. Epub 2022 Nov 20.

## [Consistent trajectories of rhinitis control and treatment in 16,177 weeks: The MASK-air® longitudinal study](#)

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[Casale](#)<sup>31</sup>, [Lorenzo Cecchi](#)<sup>32</sup>, [Tomas Chivato](#)<sup>33</sup>, [Derek K Chu](#)<sup>4</sup>, [Cemal Cingi](#)<sup>34</sup>, [Elísio M Costa](#)<sup>35</sup>, [Alvaro A Cruz](#)<sup>36</sup>, [Stefano Del Giacco](#)<sup>37</sup>, [Philippe Devillier](#)<sup>38</sup>, [Patrik Eklund](#)<sup>39</sup>, [Wytse J Fokkens](#)<sup>40</sup>, [Bilun Gemicioglu](#)<sup>41</sup>, [Tari Haahtela](#)<sup>42</sup>, [Juan Carlos Ivancevich](#)<sup>43</sup>, [Zhanat Ispayeva](#)<sup>44</sup>, [Marek Jutel](#)<sup>45</sup>, [Piotr Kuna](#)<sup>46</sup>, [Igor Kaidashev](#)<sup>47</sup>, [Musa Khaitov](#)<sup>48 49</sup>, [Helga Kraxner](#)<sup>50</sup>, [Daniel Laune](#)<sup>51</sup>, [Brian Lipworth](#)<sup>52</sup>, [Renaud Louis](#)<sup>53</sup>, [Michael Makris](#)<sup>54</sup>, [Riccardo Monti](#)<sup>55</sup>, [Mario Morais-Almeida](#)<sup>56</sup>, [Ralph Mösges](#)<sup>57</sup>, [Marek Niedozytko](#)<sup>58</sup>, [Nikolaos G Papadopoulos](#)<sup>59</sup>, [Vincenzo Patella](#)<sup>60</sup>, [Nhân Pham-Thi](#)<sup>61</sup>, [Frederico S Regateiro](#)<sup>62 63 64</sup>, [Sietze Reitsma](#)<sup>65</sup>, [Philip W Rouadi](#)<sup>66 67</sup>, [Boleslaw Samolinski](#)<sup>68</sup>, [Aziz Sheikh](#)<sup>69</sup>, [Milan Sova](#)<sup>70</sup>, [Ana Todo-Bom](#)<sup>71</sup>, [Luis Taborda-Barata](#)<sup>72 73 74</sup>, [Sanna Toppila-Salmi](#)<sup>42</sup>, [Joaquin Sastre](#)<sup>75</sup>, [Ioanna Tsiligianni](#)<sup>76 77</sup>, [Arunas Valiulis](#)<sup>78</sup>, [Olivier Vandenplas](#)<sup>79</sup>, [Dana Wallace](#)<sup>80</sup>, [Susan Wasserman](#)<sup>81</sup>, [Arzu Yorgancioglu](#)<sup>82</sup>, [Mihaela Zidarn](#)<sup>83 84</sup>, [Torsten Zuberbier](#)<sup>23 24</sup>, [Joao A Fonseca](#)<sup>1 2 3</sup>, [Jean Bousquet](#)<sup>23 24 85</sup>

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- PMID: 36325824
- DOI: [10.1111/all.15574](https://doi.org/10.1111/all.15574)

## Abstract

**Introduction:** Data from mHealth apps can provide valuable information on rhinitis control and treatment patterns. However, in MASK-air®, these data have only been analyzed cross-sectionally, without considering the changes of symptoms over time. We analyzed data from MASK-air® longitudinally, clustering weeks according to reported rhinitis symptoms.

**Methods:** We analyzed MASK-air® data, assessing the weeks for which patients had answered a rhinitis daily questionnaire on all 7 days. We firstly used k-means clustering algorithms for longitudinal data to define clusters of weeks according to the trajectories of reported daily rhinitis symptoms. Clustering was applied separately for weeks when medication was reported or not. We compared obtained clusters on symptoms and rhinitis medication patterns. We then used the latent class mixture model to assess the robustness of results.

**Results:** We analyzed 113,239 days (16,177 complete weeks) from 2590 patients (mean age ± SD = 39.1 ± 13.7 years). The first clustering algorithm identified ten clusters among weeks with medication use: seven with low variability in rhinitis control during the week and three with highly-variable control. Clusters with poorly-controlled rhinitis displayed a higher frequency of rhinitis co-medication, a more frequent change of medication schemes and more pronounced seasonal patterns. Six clusters were identified in weeks when no rhinitis medication was used, displaying similar control patterns. The second clustering method provided similar results. Moreover, patients displayed consistent levels of rhinitis control, reporting several weeks with similar levels of control.

**Conclusions:** We identified 16 patterns of weekly rhinitis control. Co-medication and medication change schemes were common in uncontrolled weeks, reinforcing the hypothesis that patients treat themselves according to their symptoms.

**Keywords:** mobile health; patient-reported outcomes; real-world data; rhinitis.

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. 2023 Apr;37(2):340-346.

doi: 10.1111/fcp.12847. Epub 2022 Nov 25.

## [Survey the effect of drug treatment on modulation of cytokines gene expression in allergic rhinitis](#)

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- PMID: 36314138
- DOI: [10.1111/fcp.12847](https://doi.org/10.1111/fcp.12847)

### Abstract

Allergic rhinitis as common airway disease has high prevalence in all peoples worldwide. In allergic diseases, Th2 cells release type 2 cytokines that support the inflammation in airways. All the drugs used for allergic rhinitis do not cure completely, and the choice of drugs according to cost and efficacy is very important in all groups of atopic patients. Therefore, in this study, the effect of commercial drugs on cytokine gene expression has been studied. Male Balb/c mice were divided into six groups. Allergic rhinitis was induced in five of the six groups with ovalbumin, and four of these five groups were treated with salbutamol, budesonide, theophylline, and montelukast. The fifth group was used as positive control group and the sixth group as negative control group. For the survey, RNA was extracted, cDNA was synthesized, and quantitative real-time PCR was done for 21 genes. The four drugs had different effects on mRNA expression of cytokines (IL-1b, 2, 4, 5, 7, 8, 9, 11, 12, 13, 17, 18, 22, 25, 31, 33, 37, IFN- $\gamma$ , TNF- $\alpha$ , TGF- $\beta$ 1, and eotaxin) in the allergic rhinitis groups. Salbutamol can be used during pregnancy and breastfeeding, but it has some side effects. Budesonide in the inhaled form is generally safe in pregnancy. Theophylline cannot control allergic attack in the long run. Montelukast is not useful in the treatment of acute allergic attacks. Immunomodulatory and anti-inflammatory effects of drugs in control of allergic rhinitis via Th2 cytokines can be new approaches in molecular medicine.

**Keywords:** allergy; asthma; corticosteroid; drugs; leukotriene;  $\beta$ 2 agonists.

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. 2023 Apr;280(4):1775-1784.

doi: 10.1007/s00405-022-07704-0. Epub 2022 Oct 22.

# Nasal eosinophilia as a preliminary discriminative biomarker of non-allergic rhinitis in every day clinical pediatric practice

[Athina Papadopoulou](#)<sup>1,2</sup>, [Stavroula Lambidi](#)<sup>3</sup>, [Theano Lagousi](#)<sup>4</sup>, [Maria Syrrou](#)<sup>5</sup>, [Fani Giannoula](#)<sup>4</sup>, [Efstathia Staikou](#)<sup>5</sup>, [Stavroula Kostaridou](#)<sup>6</sup>, [Despoina-Zoe T Mermiri](#)<sup>4</sup>

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- PMID: 36271956
- DOI: [10.1007/s00405-022-07704-0](https://doi.org/10.1007/s00405-022-07704-0)

## Abstract

**Background:** Non-allergic rhinitis (NAR) in children, named local allergic rhinitis (LAR) and non-allergic rhinitis with eosinophilia syndrome (NARES), are recently termed entities in childhood characterized by symptoms suggestive of allergic rhinitis in the absence of systemic atopy. Nasal eosinophils (nEo) are the principal cells involved in the allergy inflammation and nasal allergen provocation test is the gold standard method for the diagnosis, albeit with several limitations. The aim of this study was to validate the presence of nEo in combination with the therapeutic response to nasal steroids, as a preliminary discriminator of NAR in real life data.

**Methods:** In a prospective cohort study, 128 children (63.3% male, aged  $72 \pm 42$  m) with history of NAR were enrolled and followed up for  $52 \pm 32$  m. Nasal cytology was performed and nasal steroids trial was recommended initially in all and repeatedly in relapsing cases. Response to therapy was clinically evaluated using 10-VAS.

**Results:** Significant nEo was found in 59.3% of the cases and was related to reported dyspnea episodes. 23.4% had no response to therapy, whereas 51.5% were constantly good responders. Response to therapy was related to nEo and a cutoff point of 20% was defined as the most reliable biological marker with 94% sensitivity and 77% specificity.

**Conclusions:** In children with symptoms of NAR, the presence of nEo  $> 20\%$  constantly responding to nasal steroid therapy, is a clear indicator of atopy. In an everyday clinical setting, it emerged as an easy, preliminary, cell biomarker suggestive of further investigation such as NAPT, to discriminate LAR from NARES.

**Keywords:** Biomarker; Children; Nasal eosinophils; Nasal steroids; Non-allergic rhinitis.

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. 2023 Apr;280(4):1741-1755.

doi: 10.1007/s00405-022-07679-y. Epub 2022 Oct 15.

# [Dupilumab \(Dupixent®\) tends to be an effective therapy for uncontrolled severe chronic rhinosinusitis with nasal polyps: real data of a single-centered, retrospective single-arm longitudinal study from a university hospital in Germany](#)

[Florian Jansen](#)<sup>1,2</sup>, [Benjamin Becker](#)<sup>3</sup>, [Jödis K Eden](#)<sup>3</sup>, [Philippe C Breda](#)<sup>3</sup>, [Amra Hot](#)<sup>4</sup>, [Tim Oqueka](#)<sup>3</sup>, [Christian S Betz](#)<sup>3</sup>, [Anna S Hoffmann](#)<sup>3</sup>

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- PMID: 36242612

- PMID: [PMC9988751](#)
- DOI: [10.1007/s00405-022-07679-y](#)

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## Abstract

**Introduction:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory disease, which is usually type 2-mediated in the western hemisphere, associated with severe therapeutic and socioeconomic challenges. The first targeted systemic treatment option for severe uncontrolled CRSwNP is a human monoclonal antibody against the interleukin-4 receptor  $\alpha$  (IL-4R $\alpha$ ) subunit called dupilumab, which was approved for subcutaneous administration in Germany in October 2019. The purpose of this study is to investigate the efficacy of dupilumab in real life in patients treated with dupilumab in label according to license in our department in 2019-2021.

**Materials and methods:** Since October 2019, we have investigated 40 patients (18 men, 22 women) treated with dupilumab in a single-center, retrospective single-arm longitudinal study. The following parameters were collected before treatment (baseline), at 1 month, 4 months, 7 months, 10 months, and 13 months: the Sino-Nasal Outcome Test-22 (SNOT-22), the forced expiratory pressure in 1 s (FEV-1), the olfactometry using Sniffin' Sticks-12 identification test (SSIT), a visual analog scale of the total complaints, the Nasal Polyp Score (NPS), histologic findings as well as total serum IgE, eosinophilic cationic protein in serum and blood eosinophils.

**Results:** The average age was 52.7 years ( $\pm$  15.3). The follow-up period was 13 months. The SNOT-22 average was 60 points ( $\pm$  22.2) at the first visit, 28.2 points ( $\pm$  17.1) after 4 months and 20.8 points ( $\pm$  17.7) after 13 months. The NPS was 4.3 points ( $\pm$  1.5), after 4 months 2.1 points ( $\pm$  1.3) and after 13 months 1.4 points ( $\pm$  1.1). Olfactometry showed 3.2 points ( $\pm$  3.7) at the baseline, 7.0 points ( $\pm$  4.0) after 4 months and 7.8 points ( $\pm$  3.5) after 13 months. The other parameters also improved. Most parameters showed linear dependence in the slopes under therapy ( $p < 0.001$ ). Adverse side effects were mostly only mild, and no rescue therapy was needed.

**Conclusion:** There is a clear improvement in the medical condition and symptoms in all categories mentioned under therapy with dupilumab, as well as a reduction in the need for systemic glucocorticoids and revision surgery as rescue treatment. Our results show that dupilumab tends to be an effective therapy alternative for severe CRSwNP.



**Keywords:** Biologic; CRSwNP; Dupilumab; Monoclonal antibody; Nasal polyposis; Type 2 inflammation.

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## Conflict of interest statement

ASH reports service on advisory board and receiving honoraria for lectures and travel expenses from Sanofi, Novartis and GSK. There are no conflicts of interest for any of the other authors.

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. 2023 Apr;78(4):1104-1112.

doi: 10.1111/all.15536. Epub 2022 Oct 11.

# Maternal heated tobacco product use during pregnancy and allergy in offspring

[Masayoshi Zaitzu](#)<sup>1</sup>, [Kenta Kono](#)<sup>2</sup>, [Yoshihiko Hosokawa](#)<sup>3</sup>, [Manabu Miyamoto](#)<sup>4</sup>, [Keiko Nanishi](#)<sup>5</sup>, [Sumiyo Okawa](#)<sup>6</sup>, [Shinji Niki](#)<sup>1</sup>, [Kyo Takahashi](#)<sup>2</sup>, [Shigemi Yoshihara](#)<sup>4</sup>, [Gen Kobashi](#)<sup>2</sup>, [Takahiro Tabuchi](#)<sup>7</sup>

Affiliations [expand](#)

- PMID: 36176042

- DOI: [10.1111/all.15536](https://doi.org/10.1111/all.15536)

## Abstract

**Background:** Little is known about the association between maternal use of heated tobacco products (HTPs) during pregnancy and the onset of allergy among offspring. This study aimed to determine whether maternal HTP smoking is associated with allergy in their offspring and to evaluate the potential dose-response association.

**Methods:** In this web-based, cross-sectional survey conducted in July and August 2021 in Japan, we investigated 5688 pairs of postpartum women and infants (<3 years). Clinical diagnoses of infant asthma, rhinitis, conjunctivitis, or atopic dermatitis were reported. Using multilevel Poisson regression, we estimated the prevalence ratios (PRs) and 95% confidence intervals (CIs) of allergy in infants with HTP smoking categories cross-classified by pregnancy periods, and adjusted for potential covariates including maternal cigarette smoking and partner's smoking status. Non-smokers served as the reference group.

**Results:** In total, 2.4% women smoked HTPs during pregnancy. Allergy occurred in 7.8% of the infants. The prevalence of allergy increased among the offspring of current HTP smokers during pregnancy at 15.2% (PR = 1.98, 95% CI 1.28-3.05); this association was the most pronounced during the first trimester but attenuated before pregnancy and postpartum. Dose-response associations were observed, for example a one-unit increase in daily maternal HTP use during pregnancy was associated with a 5% increase in allergy onset. Sub-group analyses excluding cigarette smokers during pregnancy and sensitivity analyses using the International Study of Asthma and Allergies in Childhood questionnaire showed a similar pattern.

**Conclusions:** Maternal HTP smoking during pregnancy is associated with allergy in the offspring.

**Keywords:** heated tobacco products; infant allergy; maternal exposure; pregnancy; smoking.

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. 2023 Apr;168(4):862-867.

doi: 10.1177/01945998221120188. Epub 2023 Jan 29.

# Patient Perspectives on Acute Exacerbations of Chronic Rhinosinusitis: A Qualitative Study

[Victoria Walker<sup>1</sup>](#), [Michal Trope<sup>1</sup>](#), [Antar A Tichavakunda<sup>2</sup>](#), [Marlene M Speth<sup>3</sup>](#), [Ahmad R Sedaghat<sup>1</sup>](#), [Katie M Phillips<sup>1</sup>](#)

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- PMID: 36040819
- DOI: [10.1177/01945998221120188](https://doi.org/10.1177/01945998221120188)

## Abstract

**Objective:** Acute exacerbations of chronic rhinosinusitis (AECRS) are currently defined as a transient worsening of symptoms that return to baseline. This definition is narrow and can only be made retrospectively. The literature has studied this phenomenon from the physician perspective, yet a key stakeholder's-the patient's perspective is not well elucidated in the literature. To understand AECRS from the patient's perspective, we performed this study to further clarify this phenomenon.

**Study design:** Basic qualitative study via patient interviews using constant comparative methodology was conducted.

**Setting:** Tertiary care academic center.

**Methods:** Two of the authors served as coders, and via group discussion, a common codebook was created and used to identify recurrent themes. The themes were analyzed for meaning and conclusions were summarized.

**Results:** Ten interviews were conducted with chronic rhinosinusitis (CRS) patients. Recurring themes included the following: (1) patients identify with the term flare or sinus infection more than exacerbation; (2) consistent with the current definition, patients identify AECRS by worsening sinonasal symptoms but also relate secondary symptoms, including poor sleep, fatigue, exacerbation of lower respiratory tract symptoms, and malaise to AECRS; and (3) patients are greatly affected by AECRS via decreased quality of life (QOL), worsening of general health, and decreasing productivity.

**Conclusion:** Beyond worsening of sinonasal symptoms, the concept of AECRS reflects a more complex construct to patients with associated extranasal symptoms and systemic manifestations. In addition, AECRS have a large impact on patients, and therefore, understanding this component of CRS is pivotal in improving disease control and QOL in this patient population.

**Keywords:** acute exacerbations; asthma; chronic rhinosinusitis; patient perspective; productivity; qualitative study; quality of life; sinonasal symptoms; sinus infections.

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. 2023 Apr;168(4):628-634.

# Association of Sinonasal Computed Tomography Scores to Patient-Reported Outcome Measures: A Systematic Review and Meta-analysis

[Tiffany Chen](#)<sup>1</sup>, [Shreya Chidarala](#)<sup>1</sup>, [Gabrielle Young](#)<sup>1</sup>, [Seth S Jeong](#)<sup>1</sup>, [Shaun A Nguyen](#)<sup>1</sup>, [Thomas S Edwards](#)<sup>1</sup>, [Rodney J Schlosser](#)<sup>1</sup>

Affiliations expand

- PMID: 35917187
- DOI: [10.1177/01945998221114078](https://doi.org/10.1177/01945998221114078)

## Abstract

**Objective:** To perform a systematic review of proposed sinus computed tomography (CT) scoring systems and determine their association with patient-reported outcome measures (PROMs).

**Data sources:** PubMed, CINAHL, Scopus, and Cochrane Library.

**Review methods:** A systematic search was conducted following the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses) for studies describing CT scores and PROMs in patients with chronic rhinosinusitis.

**Results:** A total of 144 studies were included. Out of 20,741 patients, 53.6% were male and 55.5% had nasal polyposis. A meta-analysis of correlations revealed a moderate correlation between Lund-McKay (LM) and the 22-item Sinonasal Outcome Test (SNOT-22;  $r = 0.434$ ,  $P < .001$ ) and a weaker correlation between LM and the 20-item Sinonasal Outcome Test (SNOT-20;  $r = 0.257$ ,  $P = .039$ ). Meta-regression also revealed a weak association between LM and SNOT-20 ( $n = 25$  studies) but no significant associations between Zinreich score and SNOT-22 or LM scores and PROMs, including SNOT-22 ( $n = 94$  studies), Rhinosinusitis Disability Index ( $n = 25$ ), nasal obstruction visual analog scale ( $n = 15$ ), Chronic Sinusitis Survey ( $n = 12$ ), Total Nasal Symptom Score ( $n = 4$ ), Total Symptom Score ( $n = 3$ ), and 12-Item Short Form Health Survey ( $n = 3$ ).

**Conclusion:** There is essentially little association between radiologic grade and PROMs. CT grading systems with improved clinical utility are needed.

**Keywords:** Lund-Mackay; SNOT-22; Total Nasal Symptom Score; chronic rhinosinusitis; computed tomography; nasal congestion; visual analog scale.

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- [45 references](#)

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Laryngoscope

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. 2023 Apr;133(4):722-731.

doi: 10.1002/lary.30306. Epub 2022 Jul 15.

# Intranasal Anticholinergics for Treatment of Chronic Rhinitis: Systematic Review and Meta-Analysis

[Jonathan C Pang](#)<sup>1</sup>, [Milind Vasudev](#)<sup>1</sup>, [Amy T Du](#)<sup>1</sup>, [Madeline M Nottoli](#)<sup>1</sup>, [Katherine Dang](#)<sup>1</sup>, [Edward C Kuan](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 35838014

- DOI: [10.1002/lary.30306](https://doi.org/10.1002/lary.30306)

# Abstract

**Objective:** Topical intranasal anticholinergics are commonly prescribed for the relief of chronic rhinitis and associated symptoms, warranting thorough assessment of the supporting evidence. The present study aimed to evaluate the safety and efficacy of anticholinergic nasal sprays in the management of allergic and non-allergic rhinitis symptom severity and duration.

**Methods:** A search encompassing the Cochrane Library, PubMed/MEDLINE, and Scopus databases was conducted. Primary studies describing rhinorrhea, nasal congestion, and/or postnasal drip outcomes in rhinitis patients treated with an anticholinergic spray were included for review.

**Results:** The search yielded 1,029 unique abstracts, of which 12 studies (n = 2,024) met inclusion criteria for qualitative synthesis and 9 (n = 1,920) for meta-analysis. Median follow-up was 4 weeks and ipratropium bromide was the most extensively trialed anticholinergic. Compared to placebo, anticholinergic treatment was demonstrated to significantly reduce rhinorrhea severity scores (standardized mean difference [95% CI] = -0.77 [-1.20, -0.35]; -0.43 [-0.72, -0.13]) and duration (-0.62 [-0.95, -0.30]; -0.29 [-0.47, -0.10]) in allergic and non-allergic rhinitis patients respectively. Benefit was less consistent for nasal congestion, postnasal drip, and sneezing symptoms. Reported adverse effects included nasal mucosa dryness or irritation, epistaxis, headaches, and pharyngitis, though comparison to placebo found significantly greater risk for epistaxis only (risk ratio [95% CI] = 2.19 [1.22, 3.93]).

**Conclusion:** Albeit treating other symptoms with less benefit, anticholinergic nasal sprays appear to be safe and efficacious in reducing rhinorrhea severity and duration in both rhinitis etiologies. This evidence supports their continued use in the treatment of rhinitis-associated rhinorrhea.

**Level of evidence:** 1 Laryngoscope, 133:722-731, 2023.

**Keywords:** anticholinergic; meta-analysis; rhinitis; rhinorrhea; systematic review.

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- [45 references](#)

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Randomized Controlled Trial

J Laryngol Otol

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. 2023 Apr;137(4):432-437.

doi: 10.1017/S0022215122001219. Epub 2022 May 18.

# Quail egg homogenate with zinc as adjunctive therapy in seasonal allergic rhinitis: a randomised, controlled trial

[C Andaloro](#)<sup>1</sup>, [A M Saibene](#)<sup>2</sup>, [I La Mantia](#)<sup>1</sup>

Affiliations expand

- PMID: 35582999
- DOI: [10.1017/S0022215122001219](https://doi.org/10.1017/S0022215122001219)

**Free article**

## Abstract

**Objective:** Because most available treatments for managing seasonal allergic rhinitis show some side effects without reducing recurrence, natural anti-allergic products could represent an interesting treatment addition. This study aimed to analyse the efficacy and tolerance of quail egg as adjunctive therapy in seasonal allergic rhinitis.

**Method:** In a Consolidated Standards of Reporting Trials compliant framework, patients with seasonal allergic rhinitis were prospectively randomised to receive mometasone nasal spray for four weeks or the same topical corticosteroid therapy plus commercially available oral quail egg and zinc tablets.



**Results:** Forty patients were enrolled. The mometasone + quail egg and zinc tablets group showed a greater reduction in nasal itching, sneezing and total nasal symptom scores than the mometasone nasal spray only group. A higher proportion of participants in the mometasone + quail egg and zinc tablets group had good rhinitis control than in the mometasone nasal spray only group, with no need for rescue medications.

**Conclusion:** Despite the need for a further larger study, quail egg preliminarily appears to be an effective adjunct to topical steroid therapy in seasonal allergic rhinitis.

**Keywords:** Anti-Allergic Agents; Mometasone Furoate; Quail; Seasonal Allergic Rhinitis.

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Ann Otol Rhinol Laryngol

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. 2023 Apr;132(4):460-469.

doi: 10.1177/00034894221093890. Epub 2022 May 12.

## [Nasal Nitric Oxide as a Biomarker in the Diagnosis and Treatment of Sinonasal Inflammatory Diseases: A Review of the Literature](#)

[Jacob J Benedict](#)<sup>1</sup>, [Matthew Lelegren](#)<sup>1</sup>, [Joseph K Han](#)<sup>1</sup>, [Kent Lam](#)<sup>1</sup>

Affiliations expand

- PMID: 35549446

- DOI: [10.1177/00034894221093890](https://doi.org/10.1177/00034894221093890)

## Abstract

**Objective:** To critically review the literature on nasal nitric oxide (nNO) and its current clinical and research applicability in the diagnosis and treatment of different sinonasal inflammatory diseases, including acute bacterial rhinosinusitis (ABRS), allergic rhinitis (AR), and chronic rhinosinusitis (CRS).

**Methods:** A search of the PubMed database was conducted to include articles on nNO and sinonasal diseases from January 2003 to January 2020. All article titles and abstracts were reviewed to assess their relevance to nNO and ABRS, AR, or CRS. After selection of the manuscripts, full-text reviews were performed to synthesize current understandings of nNO and its applications to the various sinonasal inflammatory diseases.

**Results:** A total of 79 relevant studies from an initial 559 articles were identified using our focused search and review criteria. nNO has been consistently shown to be decreased in ABRS and CRS, especially in cases with nasal polyps. While AR is associated with elevations in nNO, nNO levels have also been found to be lower in AR cases with higher symptom severity. The obstruction of the paranasal sinuses is speculated to be an important variable in the relationship between nNO and the sinonasal diseases. Treatment of these diseases appears to affect nNO through the reduction of inflammatory disease burden and also mitigation of sinus obstruction.

**Conclusion:** nNO has been of increasing interest to researchers and clinicians over the last decade. The most compelling data for nNO as a clinical tool involve CRS. nNO can be used as a marker of ostiomeatal complex patency. Variations in measurement techniques and technology continue to impede standardized interpretation and implementation of nNO as a biomarker for sinonasal inflammatory diseases.

**Keywords:** allergic rhinitis; chronic rhinosinusitis; fractionated exhaled nitric oxide; nasal nitric oxide; nasal polyps; nitric oxide.

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. 2023 Apr;133(4):755-763.

doi: 10.1002/lary.30129. Epub 2022 Apr 8.

# Demographic Disparities in the Federal Drug Approval Process for Allergic Rhinitis Medications

[Andi Liebowitz](#)<sup>1</sup>, [Daniel B Spielman](#)<sup>1</sup>, [Rodney J Schlosser](#)<sup>2</sup>, [Michael G Stewart](#)<sup>3</sup>, [David A Gudis](#)<sup>1</sup>

Affiliations expand

- PMID: 35394648

- DOI: [10.1002/lary.30129](https://doi.org/10.1002/lary.30129)

## Abstract

**Objective:** Demographic minorities are underrepresented in clinical trials. For the approval of new drug applications (NDAs), the Food and Drug Administration (FDA) has asserted that clinical trial enrollment should represent the demographics of patients likely to receive the trial drug. The aim of this study is to assess the demographics of clinical trials included in NDAs and biologics license applications (BLAs) approved by the FDA since 1990 for allergic rhinitis (AR), a condition whose demographic prevalence mirrors the US population.

**Methods:** Federal Freedom of Information Act requests were submitted to the US government to obtain documents related to all relevant NDAs and BLAs. The Drugs@FDA database was queried for all clinical trial documentation. Demographic data were extracted from clinical trials used to inform FDA approval for AR pharmacotherapies. Demographics were analyzed relative to national US Census data.

**Results:** Since 1990, 22 drugs have been approved for AR. The racial, ethnic, and sex composition of all included study populations differed significantly ( $p < 0.05$ ) from the demographics of AR and from US Census data. Most NDAs and BLAs included

overrepresentation of White participants and underrepresentation of Black, Asian, Pacific Island, Native American, and Hispanic participants.

**Conclusion:** The patients enrolled in clinical trials used to inform FDA approval for AR pharmacotherapeutics do not represent the demographics of the United States or the demographics of AR. The clinical significance of unrepresentative demography between study and treatment populations has been examined for several medical disorders, but has not been studied for AR.

**Level of evidence:** 4 Laryngoscope, 133:755-763, 2023.

**Keywords:** allergic rhinitis; clinical trial enrollment; health care disparities; socioeconomic disparities.

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Otolaryngol Head Neck Surg

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. 2023 Apr;168(4):643-657.

doi: 10.1177/01945998221087664. Epub 2023 Feb 5.

## [Systemic Steroids for Otolaryngology-Head and Neck Surgery Disorders: An Evidence-Based Primer for Clinicians](#)

[Edward D McCoul](#)<sup>1</sup>, [Uchechukwu C Megwalu](#)<sup>2</sup>, [Stephanie Joe](#)<sup>3</sup>, [Raluca Gray](#)<sup>4</sup>, [Daniel C O'Brien](#)<sup>5</sup>, [Elisabeth H Ference](#)<sup>6</sup>, [Victoria S Lee](#)<sup>3</sup>, [Prayag S Patel](#)<sup>7</sup>, [Marco A Figueroa-Morales](#)<sup>8</sup>, [Jennifer J Shin](#)<sup>9</sup>, [Michael J Brenner](#)<sup>10</sup>

Affiliations expand

- PMID: 35349383
- DOI: [10.1177/01945998221087664](https://doi.org/10.1177/01945998221087664)

## Abstract

**Objective:** To offer pragmatic, evidence-informed guidance on the use of systemic corticosteroids (SCS) for common otolaryngologic disorders.

**Data sources:** PubMed, Cochrane Library, and American Academy of Otolaryngology-Head and Neck Surgery Foundation clinical practice guidelines.

**Review methods:** A comprehensive search of published literature through November 2021 was conducted on the efficacy of SCS, alone or in combination with other treatments, for managing disorders in otolaryngology and the subspecialties. Clinical practice guidelines, systematic reviews, and randomized controlled trials, when available, were preferentially retrieved. Interventions and outcomes of SCS use were compiled to generate summary tables and narrative synthesis of findings.

**Conclusions:** Evidence on the effectiveness of SCS varies widely across otolaryngology disorders. High-level evidence supports SCS use for Bell's palsy, sinonasal polyposis, and lower airway disease. Conversely, evidence is weak or absent for upper respiratory tract infection, eustachian tube dysfunction, benign paroxysmal positional vertigo, adenotonsillar hypertrophy, or nonallergic rhinitis. Evidence is indeterminate for acute laryngitis, acute pharyngitis, acute sinusitis, angioedema, chronic rhinosinusitis without polyps, Ménière's disease, postviral olfactory loss, postoperative nerve paresis/paralysis, facial pain, and sudden sensorineural hearing loss.

**Implications for practice:** Clinicians should bring an evidence-informed lens to SCS prescribing to best counsel patients regarding the risks, anticipated benefits, and limited data on long-term effects. Alternate routes of corticosteroid administration-such as sprays, drops, inhalers, and intralesional injections-may be preferable for many disorders, particularly those that are self-limited or require a prolonged duration of therapy. Prudent use of SCS reduces the risk of medication-related adverse effects. Clinicians who are conversant with high-level evidence can achieve optimal outcomes and stewardship when prescribing SCS.

**Keywords:** Bell palsy; Bell's palsy; Meniere's disease; adenoid; angioedema; anosmia; corticosteroid; dysphonia; edema; eustachian tube dysfunction; facial pain; facial palsy; facial paralysis; facial paresis; hearing loss; hyposmia; laryngitis; laryngotracheal stenosis; nasal polyposis; olfactory dysfunction; optic neuropathy; otitis media; pediatric; peritonsillar abscess; phonotrauma; rhinitis; rhinosinusitis; sinonasal; sinusitis; smell; steroid; stewardship; subglottic stenosis; sudden sensorineural hearing loss; tonsillectomy; upper respiratory tract infection; vertigo; vestibular neuronitis; vocal fold.

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. 2022 Jan 31;38(1):181-186.

doi: 10.1515/reveh-2021-0158. Print 2023 Mar 28.

## [Association between food additives and prevalence of allergic reactions in children: a systematic review](#)

[Parisa Sadighara](#)<sup>1</sup>, [Mehdi Safta](#)<sup>2,3</sup>, [Intissar Limam](#)<sup>2,4</sup>, [Kiandokht Ghanati](#)<sup>5</sup>, [Zahra Nazari](#)<sup>6</sup>, [Marzieh Karami](#)<sup>1</sup>, [Amirhossein Abedini](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 35106984

- DOI: [10.1515/reveh-2021-0158](https://doi.org/10.1515/reveh-2021-0158)

## Abstract

Food additives contain synthetic and natural chemical compounds and are one of the causes of food allergies. In this regard, it is necessary to recognize the food additives that are of special interest for children. In this survey, the relation between food additives and allergic reactions and attention-deficit hyperactivity disorders in children was studied. The research studies with keywords "allergic reactions", "hypersensitivity", "food additives" and "children" were searched in PubMed, Scopus, Science Direct, Web of Science, and SID databases, from 1984 to 2020. Three hundred twenty-seven studies were obtained and only seven articles were finally selected according to exclusion and inclusion criteria. In the final review, seven articles were selected to investigate the relationship between food additives and hypersensitivity reactions. Some clinical factors such as urticaria, eczema, rhinitis and gastrointestinal symptoms and the prevalence of laboratory evidence in atopic children are due to increased exposure to food additives including artificial colors and sweeteners, preservatives, and monosodium glutamate. Clinical signs and laboratory evidence prove a significant association between some food additives and allergenic adverse reactions. It was also found that food additives such as artificial colors and sweeteners, preservatives, and monosodium glutamate are responsible for most cases of hypersensitivity in children, and the prevalence of hypersensitivity to food additives was estimated to be about 1.2% based on data extracted from studies.

**Keywords:** child; color; immune reaction; monosodium glutamate; preservatives; sweetener.

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- [27 references](#)

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Publication types, MeSH terms, Substancesexpand

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# CHRONIC COUGH

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Am J Respir Crit Care Med

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. 2023 Mar 30.

doi: 10.1164/rccm.202211-2128LE. Online ahead of print.

# Efficacy and Safety of Gefapixant for Refractory or Unexplained Chronic Cough Over 52 Weeks

[Surinder S Birring<sup>1</sup>](#), [Peter V Dicpinigaitis<sup>2</sup>](#), [Jaclyn A Smith<sup>3,4</sup>](#), [Alyn H Morice<sup>5</sup>](#), [Lorcan P McGarvey<sup>6</sup>](#), [Ian D Pavord<sup>7</sup>](#), [Allison Martin Nguyen<sup>8</sup>](#), [Jonathan Schelfhout<sup>8</sup>](#), [Qing Li<sup>8</sup>](#), [Beata Iskold<sup>8</sup>](#), [Stuart A Green<sup>9</sup>](#), [George Philip<sup>10</sup>](#), [David R Muccino<sup>8</sup>](#), [Carmen La Rosa<sup>8</sup>](#)

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- PMID: 36996347
- DOI: [10.1164/rccm.202211-2128LE](https://doi.org/10.1164/rccm.202211-2128LE)

*No abstract available*

**Keywords:** cough.

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. 2023 Mar 30;18(3):e0283758.

doi: 10.1371/journal.pone.0283758. eCollection 2023.

# Chronic cough in post-COVID syndrome: Laryngeal



# electromyography findings in vagus nerve neuropathy

[Patricia García-Vicente<sup>1</sup>](#), [Antonio Rodríguez-Valiente<sup>1</sup>](#), [Carmen Górriz Gil<sup>1</sup>](#), [Reyes Márquez Altemir<sup>1</sup>](#), [Francisco Martínez-Pérez<sup>2</sup>](#), [Luis Fernando López-Pajaro<sup>2</sup>](#), [Jose Ramón García-Berrocal<sup>1</sup>](#)  
Affiliations expand

- PMID: 36996121
- PMCID: [PMC10062549](#)
- DOI: [10.1371/journal.pone.0283758](#)

## Abstract

**Background:** Despite being a new entity, there is a large amount of information on the characteristics of SARS-CoV-2 infection and the symptoms of the acute phase; however, there are still many unknowns about the clinical features and pathophysiology of post-COVID syndrome. Refractory chronic cough is one of the most prevalent symptoms and carries both a medical problem and a social stigma. Many recent studies have highlighted the role of SARS-CoV-2 neurotropism, but no studies have demonstrated vagus nerve neuropathy as a cause of persistent chronic cough or other COVID-19 long-term effects.

**Objective:** The main objective was to assess the involvement of the vagus nerve neuropathy as a cause of chronic cough and other post-COVID syndrome symptoms.

**Material and methods:** This was a single-center observational study with prospective clinical data collected from 38 patients with chronic cough and post-COVID-19 syndrome. Clinical characteristics and laryngeal electromyographic findings were analyzed.

**Results:** Clinical data from 38 patients with chronic cough after 12 weeks of the acute phase of COVID-19 infection were analyzed. Of these patients, 81.6% suffered from other post-COVID conditions and, 73.6% reported fluctuating evolution of symptoms. Laryngeal electromyography (LEMG) of the thyroarytenoid (TA) muscles and cricothyroid (CT) muscles was pathological in 76.3% of the patients. Of the patients with abnormal LEMG, chronic denervation was the most frequent finding (82.8%), 10.3% presented acute denervation signs, and 6.9% presented myopathic pattern in LEMG.

**Conclusions:** LEMG studies suggest the existence of postviral vagus nerve neuropathy after SARS-CoV-2 infection that could explain chronic cough in post-COVID syndrome.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

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

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. 2023 Apr;32(4):1043-1051.

doi: 10.1007/s11136-022-03319-4. Epub 2023 Mar 11.

# The effects of greater frequency of two most prevalent bothersome acute respiratory symptoms on health-related quality of life in the 2020 US general population

[John E Ware Jr](#)<sup>1,2</sup>, [Graça Coutinho](#)<sup>3</sup>, [Adam B Smith](#)<sup>4</sup>, [Evi Tselenti](#)<sup>4</sup>, [Anuradha Kulasekaran](#)<sup>5</sup>

Affiliations [expand](#)

- PMID: 36905563
- PMCID: [PMC10007648](#)
- DOI: [10.1007/s11136-022-03319-4](#)

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# Abstract

**Purpose:** Upper respiratory tract infections (URTI) and related symptoms are widespread and a common reason for visiting primary care with cough and sore throat being most prevalent. Despite their impact on daily activities, no studies have explored the impact on health-related quality of life (HRQOL) in representative general populations. We aimed to understand the short-term impact of the two most prevalent URTI symptoms on HRQOL.

**Methods:** Online 2020 surveys including acute ( $\leq 4$  weeks) respiratory symptoms (sore throat and cough) and SF-36® health survey (all with 4-week recall) were analysed using analysis of covariance (ANCOVA) in comparison with adult US population norms. Linear T-score transformation of SF-6D utility (ranging from 0 to 1) enabled direct comparisons with SF-36.

**Results:** In total, 7563 US adults responded (average age: 52 years; range: 18-100 years). Sore throat and cough lasting at least several days were experienced by 14% and 22% participants, respectively. Chronic respiratory conditions were reported by 22% of the sample. A clear and consistent pattern of group HRQOL means declining significantly ( $p < 0.001$ ) for acute cough and sore throat symptom presence and severity. Declines were observed on SF-36 physical (PCS) and mental component (MCS) and health utility (SF-6D) scores controlling for covariates. Those reporting respiratory symptoms 'most days' declined  $\geq 0.5$  standard deviation (minimal important difference [MID]) worse with averages at the 19th and 34th centiles for cough on the PCS and MCS, and 21st to 26th centile for sore throat.

**Conclusion:** Declines in HRQOL with acute cough and sore throat symptoms consistently exceeded MID standards and should not be ignored as self-limiting without intervention. Future studies on early self-care for symptom relief and its implications on HRQOL and health economics would be valuable to understand the benefits on healthcare burden and need for updating treatment guidelines.

**Keywords:** Acute cough; Acute sore throat; Health-related quality of life; Minimally important difference; Respiratory symptoms; SF-36; SF-6D.

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## Conflict of interest statement

GC, ABS, ET, and AK are employees of Reckitt Health. JW has received US federal grants from National Institutes of Health (NIH), National Institute on Aging (NIA), and Agency for Healthcare Research and Quality (AHRQ), unrestricted research grants from foundations and industry and honoraria from academic institutions, and is a principal shareholder of John Ware Research Group, Inc.

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

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Respirology

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. 2023 Apr;28(4):339-349.

doi: 10.1111/resp.14479. Epub 2023 Mar 2.

# Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand

[Anne B Chang](#)<sup>1 2 3</sup>, [Scott C Bell](#)<sup>4 5 6</sup>, [Catherine A Byrnes](#)<sup>7 8</sup>, [Paul Dawkins](#)<sup>9 10</sup>, [Anne E Holland](#)<sup>11 12 13</sup>, [Emma Kennedy](#)<sup>14 15 16</sup>, [Paul T King](#)<sup>17</sup>, [Pamela Laird](#)<sup>18 19 20</sup>, [Sarah Mooney](#)<sup>9 21</sup>, [Lucy Morgan](#)<sup>22</sup>, [Marianne Parsons](#)<sup>23</sup>, [Betty Poot](#)<sup>24 25</sup>, [Maree Toombs](#)<sup>26</sup>, [Paul J Torzillo](#)<sup>27 28</sup>, [Keith Grimwood](#)<sup>29 30</sup>

Affiliations expand

- PMID: 36863703
- DOI: [10.1111/resp.14479](https://doi.org/10.1111/resp.14479)

**Free article**

## Abstract

This position statement, updated from the 2015 guidelines for managing Australian and New Zealand children/adolescents and adults with chronic suppurative lung disease (CSLD) and bronchiectasis, resulted from systematic literature searches by a multi-disciplinary team that included consumers. The main statements are: Diagnose CSLD and bronchiectasis early; this requires awareness of bronchiectasis symptoms and its co-existence with other respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease). Confirm bronchiectasis with a chest computed-tomography scan, using age-appropriate protocols and criteria in children. Undertake a baseline panel of investigations. Assess baseline severity, and health impact, and develop individualized management plans that include a multi-disciplinary approach and coordinated care between healthcare providers. Employ intensive treatment to improve symptom control, reduce exacerbation frequency, preserve lung function, optimize quality-of-life and enhance survival. In

children, treatment also aims to optimize lung growth and, when possible, reverse bronchiectasis. Individualize airway clearance techniques (ACTs) taught by respiratory physiotherapists, encourage regular exercise, optimize nutrition, avoid air pollutants and administer vaccines following national schedules. Treat exacerbations with 14-day antibiotic courses based upon lower airway culture results, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients with severe exacerbations and/or not responding to outpatient therapy are hospitalized for further treatments, including intravenous antibiotics and intensive ACTs. Eradicate *Pseudomonas aeruginosa* when newly detected in lower airway cultures. Individualize therapy for long-term antibiotics, inhaled corticosteroids, bronchodilators and mucoactive agents. Ensure ongoing care with 6-monthly monitoring for complications and co-morbidities. Undertake optimal care of underserved peoples, and despite its challenges, delivering best-practice treatment remains the overriding aim.

**Keywords:** adolescents; adults; bronchiectasis; children; evidence base practice; systematic review.

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. 2023 Apr;64(4):409-412.

doi: 10.1007/s00108-022-01466-x. Epub 2023 Jan 27.

## [\[Gefapixant in the treatment of chronic coughing\]](#)

[Article in German]

[T Kühlein](#)<sup>1</sup>, [C Hasford](#)<sup>2</sup>, [S Nitschmann](#)<sup>3</sup>

Affiliations [expand](#)

- PMID: 36705677

- DOI: [10.1007/s00108-022-01466-x](https://doi.org/10.1007/s00108-022-01466-x)

*No abstract available*

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MeSH terms, Substances [expand](#)

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Eur Respir Rev

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. 2023 Jan 25;32(167):220141.

doi: 10.1183/16000617.0141-2022. Print 2023 Mar 31.

# [Mucolytics for acute exacerbations of chronic obstructive pulmonary disease: a meta-analysis](#)

[Efthymia Papadopoulos](#)<sup>1</sup>, [Jan Hansel](#)<sup>2</sup>, [Zsolt Lazar](#)<sup>3</sup>, [Konstantinos Kostikas](#)<sup>4</sup>, [Stavros Tryfon](#)<sup>1</sup>, [Jørgen Vestbo](#)<sup>5,6</sup>, [Alexander G Mathioudakis](#)<sup>7,6</sup>

[Affiliations expand](#)

- PMID: 36697209
- PMCID: [PMC9879332](#)
- DOI: [10.1183/16000617.0141-2022](https://doi.org/10.1183/16000617.0141-2022)

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## Abstract

This meta-analysis explored the safety and effectiveness of mucolytics as an add-on treatment for chronic obstructive pulmonary disease (COPD) exacerbations. Based on a pre-registered protocol and following Cochrane methods, we systematically searched for relevant randomised or quasi-randomised controlled trials (RCTs). We used the Risk of Bias v2 tool for appraising the studies and performed random-effect meta-analyses when appropriate. We assessed certainty of evidence using GRADE. This meta-analysis included 24 RCTs involving 2192 patients with COPD exacerbations, entailing at least some concerns of methodological bias. We demonstrated with moderate certainty that mucolytics increase the rate of treatment success (relative risk 1.37, 95% CI 1.08-1.73, n=383), while they also exert benefits on overall symptom scores (standardised mean difference 0.86, 95% CI 0.63-1.09, n=316), presence of cough at follow-up (relative risk 1.93, 95% CI 1.15-3.23) and ease of expectoration (relative risk 2.94, 95% CI 1.68-5.12). Furthermore, low or very low certainty evidence suggests mucolytics may also reduce future risk of exacerbations and improve health-related quality of life, but do not impact on breathlessness, length of hospital stay, indication for higher level of care or serious adverse events. Overall, mucolytics could be considered for COPD exacerbation management. These findings should be validated in further, rigorous RCTs.

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## Conflict of interest statement

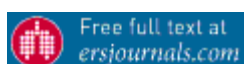
Conflicts of interest: The authors declare no conflict of interest related to this work. E. Papadopoulou, J. Hansel, and Z. Lazar report no conflict of interest. K. Kostikas reports grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir, consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, ELPEN, GSK, Menarini, Novartis and Sanofi Genzyme, honoraria from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GILEAD, GSK, Menarini, MSD, Novartis, Sanofi Genzyme and WebMD. S. Tryfon reports honoraria from Menarini, Boehringer-Ingelheim and ELPEN, support for attending meetings from Chiesi and Menarini, and patents with GSK, AstraZeneca and ELPEN, not related to this work. J. Vestbo reports consulting fees and/or honoraria from ALK-Abello, AstraZeneca, Boehringer Ingelheim, GSK and TEVA, not related to this work. A.G. Mathioudakis reports a research grant from Boehringer Ingelheim, not related to this work.

- [75 references](#)
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J Asthma

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. 2023 Apr;60(4):769-783.

doi: 10.1080/02770903.2022.2094803. Epub 2022 Jul 10.

# Usefulness of simultaneous impulse oscillometry and spirometry with airway response to bronchodilator in the diagnosis of asthmatic cough

[Namiko Taniuchi](#)<sup>1,2</sup>, [Mitsunori Hino](#)<sup>1,2</sup>, [Akiko Yoshikawa](#)<sup>1,2</sup>, [Akihiko Miyanaga](#)<sup>1,2</sup>, [Yosuke Tanaka](#)<sup>2</sup>, [Masahiro Seike](#)<sup>2</sup>, [Akihiko Gemma](#)<sup>2</sup>

Affiliations expand

- PMID: 35759776
- DOI: [10.1080/02770903.2022.2094803](https://doi.org/10.1080/02770903.2022.2094803)

## Abstract

**Objective:** Some of the most common causes of chronic cough include cough variant asthma (CVA), bronchial asthma (BA), and asthma-COPD overlap (ACO). Although there is some overlap in the etiology of these diseases, it is clinically important to attempt an early differential diagnosis due to treatment strategies and prognoses. **Methods:** Spirometry and impulse oscillometry (IOS) before and after bronchodilator inhalation were analyzed for clinically diagnosed CVA (cCVA,  $n = 203$ ), BA (cBA,  $n = 222$ ), and ACO (cACO,  $n = 61$ ). **Results:** A significant difference in  $\Delta FEV_1$  was observed between cBA and cCVA ( $\Delta FEV_1$  improvement of 122.5 mL/5.4% and 65.7 mL/2.2%, respectively), but no difference was observed in  $\Delta PEF$ ,  $\Delta V_{50}$ , or  $\Delta V_{25}$ . Except for R20 (resistance at 20 Hz), significant differences between the three groups were observed in IOS. In IOS, cCVA and cBA showed comparable peripheral airway response to bronchodilator which was thought to be commensurate with changes in  $V_{50}$  and  $V_{25}$ . cACO improved  $\Delta FEV_1$  improvement of 81.0 mL/6.2% and was distinguished by a downward respiratory system reactance (Xrs) waveform with a limited bronchodilator response.  $FEV_1/FVC$ ,  $\%FEV_1$ , and  $\%V_{25}$  had relatively strong correlations with the three IOS parameters, X5 (reactance at 5 Hz), resonant frequency (Fres), and low-frequency reactance area (ALX), in the correlation between IOS and spirometers. **Conclusion:** Changes in IOS parameters were more sensitive in this study than changes in  $FEV_1$  or the flow-volume curve. Considering the benefits and relevance of the two different tests, simultaneous IOS and spirometry testing were useful in the diagnosis of asthmatic cough.

**Keywords:** IOS; Impulse oscillometry; asthma; chronic cough; spirometry.

SUPPLEMENTARY INFO



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Pediatr Nephrol

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. 2023 Apr;38(4):1029-1031.

doi: 10.1007/s00467-022-05647-6. Epub 2022 Jun 20.

# Chronic cough in an adolescent with infantile onset of hypokalemic hypochloremic metabolic alkalosis: Answers

[Emre Leventoğlu<sup>1</sup>](#), [Bahriye Uzun Kenan<sup>2</sup>](#), [Eylül Pınar Çakır<sup>3</sup>](#), [Zeynep İlkşen Hocoğlu<sup>3</sup>](#), [Tuğba Şişmanlar Eyüboğlu<sup>3</sup>](#), [Bahar Büyükkaragöz<sup>2</sup>](#), [Ayşe Tana Aslan<sup>3</sup>](#), [Oğuz Söylemezoğlu<sup>2</sup>](#)

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- DOI: [10.1007/s00467-022-05647-6](https://doi.org/10.1007/s00467-022-05647-6)

*No abstract available*

**Keywords:** Acute pancreatitis; CFTR gene; Chronic cough; Cystic fibrosis; Infant; Pseudo-Bartter syndrome.

- [25 references](#)

SUPPLEMENTARY INFO

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. 2023 Apr;38(4):1027-1028.

doi: 10.1007/s00467-022-05641-y. Epub 2022 Jun 20.

# Chronic cough in an adolescent with infantile onset of hypokalemic hypochloremic metabolic alkalosis: Questions

[Emre Leventoğlu<sup>1</sup>](#), [Bahriye Uzun Kenan<sup>2</sup>](#), [Eylül Pınar Çakır<sup>3</sup>](#), [Zeynep İlkşen Hocoğlu<sup>3</sup>](#), [Tuğba Şişmanlar Eyüboğlu<sup>3</sup>](#), [Bahar Büyükkaragöz<sup>2</sup>](#), [Ayşe Tana Aslan<sup>3</sup>](#), [Oğuz Söylemezoğlu<sup>2</sup>](#)

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- PMID: 35723734
- DOI: [10.1007/s00467-022-05641-y](https://doi.org/10.1007/s00467-022-05641-y)

*No abstract available*

**Keywords:** Acute pancreatitis; Antenatal Bartter syndrome; Chronic cough; Infant.

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# BRONCHIECTASIS

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Diagn Interv Radiol

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. 2023 Mar 29;29(2):291-299.

doi: 10.4274/dir.2023.221959. Epub 2023 Mar 8.

## Photon-counting computed tomography in the assessment of rheumatoid arthritis-associated interstitial lung disease: an initial experience

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- PMID: 36987949
- DOI: [10.4274/dir.2023.221959](https://doi.org/10.4274/dir.2023.221959)

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## Abstract

**Purpose:** Interstitial lung disease (ILD) accounts for a significant proportion of mortality and morbidity in patients with rheumatoid arthritis (RA). The aim of this cross-sectional study is to evaluate the performance of novel photon-counting detector computed tomography (PCD-CT) in the detection of pulmonary parenchymal involvement.

**Methods:** Sixty-one patients with RA without a previous definitive diagnosis of ILD underwent high-resolution (HR) (0.4 mm slice thickness) and ultra-high-resolution (UHR) (0.2 mm slice thickness) PCDCT examination. The extent of interstitial abnormalities [ground-glass opacity

(GGO), reticulation, bronchiectasis, and honeycombing] were scored in each lobe using a Likert-type scale. Total ILD scores were calculated as the sum of scores from all lobes.

**Results:** Reticulation and bronchiectasis scores were higher in the UHR measurements taken compared with the HR protocol [median (quartile 1, quartile 3): 2 (0, 3.5) vs. 0 (0, 3),  $P < 0.001$  and 2 (0, 2) vs. 0 (0, 2),  $P < 0.001$ , respectively]; however, GGO and honeycombing scores did not differ [2 (2, 4) vs. 2 (2, 4),  $P = 0.944$  and 0 (0, 0) vs. 0 (0, 0),  $P = 0.641$ , respectively]. Total ILD scores from both HR and UHR scans showed a mild negative correlation in diffusion capacity for carbon monoxide (HR:  $r = -0.297$ ,  $P = 0.034$ ; UHR:  $r = -0.294$ ,  $P = 0.036$ ). The pattern of lung parenchymal involvement did not differ significantly between the two protocols. The HR protocol had significantly lower volume CT dose index [0.67 (0.69, 1.06) mGy], total dose length product [29 (24.48, 33.2) mGy\*cm] compared with UHR scans [8.18 (6.80, 9.23) mGy,  $P < 0.001$  and 250 (218, 305) mGy\*cm,  $P < 0.001$ ].

**Conclusion:** UHR PCD-CT provides more detailed information on ILD in patients with RA than low-dose HR PCDCT. HR PCD-CT image acquisition with a low effective radiation dose may serve as a valuable, low-radiation screening tool in the selection of patients for further, higher-dose UHR PCD-CT screening.

**Keywords:** CT; high-resolution; low-dose; lung; photon-counting; ultra-high-resolution.

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MeSH termsexpand

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Review

Eur Respir Rev



. 2023 Mar 8;32(167):220202.

doi: 10.1183/16000617.0202-2022. Print 2023 Mar 31.

## Strength of association between comorbidities and asthma: a meta-analysis

- PMID: 36889783
- PMCID: [PMC10032614](#)
- DOI: [10.1183/16000617.0202-2022](#)

### Free PMC article

## Abstract

**Background:** The strength of association between comorbidities and asthma has never been ranked in relation to the prevalence of the comorbidity in the nonasthma population. We investigated the strength of association between comorbidities and asthma.

**Methods:** A comprehensive literature search was performed for observational studies reporting data on comorbidities in asthma and nonasthma populations. A pairwise meta-analysis was performed and the strength of association calculated by anchoring odds ratios and 95% confidence intervals with the rate of comorbidities in nonasthma populations *via* Cohen's *d* method. Cohen's *d*=0.2, 0.5 and 0.8 were cut-off values for small, medium and large effect sizes, respectively; very large effect size resulted for Cohen's *d*>0.8. The review was registered in the PROSPERO database; identifier number CRD42022295657.

**Results:** Data from 5 493 776 subjects were analysed. Allergic rhinitis (OR 4.24, 95% CI 3.82-4.71), allergic conjunctivitis (OR 2.63, 95% CI 2.22-3.11), bronchiectasis (OR 4.89, 95% CI 4.48-5.34), hypertensive cardiomyopathy (OR 4.24, 95% CI 2.06-8.90) and nasal congestion (OR 3.30, 95% CI 2.96-3.67) were strongly associated with asthma (Cohen's *d*>0.5 and ≤0.8); COPD (OR 6.23, 95% CI 4.43-8.77) and other chronic respiratory diseases (OR 12.85, 95% CI 10.14-16.29) were very strongly associated with asthma (Cohen's *d*>0.8). Stronger associations were detected between comorbidities and severe asthma. No bias resulted according to funnel plots and Egger's test.

**Conclusion:** This meta-analysis supports the relevance of individualised strategies for disease management that look beyond asthma. A multidimensional approach should be used to assess whether poor symptom control is related to uncontrolled asthma or to uncontrolled underlying comorbidities.

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## Conflict of interest statement

Conflict of interest: P. Rogliani participated as a lecturer and advisor in scientific meetings and courses under the sponsorship of Almirall, AstraZeneca, Biofutura, Boehringer Ingelheim, Chiesi Farmaceutici, GlaxoSmithKline, Menarini Group, Mundipharma, and Novartis, and her department

was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici Novartis, and Zambon, outside the submitted work. Conflict of interest: R. Laitano has nothing to disclose. Conflict of interest: J. Ora has nothing to disclose. Conflict of interest: R. Beasley reports grants and personal fees from AstraZeneca, grants from GlaxoSmithKline and Genentech, personal fees from Avillion and Theravance, outside the submitted work. Conflict of interest: L. Calzetta has participated as advisor in scientific meetings under the sponsorship of Boehringer Ingelheim and Novartis; received nonfinancial support from AstraZeneca; a research grant partially funded by Chiesi Farmaceutici, Boehringer Ingelheim, Novartis, and Almirall; is or has been a consultant to ABC Farmaceutici, Edmond Pharma, Zambon, Verona Pharma, and Ockham Biotech; and his department was funded by Almirall, Boehringer Ingelheim, Chiesi Farmaceutici, Novartis, and Zambon, outside the submitted work.

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. 2023 Apr;28(4):339-349.

doi: 10.1111/resp.14479. Epub 2023 Mar 2.

## [Thoracic Society of Australia and New Zealand \(TSANZ\) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand](#)

[Anne B Chang](#)<sup>1 2 3</sup>, [Scott C Bell](#)<sup>4 5 6</sup>, [Catherine A Byrnes](#)<sup>7 8</sup>, [Paul Dawkins](#)<sup>9 10</sup>, [Anne E Holland](#)<sup>11 12 13</sup>, [Emma Kennedy](#)<sup>14 15 16</sup>, [Paul T King](#)<sup>17</sup>, [Pamela Laird](#)<sup>18 19 20</sup>, [Sarah Mooney](#)<sup>9 21</sup>, [Lucy](#)

[Morgan](#)<sup>22</sup>, [Marianne Parsons](#)<sup>23</sup>, [Betty Poot](#)<sup>24 25</sup>, [Maree Toombs](#)<sup>26</sup>, [Paul J Torzillo](#)<sup>27 28</sup>, [Keith Grimwood](#)<sup>29 30</sup>

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- PMID: 36863703
- DOI: [10.1111/resp.14479](https://doi.org/10.1111/resp.14479)

**Free article**

## Abstract

This position statement, updated from the 2015 guidelines for managing Australian and New Zealand children/adolescents and adults with chronic suppurative lung disease (CSLD) and bronchiectasis, resulted from systematic literature searches by a multi-disciplinary team that included consumers. The main statements are: Diagnose CSLD and bronchiectasis early; this requires awareness of bronchiectasis symptoms and its co-existence with other respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease). Confirm bronchiectasis with a chest computed-tomography scan, using age-appropriate protocols and criteria in children. Undertake a baseline panel of investigations. Assess baseline severity, and health impact, and develop individualized management plans that include a multi-disciplinary approach and coordinated care between healthcare providers. Employ intensive treatment to improve symptom control, reduce exacerbation frequency, preserve lung function, optimize quality-of-life and enhance survival. In children, treatment also aims to optimize lung growth and, when possible, reverse bronchiectasis. Individualize airway clearance techniques (ACTs) taught by respiratory physiotherapists, encourage regular exercise, optimize nutrition, avoid air pollutants and administer vaccines following national schedules. Treat exacerbations with 14-day antibiotic courses based upon lower airway culture results, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients with severe exacerbations and/or not responding to outpatient therapy are hospitalized for further treatments, including intravenous antibiotics and intensive ACTs. Eradicate *Pseudomonas aeruginosa* when newly detected in lower airway cultures. Individualize therapy for long-term antibiotics, inhaled corticosteroids, bronchodilators and mucoactive agents. Ensure ongoing care with 6-monthly monitoring for complications and co-morbidities. Undertake optimal care of underserved peoples, and despite its challenges, delivering best-practice treatment remains the overriding aim.

**Keywords:** adolescents; adults; bronchiectasis; children; evidence base practice; systematic review.

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- [26 references](#)

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# Cystic fibrosis and primary ciliary dyskinesia: Similarities and differences

[Rute Pereira](#)<sup>1</sup>, [Telma Barbosa](#)<sup>2</sup>, [Ana Lúcia Cardoso](#)<sup>3</sup>, [Rosália Sá](#)<sup>4</sup>, [Mário Sousa](#)<sup>5</sup>

Affiliations [expand](#)

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- DOI: [10.1016/j.rmed.2023.107169](https://doi.org/10.1016/j.rmed.2023.107169)

## Free article

## Abstract

Cystic fibrosis (CF) and Primary ciliary dyskinesia (PCD) are both rare chronic diseases, inherited disorders associated with multiple complications, namely respiratory complications, due to impaired mucociliary clearance that affect severely patients' lives. Although both are classified as rare diseases, PCD has a much lower prevalence than CF, particularly among Caucasians. As a result, CF is well studied, better recognized by clinicians, and with some therapeutic approaches already available. Whereas PCD is still largely unknown, and thus the approach is based on consensus guidelines, expert opinion, and extrapolation from the larger evidence base available for patients with CF. Both diseases have some clinical similarities but are very different, necessitating different treatment by specialists who are familiar with the complexities of each disease. This review aims to provide an overview of the knowledge about the two diseases with a focus on the similarities and differences between both in terms of disease mechanisms, common clinical manifestations, genetics and the most relevant therapeutic options. We hoped to raise clinical awareness about PCD, what it is, how it differs from CF, and how much information is still lacking. Furthermore, this review emphasises the fact that both diseases require ongoing research to find better treatments and, in particular for PCD, to fill the medical and scientific gaps.



**Keywords:** Clinical awareness; Cystic fibrosis (CF); Mucociliary clearance; Primary ciliary dyskinesia (PCD); Rare diseases.

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## Conflict of interest statement

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

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Respir Med



. 2023 Apr;209:107167.

doi: 10.1016/j.rmed.2023.107167. Epub 2023 Feb 16.

# Racial and ethnic differences in patients enrolled in the national bronchiectasis and nontuberculous mycobacteria research registry

[P J McShane](#)<sup>1</sup>, [R Choate](#)<sup>2</sup>, [M Johnson](#)<sup>3</sup>, [D J Maselli](#)<sup>4</sup>, [K L Winthrop](#)<sup>5</sup>, [M L Metersky](#)<sup>6</sup>; [Bronchiectasis and NTM Research Registry Investigators](#)

Affiliations expand

- PMID: 36804343
- DOI: [10.1016/j.rmed.2023.107167](https://doi.org/10.1016/j.rmed.2023.107167)

# Abstract

Demographic and socioeconomic factors are recognized to contribute to disparities in healthcare outcomes. Originally, bronchiectasis was described in a population of predominantly White ethnic group of patients in which racial disparity could not be identified. The U.S. Bronchiectasis Research Registry (BRR), a centralized database of adult patients with bronchiectasis and/or NTM from 18 clinical institutions across the U.S., was created to support the research of this condition. The aim of this study is to describe the racial and ethnic distribution of patients enrolled in the BRR and evaluate factors associated with healthcare disparities within manifestations of and/or the care delivered to this population. At the time of this study, 3600 patients with bronchiectasis and/or NTM were enrolled in the BRR. Of those, 3510 participants were included in these analyses. The population was predominantly non-Hispanic White (n = 3143, 89.5%), followed by Hispanic or Latino (n = 149, 4.3%), Asian (n = 130, 3.7%) and non-Hispanic Black (n = 88, 2.5%) participants. Testing for cystic fibrosis, immunoglobulin deficiency, and mycobacteria was not different between races, but non-Hispanic Black patients were tested less frequently for alpha-1 antitrypsin (A1AT) deficiency compared to other groups (P = 0.01). The four groups did not differ in the proportion of *Pseudomonas aeruginosa* or *Hemophilus influenzae*. There was no statistically significant difference in use of high-frequency chest wall oscillation, pulmonary rehabilitation services, or suppressive macrolide treatment across the groups (P > 0.05). There is a disproportionately high percentage of non-Hispanic White patients compared to non-Hispanic Black patients and Hispanic or Latino patients in the BRR. However, we found an overall similarity of care of BRR patients, regardless of racial and ethnic group.

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## Conflict of interest statement

**Declaration of competing interest** The authors declare no financial relationships, compensation or intellectual property related to the work in this manuscript.

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Eur Respir Rev

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. 2023 Jan 11;32(167):220154.

# Role of inhaled antibiotics in the era of highly effective CFTR modulators

J Stuart Elborn<sup>1</sup>, Francesco Blasi<sup>2,3</sup>, Pierre-Régis Burgel<sup>4,5</sup>, Daniel Peckham<sup>6</sup>

Affiliations expand

- PMID: 36631132
- PMCID: [PMC9879329](#)
- DOI: [10.1183/16000617.0154-2022](#)

**Free PMC article**

## Abstract

Recurrent and chronic bacterial infections are common in people with cystic fibrosis (CF) and contribute to lung function decline. Antibiotics are the mainstay in the treatment of exacerbations and chronic bacterial infection in CF. Inhaled antibiotics are effective in treating chronic respiratory bacterial infections and eradicating *Pseudomonas aeruginosa* from the respiratory tract, with limited systemic adverse effects. In the past decade, highly effective cystic fibrosis transmembrane conductance regulator (CFTR) modulators have become a new therapy that partially corrects/opens chloride transport in patients with selected CFTR mutations, restoring mucus hydration and improving mucociliary clearance. The recent triple CFTR modulator combination is approved for ~80-90% of the CF population and significantly reduces pulmonary exacerbations and improves respiratory symptoms and lung function. CFTR modulators have shifted the focus from symptomatic treatment to personalised/precision medicine by targeting genotype-specific CFTR defects. While these are highly effective, they do not fully normalise lung physiology, stop inflammation or resolve chronic lung damage, such as bronchiectasis. The impact of these new drugs on lung health is likely to change the future management of chronic pulmonary infections in people with CF. This article reviews the role of inhaled antibiotics in the era of CFTR modulators.

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## Conflict of interest statement

Conflict of interest: J.S. Elborn holds a joint public–private grant from the European commission in the innovative medicines initiative with Novartis AG and Spexsis; he worked as a paid consultant for Vertex Pharmaceuticals and Viatrix Inc.; and has been a paid speaker for many pharmaceutical companies over 30 years in respiratory medicine. Conflict of interest: F. Blasi receives financial grants from AstraZeneca, Chiesi Farmaceutici S.p.A and Insmed Inc.; he works as a paid consultant for Menarini and Zambon; and receives speaker fees from AstraZeneca, Chiesi Farmaceutici S.p.A,

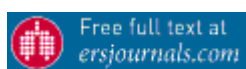
GlaxoSmithKline, Guidotti, Grifols, Insmmed Inc., Menarini, Novartis AG, Sanofi-Genzyme, Viartis Inc., Vertex Pharmaceuticals and Zambon. Conflict of interest: P-R. Burgel received financial grants from GlaxoSmithKline and Vertex Pharmaceuticals and was a paid consultant for AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici S.p.A, GlaxoSmithKline, Insmmed Inc., Novartis AG, Pfizer Inc., Vertex Pharmaceuticals and Zambon. Conflict of interest: D. Peckham received a noncommercial financial grant from Gilead Sciences; and has been a paid consultant and speaker in advisory boards for multiple pharmaceutical companies.

- [71 references](#)

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#### Multicenter Study

Pediatr Pulmonol

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. 2023 Apr;58(4):1127-1135.

doi: 10.1002/ppul.26303. Epub 2023 Jan 9.

## Primary ciliary dyskinesia: A multicenter survey on clinical practice and patient management in Italy

[Nicola Ullmann](#)<sup>1</sup>, [Francesca Santamaria](#)<sup>2</sup>, [Annalisa Allegorico](#)<sup>1</sup>, [Valentina Fainardi](#)<sup>3</sup>, [Melissa Borrelli](#)<sup>2</sup>, [Valentina A Ferraro](#)<sup>4</sup>, [Elena Proietti](#)<sup>5</sup>, [Giuseppe F Parisi](#)<sup>6</sup>, [Vittorio Romagnoli](#)<sup>7</sup>, [Francesca Lucca](#)<sup>8</sup>, [Marcella Gallucci](#)<sup>9</sup>, [Luigi Mappa](#)<sup>10</sup>, [Mara Lelli](#)<sup>11</sup>, [Doriana Amato](#)<sup>12</sup>, [Laura Petrarca](#)<sup>13</sup>, [Giuseppe Cimino](#)<sup>14</sup>, [Oliviero Sacco](#)<sup>15</sup>, [Claudia Calogero](#)<sup>16</sup>, [Maria Francesca Patria](#)<sup>11</sup>, [Angelo Acquafredda](#)<sup>17</sup>, [Annalisa Ferlisi](#)<sup>18</sup>, [Massimo Maschio](#)<sup>19</sup>, [Ahmad Kantar](#)<sup>20</sup>, [Renato Cutrera](#)<sup>1</sup>

Affiliations expand

- PMID: 36588099

- DOI: [10.1002/ppul.26303](https://doi.org/10.1002/ppul.26303)

## Abstract

**Introduction:** There are no recent data on primary ciliary dyskinesia (PCD) distribution, diagnosis and treatment in Italy.

**Methods:** A descriptive study based on a survey questionnaire. It consisted of three sections (patients, diagnosis, and treatment), and sent to all the Italian PCD Centers.

**Results:** Questionnaires obtained from 20/22 centers in 12/20 regions showed that the total number of PCD patients treated at the participating centers was of 416. Out of all centers, 55% follow <20 patients, two centers have >40 patients, and 75% follow both pediatric and adults. Age at diagnosis was between 4 and 8 years in 45% of the centers, <3 years in three centers. Nasal nitric oxide, transmission electron microscopy and ciliary high-speed video microscopy are performed in 75%, 90%, and 40% of centers, respectively. Immunofluorescence is available in five centers. Genetic analysis is offered in 55% of the centers, and in seven centers >50% of the patients have a known genetic profile. Patients treated at all centers receive inhaled saline solutions, corticosteroids and chest physiotherapy. Prophylactic antibiotics and mucolytics are prescribed in 95% and 50% of the centers, respectively. Pseudomonas infection is treated with oral or inhaled antibiotics.

**Conclusions:** Many Italian centers care for a small number of pediatric and adult patients, and diagnosis is often delayed. We found a great variability in the available diagnostic procedures, as well in the prescribed therapies. Our study will help to uniform diagnostic algorithm and share treatments protocols for PCD in Italy and allowed to set specific national goals.

**Keywords:** children; diagnosis; management; primary ciliary dyskinesia; treatment.

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- [28 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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. 2023 Apr;307(1):e221145.

# Radiologic and Histologic Correlates of Early Interstitial Lung Changes in Explanted Lungs

[Stijn E Verleden](#)<sup>1</sup>, [Arno Vanstapel](#)<sup>1</sup>, [Joseph Jacob](#)<sup>1</sup>, [Tinne Goos](#)<sup>1</sup>, [Jeroen Hendriks](#)<sup>1</sup>, [Laurens J Ceulemans](#)<sup>1</sup>, [Dirk E Van Raemdonck](#)<sup>1</sup>, [Laurens De Sadeleer](#)<sup>1</sup>, [Robin Vos](#)<sup>1</sup>, [Johanna M Kwakkel-van Erp](#)<sup>1</sup>, [Arne P Neyrinck](#)<sup>1</sup>, [Geert M Verleden](#)<sup>1</sup>, [Matthieu N Boone](#)<sup>1</sup>, [Wim Janssens](#)<sup>1</sup>, [Els Wauters](#)<sup>1</sup>, [Birgit Weynand](#)<sup>1</sup>, [Danny D Jonigk](#)<sup>1</sup>, [Johny Verschakelen](#)<sup>1</sup>, [Wim A Wuyts](#)<sup>1</sup>

Affiliations expand

- PMID: 36537894
- PMCID: [PMC7614383](#)
- DOI: [10.1148/radiol.221145](#)

## Abstract

**Background** Interstitial lung abnormalities (ILAs) reflect imaging features on lung CT scans that are compatible with (early) interstitial lung disease. Despite accumulating evidence regarding the incidence, risk factors, and prognosis of ILAs, the histopathologic correlates of ILAs remain elusive. **Purpose** To determine the correlation between radiologic and histopathologic findings in CT-defined ILAs in human lung explants. **Materials and Methods** Explanted lungs or lobes from participants with radiologically documented ILAs were prospectively collected from 2010 to 2021. These specimens were air-inflated, frozen, and scanned with CT and micro-CT (spatial resolution of 0.7 mm and 90  $\mu$ m, respectively). Subsequently, the lungs were cut and sampled with core biopsies. At least five samples per lung underwent micro-CT and subsequent histopathologic assessment with semiquantitative remodeling scorings. Based on area-specific radiologic scoring, the association between radiologic and histopathologic findings was assessed. **Results** Eight lung explants from six donors (median age at explantation, 71 years [range, 60-83 years]; four men) were included (unused donor lungs,  $n = 4$ ; pre-emptive lobectomy for oncologic indications,  $n = 2$ ). Ex vivo CT demonstrated ground-glass opacification, reticulation, and bronchiectasis. Micro-CT and histopathologic examination demonstrated that lung abnormalities were frequently paraseptal and associated with fibrosis and lymphocytic inflammation. The histopathologic results showed varying degrees of fibrosis in areas that appeared normal on CT scans. Regions of reticulation on CT scans generally had greater fibrosis at histopathologic analysis. Vasculopathy and bronchiectasis were also often present at histopathologic examination of lungs with ILAs. Fully developed fibroblastic foci were rarely observed. **Conclusion** This study demonstrated direct histologic correlates of CT-defined interstitial lung abnormalities. © RSNA, 2022 *Supplemental material is available for this article.* See also the editorial by Jeudy in this issue.

## Comment in

- [Interstitial Lung Abnormalities: The More We Learn, the Less We Know.](#)  
Jeudy J. Radiology. 2023 Apr;307(1):e222996. doi: 10.1148/radiol.222996. Epub 2022 Dec 20. PMID: 36537900 No abstract available.
- [22 references](#)
- [4 figures](#)

## SUPPLEMENTARY INFO

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. 2023 Apr;307(1):e222675.  
doi: 10.1148/radiol.222675. Epub 2022 Dec 13.

# [Artificial Intelligence Analysis of Bronchiectasis Is Predictive of Outcomes in Chronic Obstructive Pulmonary Disease](#)

[Mark L Schiebler](#)<sup>1</sup>, [Joon Beom Seo](#)<sup>1</sup>

[Affiliations expand](#)

- PMID: 36511811
- DOI: [10.1148/radiol.222675](#)

No abstract available

## Comment on

- [Artificial Intelligence-based CT Assessment of Bronchiectasis: The COPDGene Study.](#) Díaz AA, Nardelli P, Wang W, San José Estépar R, Yen A, Kligerman S, Maselli DJ, Dolliver WR, Tsao A, Orejas JL, Aliberti S, Aksamit TR, Young KA, Kinney GL, Washko GR, Silverman EK, San José Estépar R. *Radiology*. 2023 Apr;307(1):e221109. doi: 10.1148/radiol.221109. Epub 2022 Dec 13. PMID: 36511808

## SUPPLEMENTARY INFO

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. 2023 Apr;307(1):e221109.

doi: 10.1148/radiol.221109. Epub 2022 Dec 13.

# [Artificial Intelligence-based CT Assessment of Bronchiectasis: The COPDGene Study](#)

[Alejandro A Díaz](#)<sup>1</sup>, [Pietro Nardelli](#)<sup>1</sup>, [Wei Wang](#)<sup>1</sup>, [Rubén San José Estépar](#)<sup>1</sup>, [Andrew Yen](#)<sup>1</sup>, [Seth Kligerman](#)<sup>1</sup>, [Diego J Maselli](#)<sup>1</sup>, [Wojciech R Dolliver](#)<sup>1</sup>, [Andrew Tsao](#)<sup>1</sup>, [José L Orejas](#)<sup>1</sup>, [Stefano Aliberti](#)<sup>1</sup>, [Timothy R Aksamit](#)<sup>1</sup>, [Kendra A Young](#)<sup>1</sup>, [Gregory L Kinney](#)<sup>1</sup>, [George R Washko](#)<sup>1</sup>, [Edwin K Silverman](#)<sup>1</sup>, [Raúl San José Estépar](#)<sup>1</sup>

Affiliations expand

- PMID: 36511808
- DOI: [10.1148/radiol.221109](#)



# Abstract

Background CT is the standard method used to assess bronchiectasis. A higher airway-to-artery diameter ratio (AAR) is typically used to identify enlarged bronchi and bronchiectasis; however, current imaging methods are limited in assessing the extent of this metric in CT scans. Purpose To determine the extent of AARs using an artificial intelligence-based chest CT and assess the association of AARs with exacerbations over time. Materials and Methods In a secondary analysis of ever-smokers from the prospective, observational, multicenter COPDGene study, AARs were quantified using an artificial intelligence tool. The percentage of airways with AAR greater than 1 (a measure of airway dilatation) in each participant on chest CT scans was determined. Pulmonary exacerbations were prospectively determined through biannual follow-up (from July 2009 to September 2021). Multivariable zero-inflated regression models were used to assess the association between the percentage of airways with AAR greater than 1 and the total number of pulmonary exacerbations over follow-up. Covariates included demographics, lung function, and conventional CT parameters. Results Among 4192 participants (median age, 59 years; IQR, 52-67 years; 1878 men [45%]), 1834 had chronic obstructive pulmonary disease (COPD). During a 10-year follow-up and in adjusted models, the percentage of airways with AARs greater than 1 (quartile 4 vs 1) was associated with a higher total number of exacerbations (risk ratio [RR], 1.08; 95% CI: 1.02, 1.15;  $P = .01$ ). In participants meeting clinical and imaging criteria of bronchiectasis (ie, clinical manifestations with  $\geq 3\%$  of AARs  $>1$ ) versus those who did not, the RR was 1.37 (95% CI: 1.31, 1.43;  $P < .001$ ). Among participants with COPD, the corresponding RRs were 1.10 (95% CI: 1.02, 1.18;  $P = .02$ ) and 1.32 (95% CI: 1.26, 1.39;  $P < .001$ ), respectively. Conclusion In ever-smokers with chronic obstructive pulmonary disease, artificial intelligence-based CT measures of bronchiectasis were associated with more exacerbations over time. Clinical trial registration no. [NCT00608764](#) © RSNA, 2022 *Supplemental material is available for this article.* See also the editorial by Schiebler and Seo in this issue.

## Comment in

- [Artificial Intelligence Analysis of Bronchiectasis Is Predictive of Outcomes in Chronic Obstructive Pulmonary Disease.](#)  
Schiebler ML, Seo JB. *Radiology*. 2023 Apr;307(1):e222675. doi: 10.1148/radiol.222675. Epub 2022 Dec 13. PMID: 36511811 No abstract available.

## SUPPLEMENTARY INFO

Publication types, MeSH terms expand

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. 2023 Apr 1;207(7):812-814.  
doi: 10.1164/rccm.202211-2179ED.

# How to Understand a Revolution: Guts, Lungs, and Bronchiectasis

[Callie M Drohan](#)<sup>1</sup>, [Philip L Molyneaux](#)<sup>2</sup>, [Robert P Dickson](#)<sup>1,3,4</sup>

Affiliations expand

- PMID: 36473273
- DOI: [10.1164/rccm.202211-2179ED](https://doi.org/10.1164/rccm.202211-2179ED)

*No abstract available*

## Comment on

- [Microbial Dysregulation of the Gut-Lung Axis in Bronchiectasis.](#)  
Narayana JK, Aliberti S, Mac Aogáin M, Jaggi TK, Ali NABM, Ivan FX, Cheng HS, Yip YS, Vos MIG, Low ZS, Lee JXT, Amati F, Gramegna A, Wong SH, Sung JJY, Tan NS, Tsaneva-Atanasova K, Blasi F, Chotirmall SH. *Am J Respir Crit Care Med.* 2023 Apr 1;207(7):908-920. doi: 10.1164/rccm.202205-0893OC. PMID: 36288294

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Ann Am Thorac Soc

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. 2023 Apr;20(4):539-547.  
doi: 10.1513/AnnalsATS.202206-524OC.

# Airway Disease in Children with Primary Ciliary Dyskinesia: Impact of Ciliary Ultrastructure Defect and Genotype

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Affiliations expand

- PMID: 36442147
- DOI: [10.1513/AnnalsATS.202206-524OC](https://doi.org/10.1513/AnnalsATS.202206-524OC)

## Abstract

**Rationale:** Primary ciliary dyskinesia (PCD) is characterized by impaired mucociliary clearance, recurrent respiratory infections, progressive airway damage, and obstructive lung disease. Although the association of ciliary ultrastructure defect/genotype with the severity of airflow obstruction has been well characterized, their association with airway abnormalities on chest computed tomography (CT) has been minimally evaluated. **Objectives:** We sought to delineate the association of ciliary defect class/genotype with chest CT scores in children with PCD. **Methods:** Cross-sectional analysis of children with PCD ( $N = 146$ ) enrolled in a prospective multicenter observational study, stratified by defect type: outer dynein arm (ODA), ODA/inner dynein arm (IDA), IDA/microtubular disorganization (MTD), and normal/near normal ultrastructure with associated genotypes. CTs were scored using the MERAGMA-PCD (Melbourne-Rotterdam Annotated Grid Morphometric Analysis for PCD), evaluating airway abnormalities in a hierarchical order: atelectasis, bronchiectasis, bronchial wall thickening, and mucus plugging/tree-in-bud opacities. The volume fraction of each component was expressed as the percentage of total lung volume. The percentage of disease was computed as the sum of all components. Regression analyses were used to describe the association between clinical predictors and CT scores. **Results:** Acceptable chest CTs were obtained in 141 children (71 male): 57 ODA, 20 ODA/IDA, 40 IDA/MTD, and 24 normal/near normal. The mean (standard deviation) age was 8.5 (4.6) years, forced expiratory volume in 1 second ( $FEV_1$ ) percent predicted was 82.4 (19.5), and %Disease was 4.6 (3.5). Children with IDA/MTD defects had a higher %Disease compared with children with ODA defects (2.71% higher [95% confidence interval (CI), 1.37-4.06;  $P < 0.001$ ]), driven by higher %Mucus plugging (2.35% higher [1.43-3.26;  $P < 0.001$ ]). Increasing age, lower body mass index, and lower  $FEV_1$  were associated with a higher %Disease (0.23%; 95% CI, 0.11-0.35;  $P < 0.001$  and 0.03%; 95% CI, 0.01-0.04;  $P = 0.008$  and 0.05%; 95% CI, 0.01-0.08;  $P = 0.011$ , respectively). **Conclusions:** Children with IDA/MTD defects had significantly greater airway disease on CT, primarily mucus plugging, compared with children with ODA defects.

**Keywords:** PCD; bronchiectasis; computed tomography; lung function; pediatric lung disease.

## Comment in

- [Mucus Plugging in Primary Ciliary Dyskinesia.](#)  
Adaikalam S, Gaston B. *Ann Am Thorac Soc.* 2023 Apr;20(4):514-515. doi: 10.1513/AnnalsATS.202301-021ED.PMID: 37000147 No abstract available.

SUPPLEMENTARY INFO

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. 2023 Apr;307(1):e212611.

doi: 10.1148/radiol.212611. Epub 2022 Nov 15.

# Chest CT Findings in Marijuana Smokers

[Luke Murtha](#)<sup>1</sup>, [Paul Sathiadoss](#)<sup>1</sup>, [Jean-Paul Salameh](#)<sup>1</sup>, [Matthew D F McInnes](#)<sup>1</sup>, [Giselle Revah](#)<sup>1</sup>

Affiliations expand

- PMID: 36378033
- DOI: [10.1148/radiol.212611](https://doi.org/10.1148/radiol.212611)

## Abstract

**Background** Global consumption of marijuana is increasing, but there is a paucity of evidence concerning associated lung imaging findings. **Purpose** To use chest CT to investigate the effects of marijuana smoking in the lung. **Materials and Methods** This retrospective case-control study evaluated results of chest CT examinations (from October 2005 to July 2020) in marijuana smokers, nonsmoker control patients, and tobacco-only smokers. We compared rates of emphysema, airway

changes, gynecomastia, and coronary artery calcification. Age- and sex-matched subgroups were created for comparison with tobacco-only smokers older than 50 years. Results were analyzed using  $\chi^2$  tests. Results A total of 56 marijuana smokers (34 male; mean age, 49 years  $\pm$  14 [SD]), 57 nonsmoker control patients (32 male; mean age, 49 years  $\pm$  14), and 33 tobacco-only smokers (18 male; mean age, 60 years  $\pm$  6) were evaluated. Higher rates of emphysema were seen among marijuana smokers (42 of 56 [75%]) than nonsmokers (three of 57 [5%]) ( $P < .001$ ) but not tobacco-only smokers (22 of 33 [67%]) ( $P = .40$ ). Rates of bronchial thickening, bronchiectasis, and mucoid impaction were higher among marijuana smokers compared with the other groups ( $P < .001$  to  $P = .04$ ). Gynecomastia was more common in marijuana smokers (13 of 34 [38%]) than in control patients (five of 32 [16%]) ( $P = .039$ ) and tobacco-only smokers (two of 18 [11%]) ( $P = .040$ ). In age-matched subgroup analysis of 30 marijuana smokers (23 male), 29 nonsmoker control patients (17 male), and 33 tobacco-only smokers (18 male), rates of bronchial thickening, bronchiectasis, and mucoid impaction were again higher in the marijuana smokers than in the tobacco-only smokers ( $P < .001$  to  $P = .006$ ). Emphysema rates were higher in age-matched marijuana smokers (28 of 30 [93%]) than in tobacco-only smokers (22 of 33 [67%]) ( $P = .009$ ). There was no difference in rate of coronary artery calcification between age-matched marijuana smokers (21 of 30 [70%]) and tobacco-only smokers (28 of 33 [85%]) ( $P = .16$ ). Conclusion Airway inflammation and emphysema were more common in marijuana smokers than in nonsmokers and tobacco-only smokers, although variable interobserver agreement and concomitant cigarette smoking among the marijuana-smoking cohort limits our ability to draw strong conclusions. © RSNA, 2022 See also the editorial by Galvin and Franks in this issue.

## Comment in

- [Marijuana and the Vulnerable Lung: The Role of Imaging and the Need to Move Quickly.](#) Galvin J, Franks T. *Radiology*. 2023 Apr;307(1):e222745. doi: 10.1148/radiol.222745. Epub 2022 Nov 15. PMID: 36378035 No abstract available.

## SUPPLEMENTARY INFO

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. 2023 Apr;53(4):640-648.

doi: 10.1007/s00247-022-05539-9. Epub 2022 Nov 14.

# Chest magnetic resonance imaging in cystic fibrosis: technique and clinical benefits

[Daniel Gräfe](#)<sup>1</sup>, [Freerk Prenzel](#)<sup>2</sup>, [Franz Wolfgang Hirsch](#)<sup>3</sup>

Affiliations expand

- PMID: 36372855
- PMCID: [PMC10027634](#)
- DOI: [10.1007/s00247-022-05539-9](#)

**Free PMC article**

## Abstract

Cystic fibrosis (CF) is one of the most common inherited and life-shortening pulmonary diseases in the Caucasian population. With the widespread introduction of newborn screening and the development of modulator therapy, tremendous advances have been made in recent years both in diagnosis and therapy. Since paediatric CF patients tend to be younger and have lower morbidity, the type of imaging modality that should be used to monitor the disease is often debated. Computed tomography (CT) is sensitive to many pulmonary pathologies, but radiation exposure limits its use, especially in children and adolescents. Conventional pulmonary magnetic resonance imaging (MRI) is a valid alternative to CT and, in most cases, provides sufficient information to guide treatment. Given the expected widespread availability of sequences with ultra-short echo times, there will be even fewer reasons to perform CT for follow-up of patients with CF. This review aims to provide an overview of the process and results of monitoring CF with MRI, particularly for centres not specialising in the disease.

**Keywords:** Bronchiectasis; Chest; Children; Computed tomography; Cystic fibrosis; Eichinger score; Fourier decomposition; Magnetic resonance imaging; Pulmonary; Ultra-short echo times.

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## Conflict of interest statement

None

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

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Am J Respir Crit Care Med

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. 2023 Apr 1;207(7):908-920.

doi: 10.1164/rccm.202205-0893OC.

# Microbial Dysregulation of the Gut–Lung Axis in Bronchiectasis

[Jayanth Kumar Narayana](#)<sup>1</sup>, [Stefano Aliberti](#)<sup>2,3</sup>, [Micheál Mac Aogáin](#)<sup>4,5</sup>, [Tavleen Kaur Jaggi](#)<sup>1</sup>, [Nur A'tikah Binte Mohamed Ali](#)<sup>1</sup>, [Fransiskus Xavierius Ivan](#)<sup>1</sup>, [Hong Sheng Cheng](#)<sup>1</sup>, [Yun Sheng Yip](#)<sup>1</sup>, [Marcus Ivan Gerard Vos](#)<sup>1</sup>, [Zun Siong Low](#)<sup>1</sup>, [Jeannie Xue Ting Lee](#)<sup>1</sup>, [Francesco Amati](#)<sup>2,3</sup>, [Andrea Gramegna](#)<sup>6,7</sup>, [Sunny H Wong](#)<sup>1,8</sup>, [Joseph J Y Sung](#)<sup>1,8</sup>, [Nguan Soon Tan](#)<sup>1,9</sup>, [Krasimira Tsaneva-Atanasova](#)<sup>10,11</sup>, [Francesco Blasi](#)<sup>6,7</sup>, [Sanjay H Chotirmall](#)<sup>1,12</sup>

Affiliations expand

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- DOI: [10.1164/rccm.202205-0893OC](https://doi.org/10.1164/rccm.202205-0893OC)

Free article

## Abstract

**Rationale:** Emerging data support the existence of a microbial "gut-lung" axis that remains unexplored in bronchiectasis. **Methods:** Prospective and concurrent sampling of gut (stool) and lung (sputum) was performed in a cohort of  $n = 57$  individuals with bronchiectasis and subjected to bacteriome (16S rRNA) and mycobionome (18S Internal Transcribed Spacer) sequencing (total, 228 microbiomes). Shotgun metagenomics was performed in a subset ( $n = 15$ ; 30 microbiomes). Data from gut and lung compartments were integrated by weighted similarity network fusion, clustered, and subjected to co-occurrence analysis to evaluate gut-lung networks. Murine experiments were undertaken to validate specific *Pseudomonas*-driven gut-lung interactions. **Results:** Microbial

communities in stable bronchiectasis demonstrate a significant gut-lung interaction. Multibiome integration followed by unsupervised clustering reveals two patient clusters, differing by gut-lung interactions and with contrasting clinical phenotypes. A high gut-lung interaction cluster, characterized by lung *Pseudomonas*, gut *Bacteroides*, and gut *Saccharomyces*, is associated with increased exacerbations and greater radiological and overall bronchiectasis severity, whereas the low gut-lung interaction cluster demonstrates an overrepresentation of lung commensals, including *Prevotella*, *Fusobacterium*, and *Porphyromonas* with gut *Candida*. The lung *Pseudomonas*-gut *Bacteroides* relationship, observed in the high gut-lung interaction bronchiectasis cluster, was validated in a murine model of lung *Pseudomonas aeruginosa* infection. This interaction was abrogated after antibiotic (imipenem) pretreatment in mice confirming the relevance and therapeutic potential of targeting the gut microbiome to influence the gut-lung axis. Metagenomics in a subset of individuals with bronchiectasis corroborated our findings from targeted analyses. **Conclusions:** A dysregulated gut-lung axis, driven by lung *Pseudomonas*, associates with poorer clinical outcomes in bronchiectasis.

**Keywords:** bronchiectasis; gut-lung axis; metagenomics; microbiome; mycobiome.

## Comment in

- [How to Understand a Revolution: Guts, Lungs, and Bronchiectasis.](#)  
Drohan CM, Molyneaux PL, Dickson RP. *Am J Respir Crit Care Med*. 2023 Apr 1;207(7):812-814. doi: 10.1164/rccm.202211-2179ED.PMID: 36473273 No abstract available.
- [Cited by 2 articles](#)

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. 2023 Apr;39(4):785-793.

doi: 10.1080/09593985.2022.2028326. Epub 2022 Jan 27.

# Physiotherapist perspectives of airway clearance techniques in bronchiectasis



[Lisa J Franks](#)<sup>1,2</sup>, [James R Walsh](#)<sup>1,2,3</sup>, [Kathleen Hall](#)<sup>1,4</sup>, [Julie A Adsett](#)<sup>5</sup>, [Norman R Morris](#)<sup>2,3,6</sup>

Affiliations expand

- PMID: 35086432
- DOI: [10.1080/09593985.2022.2028326](https://doi.org/10.1080/09593985.2022.2028326)

## Abstract

**Introduction:** Our understanding regarding the personalization of airway clearance techniques (ACTs) in bronchiectasis is limited.

**Objective:** This study aimed to determine physiotherapist perceptions regarding the prescription of ACTs in inpatients and outpatients with bronchiectasis.

**Methods:** A single-center qualitative study using semi-structured interviews of physiotherapists who treated 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. Findings were summarized into major conceptual themes. Participant demographic data was also obtained.

**Results:** Eleven physiotherapists participated in the interviews. Central to all themes was the complexity of physiotherapy clinical decision-making regarding ACT prescription. Main themes included: organizational factors (i.e. workload, scope of service, access to resources/ACTs); patient-related factors (i.e. symptom severity, finances, disease-specific knowledge, social commitments, clinical setting, and perceived benefit); and physiotherapist/profession-related factors (i.e. clinical experience, access to professional support and education, awareness of evidence of ACTs, and evaluating ACT effectiveness).

**Conclusion:** Physiotherapists regularly and routinely prescribe ACTs for individuals with bronchiectasis allowing for a multitude of competing factors. These factors should be considered by physiotherapists to enhance the personalized prescription of ACTs and may help promote patient adherence to ACTs to improve outcomes.

**Keywords:** Physiotherapy; airway clearance techniques; bronchiectasis; physiotherapist perspectives.

- [Cited by 1 article](#)

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