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

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PLoS One

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doi: 10.1371/journal.pone.0286870. eCollection 2023.

## [Video-based teach-to-goal intervention on inhaler technique on adults with asthma and COPD: A randomized controlled trial](#)

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Affiliations expand

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- DOI: [10.1371/journal.pone.0286870](https://doi.org/10.1371/journal.pone.0286870)

## Abstract

**Background:** Incorrect use of inhalers is a problem associated with poor patient outcomes. Despite improvement in the technique after verbal educations, this deteriorates over-time requiring re-enforcement through different educative strategies. This study aimed to assess the impact of a novel video-based teach-to-goal (TTG) educational intervention on: mastery of inhaler technique, disease control, medication adherence and disease-related quality of life (QoL) over-time among asthma and COPD patients.

**Methods:** This prospective, open-label, randomized controlled trial was registered in ClinicalTrials.gov: Identifier [NCT05664347](https://clinicaltrials.gov/ct2/show/NCT05664347). After baseline assessment participants received either a verbal (control group) or a video-based (intervention group) TTG strategy. After 3-month the intervention was assessed for impact on the intended outcomes. Inhaler technique was assessed using standardized checklists, disease control using the Asthma control test and COPD assessment test respectively for asthma and COPD patients while adherence using the Morisky Green Levine scale. For QoL, the mini asthma quality of life questionnaire and the St. George respiratory questionnaire were used for asthmatic and COPD patients, respectively. Differences in outcomes between intervention-control groups were analyzed using either Chi-Square (X<sup>2</sup>)/Fisher Exact or Mann Whitney test. The impact of intervention on outcomes over-time was examined using either McNemar or Wilcoxon test.

**Results:** At baseline, intervention (n = 51) and control (n = 52) groups had comparable demographic/clinical characteristics. At follow-up, inhaler technique improved among intervention group compared to control group (93.4% vs 67%) and to baseline (93.4% to 49.5%), (P<0.05). Similarly, medication adherence ameliorated among the intervention group in comparison to control group (88.2% to 61.5%) and to baseline (88.2% to 66.7%), (P<0.05). In regards to disease control, results showed an amelioration among the intervention group compared to baseline (35.3% to 54.9%) (P<0.05). QoL scores improved significantly among asthma patients (intervention group) at follow-up vs baseline. Better scores were also observed for COPD patients compared to controls, (P<0.05).

**Conclusion:** Video-based (TTG) was effective in enhancing inhaler technique over time as well as improving disease control, medication adherence, and QoL.

**Trial registration:** ClinicalTrials.gov: [NCT05664347](https://clinicaltrials.gov/ct2/show/NCT05664347).  
<https://clinicaltrials.gov/ct2/show/NCT05664347>.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

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Nat Med

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. 2023 Jun 8.

doi: 10.1038/s41591-023-02327-2. Online ahead of print.

# An integrated cell atlas of the lung in health and disease

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Collaborators, Affiliations expand

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## Abstract

Single-cell technologies have transformed our understanding of human tissues. Yet, studies typically capture only a limited number of donors and disagree on cell type definitions. Integrating many single-cell datasets can address these limitations of individual studies and capture the variability present in the population. Here we present the integrated Human Lung Cell Atlas (HLCA), combining 49 datasets of the human respiratory system into a single atlas spanning over 2.4 million cells from 486 individuals. The HLCA presents a consensus cell type re-annotation with matching marker genes, including annotations of rare and previously undescribed cell types. Leveraging the number and diversity of individuals in the HLCA, we identify gene modules that are associated with demographic covariates such as age, sex and body mass index, as well as gene modules changing expression along the proximal-to-distal axis of the bronchial tree. Mapping new data to the HLCA enables rapid data annotation and interpretation. Using the HLCA as a reference for the study of disease, we identify shared cell states across multiple lung diseases, including SPP1<sup>+</sup> profibrotic monocyte-derived macrophages in COVID-19, pulmonary fibrosis and lung carcinoma. Overall, the HLCA serves as an example for the development and use of large-scale, cross-dataset organ atlases within the Human Cell Atlas.

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. 2023 Jun 8;61(6):2300466.

doi: 10.1183/13993003.00466-2023. Print 2023 Jun.

## The GOLD 2023 proposed taxonomy: a new tool to determine COPD etiotypes

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Affiliations expand

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- DOI: [10.1183/13993003.00466-2023](https://doi.org/10.1183/13993003.00466-2023)

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### Conflict of interest statement

Conflict of interest: J.B Soriano and D.D. Sin are current members of the European Respiratory Journal editorial board. J.B Soriano is an associate editor and D.D. Sin is the current deputy chief editor. The remaining authors have nothing to disclose.

### Comment on

- [Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary.](#)  
Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martinez FJ, Montes de Oca M, Mortimer K, Papi A, Pavord I, Roche N, Salvi S, Sin DD, Singh D, Stockley R, López Varela MV, Wedzicha JA, Vogelmeier CF. *Eur Respir J.* 2023 Apr 1;61(4):2300239. doi: 10.1183/13993003.00239-2023. Print 2023 Apr. PMID: 36858443 **Free PMC article.**

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. 2023 Jun 8;2202014.

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# [European Respiratory Society Clinical Practice Guideline: Palliative care for people with chronic obstructive pulmonary disease or interstitial lung disease](#)

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Affiliations expand

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- DOI: [10.1183/13993003.02014-2022](https://doi.org/10.1183/13993003.02014-2022)

## Abstract

There is increased awareness of palliative care needs in people with chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD). This European Respiratory

Society (ERS) task force aimed to provide recommendations for initiation and integration of palliative care into the respiratory care of adult people with COPD or ILD. The ERS task force consisted of 20 members, including representatives of people with COPD or ILD and informal caregivers. Eight questions were formulated, four in the 'Population, Intervention, Comparison, Outcome' (PICO) format. These were addressed with full systematic reviews and application of Grading of Recommendations Assessment, Development and Evaluation (GRADE) for assessing the evidence. Four additional questions were addressed narratively. An 'evidence-to-decision' framework was used to formulate recommendations. The following definition of palliative care for people with COPD or ILD was agreed: A holistic and multidisciplinary, person-centred approach aiming to control symptoms, and improve quality of life of people with serious health-related suffering because of COPD or ILD, and to support their informal caregivers. Recommendations were made regarding people with COPD or ILD and their informal caregivers to: consider palliative care when physical, psychological, social, or existential needs are identified through holistic needs assessment; offer palliative care interventions, including support for informal caregivers, in accordance with such needs; offer advance care planning in accordance with preferences; and integrate palliative care into routine COPD and ILD care. Recommendations should be reconsidered as new evidence becomes available.

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Chronic Obstr Pulm Dis

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. 2023 Jun 7.

doi: 10.15326/jcopdf.2022.0386. Online ahead of print.

## Inhaled Corticosteroids and Risk of Cardiovascular Disease in Chronic Obstructive Pulmonary Disease: A

# Systematic Review and Meta-Regression

[Krish Gadhvi](#)<sup>1</sup>, [Minnah Kandeil](#)<sup>1</sup>, [Dinushan Raveendran](#)<sup>1</sup>, [Jeewoo Choi](#)<sup>1</sup>, [Nia Davies](#)<sup>1</sup>, [AnyaNanchahal](#)<sup>1</sup>, [Oliva Wing](#)<sup>1</sup>, [Jennifer Quint](#)<sup>2</sup>, [Hannah Whittaker](#)<sup>2</sup>

Affiliations expand

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## Abstract

**Background:** Previous studies have reported mixed associations between inhaled corticosteroids (ICS) and cardiovascular disease (CVD) in people with chronic obstructive pulmonary disease (COPD). Using updated literature, we investigated the association between ICS-containing medications and CVD in COPD patients, stratified by study-related factors.

**Methods:** We searched MEDLINE and EMBASE for studies that reported effect estimates for the association between ICS-containing medications and risk of CVD in COPD patients. CVD outcomes specifically included heart failure, myocardial infarction, and stroke-related events. We conducted a random-effects meta-analysis and a meta-regression to identify effect modifying study-related factors.

**Results:** Fifteen studies met inclusion criteria and investigated the association between ICS-containing medications and risk of CVD. Pooled results from our meta-analysis showed a significant association between ICS-containing medication and reduced risk of CVD (HR 0.87, 95% confidence intervals 0.78-0.97). Study follow-up time, non-ICS comparator, and exclusion of patients with previous CVD modified the association between ICS use and risk of CVD.

**Conclusions:** Overall, we found an association between ICS-containing medications and reduced risk of CVD in COPD patients. Results from the meta-regression suggest that subgroups of COPD patients may benefit from ICS use more than others and further work is needed to determine this.

**Keywords:** COPD; cardiovascular disease; inhaled corticosteroids.



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. 2023 Jun 7;32(168):230003.

doi: 10.1183/16000617.0003-2023. Print 2023 Jun 30.

# The role of diet and nutrition in the management of COPD

[Rosanne J H C G Beijers](#)<sup>1</sup>, [Michael C Steiner](#)<sup>2</sup>, [Annemie M W J Schols](#)<sup>3</sup>

Affiliations expand

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- PMCID: [PMC10245132](#)
- DOI: [10.1183/16000617.0003-2023](#)

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## Abstract

In 2014, the European Respiratory Society published a statement on nutritional assessment and therapy in COPD. Since then, increasing research has been performed on the role of diet and nutrition in the prevention and management of COPD. Here, we provide an overview of recent scientific advances and clinical implications. Evidence for a potential role of diet and nutrition as a risk factor in the development of COPD has been accumulating and is reflected in the dietary patterns of patients with COPD. Consuming a healthy diet

should, therefore, be promoted in patients with COPD. Distinct COPD phenotypes have been identified incorporating nutritional status, ranging from cachexia and frailty to obesity. The importance of body composition assessment and the need for tailored nutritional screening instruments is further highlighted. Dietary interventions and targeted single or multi-nutrient supplementation can be beneficial when optimal timing is considered. The therapeutic window of opportunity for nutritional interventions during and recovering from an acute exacerbation and hospitalisation is underexplored.

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## Conflict of interest statement

Conflicts of interest: All authors have no conflicts of interest to declare.

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- doi: [10.1183/16000617.0028-2023](https://doi.org/10.1183/16000617.0028-2023)
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. 2023 Jun 7;32(168):220222.

doi: [10.1183/16000617.0222-2022](https://doi.org/10.1183/16000617.0222-2022). Print 2023 Jun 30.

# Pulmonary rehabilitation and physical interventions

[Thierry Troosters](#)<sup>1,2</sup>, [Wim Janssens](#)<sup>2,3</sup>, [Heleen Demeyer](#)<sup>4,2,5</sup>, [Roberto A Rabinovich](#)<sup>6,7</sup>

Affiliations expand

- PMID: 37286219
- PMCID: [PMC10245142](#)
- DOI: [10.1183/16000617.0222-2022](#)

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## Abstract

Pulmonary rehabilitation has established a status of evidence-based therapy for patients with symptomatic COPD in the stable phase and after acute exacerbations. Rehabilitation should have the possibility of including different disciplines and be offered in several formats and lines of healthcare. This review focusses on the cornerstone intervention, exercise training, and how training interventions can be adapted to the limitations of patients. These adaptations may lead to altered cardiovascular or muscular training effects and/or may improve movement efficiency. Optimising pharmacotherapy (not the focus of this review) and oxygen supplements, whole-body low- and high-intensity training or interval training, and resistance (or neuromuscular electrical stimulation) training are important training modalities for these patients in order to accommodate cardiovascular and ventilatory impairments. Inspiratory muscle training and whole-body vibration may also be worthwhile interventions in selected patients. Patients with stable but symptomatic COPD, those who have suffered exacerbations and patients waiting for or who have received lung volume reduction or lung transplantation are good candidates. The future surely holds promise to further personalise exercise training interventions and to tailor the format of rehabilitation to the individual patient's needs and preferences.

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## Conflict of interest statement

Conflict of interest: None declared.

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Respir Med

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. 2023 Jun 5;107306.

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# Breathlessness and exercise performance to predict mortality in long-term oxygen therapy - The population-based DISCOVERY study

[Filip Björklund](#)<sup>1</sup>, [Andreas Palm](#)<sup>2</sup>, [Jwan Abdulrazak Gorani](#)<sup>3</sup>, [Zainab Ahmadi](#)<sup>4</sup>, [Josefin Sundh](#)<sup>5</sup>, [Jenny Theorell-Haglöw](#)<sup>6</sup>, [Mirjam Ljunggren](#)<sup>7</sup>, [Ludger Grote](#)<sup>8</sup>, [Karin Wadell](#)<sup>9</sup>, [Magnus Ekström](#)<sup>10</sup>

Affiliations expand

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- DOI: [10.1016/j.rmed.2023.107306](https://doi.org/10.1016/j.rmed.2023.107306)

# Abstract

**Background:** Patients with chronic respiratory failure treated with long-term oxygen therapy (LTOT) often have severe breathlessness, impaired exercise performance, and high but variable mortality that is difficult to predict. We aimed to evaluate breathlessness and exercise performance upon starting LTOT as predictors of overall and short-term mortality.

**Methods:** This was a longitudinal, population-based study of patients who initiated LTOT between 2015-2018 in Sweden. Breathlessness was measured using the Dyspnea Exertion Scale, and exercise performance using the 30s-Sit-To-Stand test. Associations with overall and three-month mortality were analyzed using Cox-regression. Subgroup analyses were performed for patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) respectively. The predictive capacity of models was assessed using a C-statistic.

**Results:** A total of 441 patients (57.6% female, aged  $75.4 \pm 8.3$  years) were analyzed, of whom 141 (32%) died during a median follow-up of 260 (IQR 75-460) days. Both breathlessness and exercise performance were independently associated with overall mortality in the crude models, but only exercise performance remained independently associated with overall mortality when models were adjusted for other predictors, when short-term mortality was analyzed, or when breathlessness and exercise capacity were analyzed concurrently. The multivariable model including exercise performance but not breathlessness provided a relatively high predictive capacity for overall mortality, C-statistic 0.756 (95% CI 0.702-0.810). Similar results were seen in the COPD and ILD subgroups.

**Conclusion:** Exercise performance as measured by the 30s-STs may be useful to identify patients with higher mortality on LTOT for optimized management and follow-up.

**Keywords:** Breathlessness; Exercise performance; Long-term oxygen therapy.

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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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Am J Respir Crit Care Med

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doi: 10.1164/rccm.202302-0205LE. Online ahead of print.

# Optimal Threshold of FEV<sub>t</sub>/FVC for Detection of Airflow Limitation Associated with Structural Lung Disease

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Affiliations expand

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*No abstract available*

**Keywords:** Chronic Obstructive Pulmonary Disease; FEV1; Spirometry.

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Sci Transl Med

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doi: 10.1126/scitranslmed.abo7728. Epub 2023 Jun 7.

# Chronic airway epithelial hypoxia exacerbates injury in muco-obstructive lung disease through mucus hyperconcentration

[Yu Mikami](#)<sup>1</sup>, [Barbara R Grubb](#)<sup>1</sup>, [Troy D Rogers](#)<sup>1</sup>, [Hong Dang](#)<sup>1</sup>, [Takanori Asakura](#)<sup>1</sup>, [Pradeep Kota](#)<sup>1</sup>, [Rodney C Gilmore](#)<sup>1</sup>, [Kenichi Okuda](#)<sup>1</sup>, [Lisa C Morton](#)<sup>1</sup>, [Ling Sun](#)<sup>1</sup>, [Gang Chen](#)<sup>1</sup>, [Jason A Wykoff](#)<sup>1</sup>, [Camille Ehre](#)<sup>1,2,3</sup>, [Juan Vilar](#)<sup>1</sup>, [Catharina van Heusden](#)<sup>1</sup>, [Alessandra Livraghi-Butrico](#)<sup>1</sup>, [Martina Gentzsch](#)<sup>1,4,5</sup>, [Brian Button](#)<sup>1</sup>, [M Jackson Stutts](#)<sup>1</sup>, [Scott H Randell](#)<sup>1</sup>, [Wanda K O'Neal](#)<sup>1</sup>, [Richard C Boucher](#)<sup>1</sup>

Affiliations expand

- PMID: 37285404
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## Abstract

Unlike solid organs, human airway epithelia derive their oxygen from inspired air rather than the vasculature. Many pulmonary diseases are associated with intraluminal airway obstruction caused by aspirated foreign bodies, virus infection, tumors, or mucus plugs intrinsic to airway disease, including cystic fibrosis (CF). Consistent with requirements for luminal O<sub>2</sub>, airway epithelia surrounding mucus plugs in chronic obstructive pulmonary disease (COPD) lungs are hypoxic. Despite these observations, the effects of chronic hypoxia (CH) on airway epithelial host defense functions relevant to pulmonary disease have not been investigated. Molecular characterization of resected human lungs from individuals with a spectrum of muco-obstructive lung diseases (MOLDS) or COVID-19 identified molecular features of chronic hypoxia, including increased *EGLN3* expression, in epithelia lining mucus-obstructed airways. In vitro experiments using cultured chronically hypoxic airway epithelia revealed conversion to a glycolytic metabolic state with maintenance of cellular architecture. Chronically hypoxic airway epithelia unexpectedly exhibited increased MUC5B mucin production and increased transepithelial Na<sup>+</sup> and fluid absorption mediated by HIF1α/HIF2α-dependent up-regulation of β and γENaC (epithelial Na<sup>+</sup> channel) subunit expression. The combination of increased Na<sup>+</sup> absorption and MUC5B production generated hyperconcentrated mucus predicted to perpetuate obstruction. Single-cell and bulk RNA sequencing analyses of chronically hypoxic cultured airway epithelia revealed transcriptional changes involved in airway wall remodeling, destruction, and angiogenesis. These results were confirmed by RNA-in situ hybridization studies of lungs from individuals with MOLD. Our data suggest that chronic airway epithelial hypoxia

may be central to the pathogenesis of persistent mucus accumulation in MOLDs and associated airway wall damage.

SUPPLEMENTARY INFO

MeSH termsexpand

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Respir Care

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. 2023 Jun 6;respcare.10132.

doi: 10.4187/respcare.10132. Online ahead of print.

# [A Randomized Study to Compare Response to Bronchodilators Administered via Different Nebulizers in COPD Exacerbations](#)

[Breda Cushen](#)<sup>1</sup>, [Abir Alsaid](#)<sup>2</sup>, [Garrett Greene](#)<sup>3</sup>, [Richard W Costello](#)<sup>4</sup>

Affiliations expand

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- DOI: [10.4187/respcare.10132](https://doi.org/10.4187/respcare.10132)

## Abstract

**Background:** The recommended treatment of COPD exacerbations includes administration of short-acting bronchodilators that act to increase reverse bronchoconstriction, restore lung volumes, and relieve breathlessness. In vitro studies demonstrate vibrating mesh



nebulizers (VMNs) provide greater drug delivery to the airway compared to standard small-volume nebulizers (SVNs). We examined whether the physiological and symptom response to nebulized bronchodilators during a COPD exacerbation differed between these 2 modes of bronchodilator delivery.

**Methods:** Subjects hospitalized with a COPD exacerbation participated in a comparative clinical effectiveness study of 2 methods of nebulization. Using block randomization, 32 participants in this open-label trial were administered salbutamol 2.5 mg/ipratropium bromide 0.5 mg via vibrating mesh (VMN group,  $n = 16$ ) or small-volume jet nebulizer (SVN group,  $n = 16$ ) on one occasion. Spirometry, body plethysmography, and impulse oscillometry were performed and Borg breathlessness scores recorded pre bronchodilator and at 1 h post bronchodilator.

**Results:** Baseline demographics were comparable between groups. Mean FEV<sub>1</sub> was 48% predicted. Significant changes in lung volumes and airway impedance were seen in both groups. Inspiratory capacity (IC) increased by  $0.27 \pm 0.20$  L and  $0.21 \pm 0.20$  L in the VMN and SVN group, respectively, between group difference  $P = .40$ . FVC increased in the VMN group by  $0.41 \pm 0.40$  L compared to  $0.19 \pm 0.20$  L with SVN, between group difference  $P = .053$ ; and residual volume (RV) decreased by  $0.36 \pm 0.80$  L and  $0.16 \pm 0.50$  L in the VMN and SVN group, respectively, between group difference  $P = .41$ . The VMN group had a significant reduction in Borg breathlessness score,  $P = .034$ .

**Conclusions:** Greater improvement in symptoms, and larger absolute change in FVC, was observed in response to equivalent doses of standard bronchodilators administered by VMN, compared to SVN, but no substantial difference in change in IC.

**Keywords:** COPD exacerbation management; bronchodilator delivery; bronchodilator response; exacerbations of COPD; small-volume nebulizer; vibrating mesh nebulizer.

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Observational Study

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doi: 10.1136/bmjopen-2023-071560.

# Mortality and readmission risk for hospitalised patients with acute exacerbation of COPD with and without spirometric obstruction: a longitudinal observational study in China

[Xiaoxia Ren](#)<sup>1,2,3,4</sup>, [Ye Wang](#)<sup>5</sup>, [Ruoxi He](#)<sup>5,6</sup>, [Fen Dong](#)<sup>2,3,4,7</sup>, [Dongyan Liu](#)<sup>8</sup>, [Ting Yang](#)<sup>#9,2,3,4</sup>, [Chen Wang](#)<sup>#9,2,3,4,5</sup>

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**Free article**

## Abstract

**Objective:** To compare the clinical features and outcomes in patients with pre-chronic obstructive pulmonary disease (COPD) and COPD hospitalised for confirmed or suspected acute exacerbation of COPD (AECOPD).

**Design:** A multicentre, longitudinal observational cohort study.

**Setting:** Data were obtained from the AECOPD Inpatient Registry Study in China.

**Participants:** 5896 patients hospitalised for AECOPD between 2017 and 2021.

**Outcomes:** Patients were divided into the COPD (n=5201) and pre-COPD (n=695) groups according to the lung function test results. The outcomes of interest included all-cause, respiratory disease-related and cardiovascular disease-related deaths as well as readmissions within 30 days and 12 months after discharge. Cumulative incidence functions were used to estimate the risk of cause-specific mortality and readmission. Multivariate hazard function models were used to determine the association between lung function and outcomes.

**Results:** There were significant between-group differences in the symptoms at admission and medication use during hospitalisation. However, there was no significant between-group difference in the 30-day all-cause mortality (0.00 vs 2.23/1000 person-month (pm),  $p=0.6110$ ) and readmission (33.52 vs 30.64/1000 pm,  $p=0.7175$ ). Likewise, the 30-day and 12-month cause-specific outcomes were not significantly different between groups (30-day readmission with acute exacerbation (AE): 26.07 vs 25.11/1000 pm; 12-month all-cause mortality: 0.20 vs 0.93/1000 pm; all-cause readmission: 11.49 vs 13.75/1000 pm; readmission with AE: 9.15 vs 11.64/1000 pm,  $p>0.05$  for all comparisons). Cumulative incidence curves revealed no significant between-group differences in the 30-day and 12-month prognosis ( $p>0.05$ ). Multivariate analysis revealed no significant association of lung function categories with 30-day and 12-month mortality or readmission ( $p>0.05$  for all effect estimations).

**Conclusions:** Patients with pre-COPD have mild symptoms and similar risks for mortality and readmission during follow-up as patients with COPD. Patients with pre-COPD should receive optimal therapies before the occurrence of irreversible damage.

**Keywords:** chronic airways disease; epidemiology; respiratory medicine (see thoracic medicine).

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## Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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doi: 10.1002/14651858.CD012066.pub3.

# Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease

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Affiliations expand

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## Abstract

**Background:** Long-acting beta-agonists (LABAs), long-acting muscarinic antagonists (LAMAs), and inhaled corticosteroids (ICSs) are inhaled medications used to manage chronic obstructive pulmonary disease (COPD). When two classes of medications are required, a LAMA plus an ICS (LABA+ICS) were previously recommended within a single inhaler as the first-line treatment for managing stable COPD in people in high-risk categories. However, updated international guidance recommends a LAMA plus a LABA (LAMA+LABA). This systematic review is an update of a Cochrane Review first published in 2017.

**Objectives:** To compare the benefits and harms of LAMA+LABA versus LABA+ICS for treatment of people with stable COPD.

**Search methods:** We performed an electronic search of the Cochrane Airways Group Specialised Register, ClinicalTrials.gov, and the World Health Organization Clinical Trials

Search Portal, followed by handsearches. Two review authors screened the selected articles. The most recent search was run on 10 September 2022.

**Selection criteria:** We included parallel or cross-over randomised controlled trials of at least one month's duration, comparing LAMA+LABA and LABA+ICS for stable COPD. We included studies conducted in an outpatient setting and irrespective of blinding.

**Data collection and analysis:** Two review authors independently extracted data and evaluated risk of bias. We resolved any discrepancies through discussion. We analysed dichotomous data as odds ratios (ORs), and continuous data as mean differences (MDs), with 95% confidence intervals (CIs) using Review Manager 5. Primary outcomes were: participants with one or more exacerbations of COPD; serious adverse events; quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ) total score change from baseline; and trough forced expiratory volume in one second (FEV<sub>1</sub>). We used the GRADE framework to rate our certainty of the evidence in each meta-analysis as high, moderate, low or very low. **MAIN RESULTS:** This review updates the first version of the review, published in 2017, and increases the number of included studies from 11 to 19 (22,354 participants). The median number of participants per study was 700. In each study, between 54% and 91% (median 70%) of participants were males. Study participants had an average age of 64 years and percentage predicted FEV<sub>1</sub> of 51.5% (medians of study means). Included studies had a generally low risk of selection, performance, detection, attrition, and reporting biases. All but two studies were sponsored by pharmaceutical companies, which had varying levels of involvement in study design, conduct, and data analysis. **Primary outcomes** The odds of having an exacerbation were similar for LAMA+LABA compared with LABA+ICS (OR 0.91, 95% CI 0.78 to 1.06;  $I^2 = 61\%$ ; 13 studies, 20,960 participants; moderate-certainty evidence). The odds of having a serious adverse event were also similar (OR 1.02, 95% CI 0.91 to 1.15;  $I^2 = 20\%$ ; 18 studies, 23,183 participants; high-certainty evidence). Participants receiving LAMA+LABA had a similar improvement in quality of life, as measured by the SGRQ, to those receiving LABA+ICS (MD -0.57, 95% CI -1.36 to 0.21;  $I^2 = 78\%$ ; 9 studies, 14,437 participants; moderate-certainty evidence) but showed a greater improvement in trough FEV<sub>1</sub> (MD 0.07, 95% CI 0.05 to 0.08;  $I^2 = 73\%$ ; 12 studies, 14,681 participants; moderate-certainty evidence). **Secondary outcomes** LAMA+LABA decreased the odds of pneumonia compared with LABA+ICS from 5% to 3% (OR 0.61, 95% CI 0.52 to 0.72;  $I^2 = 0\%$ ; 14 studies, 21,829 participants; high-certainty evidence) but increased the odds of all-cause death from 1% to 1.4% (OR 1.35, 95% CI 1.05 to 1.75;  $I^2 = 0\%$ ; 15 studies, 21,510 participants; moderate-certainty evidence). The odds of achieving a minimal clinically important difference of four or more points on the SGRQ were similar between LAMA+LABA and LABA+ICS (OR 1.06, 95% CI 0.90 to 1.25;  $I^2 = 77\%$ ; 4 studies, 13,614 participants; moderate-certainty evidence).

**Authors' conclusions:** Combination LAMA+LABA therapy probably holds similar benefits to LABA+ICS for exacerbations and quality of life, as measured by the St George's Respiratory Questionnaire, for people with moderate to severe COPD, but offers a larger improvement in FEV<sub>1</sub> and a slightly lower risk of pneumonia. There is little to no difference between LAMA+LABA and LABA+ICS in the odds of having a serious adverse event. Whilst

all-cause death may be lower with LABA+ICS, there was a very small number of events in the analysis, translating to a low absolute risk. Findings are based on moderate- to high-certainty evidence from heterogeneous trials with an observation period of less than one year. This review should be updated again in a few years.

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## Conflict of interest statement

NF: none known. NH: personally received a lecture fee from AstraZeneca. AK: none known. AG: none known. TK: acted as an independent contractor, with monies paid to institution, for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis. TK also received grants with monies paid to host institution from Boehringer Ingelheim and Novartis. EO: none known. KK: worked as a freelance editor with Cochrane Airways at the time of writing but was not involved in the editorial process for this review.

## Update of

- [Long-acting muscarinic antagonist \(LAMA\) plus long-acting beta-agonist \(LABA\) versus LABA plus inhaled corticosteroid \(ICS\) for stable chronic obstructive pulmonary disease \(COPD\).](#)  
Horita N, Goto A, Shibata Y, Ota E, Nakashima K, Nagai K, Kaneko T. *Cochrane Database Syst Rev.* 2017 Feb 10;2(2):CD012066. doi: 10.1002/14651858.CD012066.pub2. PMID: 28185242 **Free PMC article. Updated.** Review.

SUPPLEMENTARY INFO

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# Airway–Occluding Mucus Plugs and Mortality in Patients With Chronic Obstructive Pulmonary Disease

[Alejandro A Diaz](#)<sup>1,2</sup>, [José L Orejas](#)<sup>1,2</sup>, [Scott Grumley](#)<sup>3</sup>, [Hrudaya P Nath](#)<sup>3</sup>, [Wei Wang](#)<sup>2,4</sup>, [Wojciech R Dolliver](#)<sup>1</sup>, [Andrew Yen](#)<sup>5</sup>, [Seth J Kligerman](#)<sup>5,6</sup>, [Kathleen Jacobs](#)<sup>5</sup>, [Padma P Manapragada](#)<sup>3</sup>, [Mostafa Abozeed](#)<sup>3</sup>, [Muhammad Usman Aziz](#)<sup>3</sup>, [Mohd Zahid](#)<sup>3</sup>, [Asmaa N Ahmed](#)<sup>3</sup>, [Nina L Terry](#)<sup>3</sup>, [Ruben San José Estépar](#)<sup>2,7</sup>, [Victor Kim](#)<sup>8</sup>, [Barry J Make](#)<sup>9</sup>, [MeiLan K Han](#)<sup>10</sup>, [Sushilkumar Sonavane](#)<sup>11</sup>, [George R Washko](#)<sup>1,2</sup>, [Michael Cho](#)<sup>1,2,12</sup>, [Raúl San José Estépar](#)<sup>2,7</sup>

Affiliations expand

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## Abstract

**Importance:** Airway mucus plugs are common in patients with chronic obstructive pulmonary disease (COPD); however, the association of airway mucus plugging and mortality in patients with COPD is unknown.

**Objective:** To determine whether airway mucus plugs identified on chest computed tomography (CT) were associated with increased all-cause mortality.

**Design, setting, and participants:** Observational retrospective analysis of prospectively collected data of patients with a diagnosis of COPD in the Genetic Epidemiology of COPD cohort. Participants were non-Hispanic Black or White individuals, aged 45 to 80 years, who smoked at least 10 pack-years. Participants were enrolled at 21 centers across the US between November 2007 and April 2011 and were followed up through August 31, 2022.

**Exposures:** Mucus plugs that completely occluded airways on chest CT scans, identified in medium- to large-sized airways (ie, approximately 2- to 10-mm lumen diameter) and categorized as affecting 0, 1 to 2, or 3 or more lung segments.

**Main outcomes and measures:** The primary outcome was all-cause mortality, assessed with proportional hazard regression analysis. Models were adjusted for age, sex, race and ethnicity, body mass index, pack-years smoked, current smoking status, forced expiratory volume in the first second of expiration, and CT measures of emphysema and airway disease.

**Results:** Among the 4483 participants with COPD, 4363 were included in the primary analysis (median age, 63 years [IQR, 57-70 years]; 44% were women). A total of 2585 (59.3%), 953 (21.8%), and 825 (18.9%) participants had mucus plugs in 0, 1 to 2, and 3 or more lung segments, respectively. During a median 9.5-year follow-up, 1769 participants (40.6%) died. The mortality rates were 34.0% (95% CI, 32.2%-35.8%), 46.7% (95% CI, 43.5%-49.9%), and 54.1% (95% CI, 50.7%-57.4%) in participants who had mucus plugs in 0, 1 to 2, and 3 or more lung segments, respectively. The presence of mucus plugs in 1 to 2 vs 0 and 3 or more vs 0 lung segments was associated with an adjusted hazard ratio of death of 1.15 (95% CI, 1.02-1.29) and 1.24 (95% CI, 1.10-1.41), respectively.

**Conclusions and relevance:** In participants with COPD, the presence of mucus plugs that obstructed medium- to large-sized airways was associated with higher all-cause mortality compared with patients without mucus plugging on chest CT scans.

## Conflict of interest statement

Conflict of Interest Disclosures: Dr Cho reported receiving grants from Bayer. Dr Diaz reported receiving personal fees from Boehringer Ingelheim and having a patent for Methods and Compositions Relating to Airway Dysfunction pending (701586-190200USPT). Dr Terry reported that she and/or her husband are general stockholders with no controlling interest in the following: Johnson & Johnson, Kimberly-Clark Corp, Microsoft Corp, Amgen Inc, Bristol Myers Squibb, Cisco Systems Inc, Medtronic, Merck & Co Inc, Procter & Gamble, Crispr Therapeutics, Nvidia, Texas Instruments, Hewlett Packard, United Health, Abbott Labs, Eli Lilly and Co, AbbVie Inc, and LyondellBasell Industries. Mr Ruben San José Estépar reported receiving grants from the National Institutes of Health (NIH) during the conduct of the study. Dr Kim reported receiving personal fees from Gala Therapeutics, the American Board of Internal Medicine critical care test writing committee, AstraZeneca, and Boehringer Ingelheim. Dr Make reported receiving grants from National Heart, Lung, and Blood Institute provided to and controlled by National Jewish Health; fees for CME activity from the American College of Chest Physicians, Eastern Pulmonary Conference, Integrity Communications, Novartis, Pri-Med, Projects in Knowledge, and WebMD; grants from the American Lung Association, AstraZeneca, and Department of Defense paid to National Jewish Health; and royalties from Wolters Kluwer Health. Dr Make also reported serving on the data and safety monitoring board for Baystate Medical Center, Quintiles Laboratories, Spiration, and the University of Wisconsin; medical advisory board for Boehringer Ingelheim and Mylan; advisory board for GlaxoSmithKline and Mount Sinai; as a consultant for Optimum Patient Care Global and Third Pole Therapeutics; and on committees for the RECOVER trial. Dr Han reported receiving grants from the NIH and



COPD Foundation and personal fees from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, Novartis, Pulmonx, Teva Pharmaceutical Industries, Verona Pharma, Merck, Mylan, Sanofi, DevPro Biopharma, Aerogen, Polarian, Regeneron, Amgen, UpToDate, Altesa Biopharma, Medscape, National Association of Colleges and Employers, MDBriefCase, and Integrity; research support paid to the institution from the NIH, Novartis, Sunovion, Nuvaire, Sanofi, AstraZeneca, Boehringer Ingelheim, Gala Therapeutics, Biodesix, the COPD Foundation, and the American Lung Association; data and safety monitoring board funds paid to the institution from Novartis and Medtronic; and stock options from Meissa Vaccines and Altesa BioSciences. Dr Washko reported receiving personal fees from Actelion, Vertex Pharmaceuticals, Intellia Therapeutics, and Janssen Pharmaceuticals; grants from the Department of Defense and Boehringer Ingelheim; and support from Pulmonx, Janssen Pharmaceuticals, and CSL Behring; and is a co-founder of Quantitative Imaging Solutions, a company focused on image analytics and software development. Dr Washko's spouse is an employee of Biogen. Dr Raúl San José Estépar reported being a founder and equity holder of Quantitative Imaging Solutions and receiving grants from Boehringer Ingelheim, contracts to serve as image core from Insmed and Lung Biotechnology; and personal fees from LeukoLab and Chiesi. No other disclosures were reported.

#### SUPPLEMENTARY INFO

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. 2023 Jun 8;76(11):1980-1988.

doi: 10.1093/cid/ciad031.

## [Prevalence and Clinical Outcomes of Respiratory Syncytial Virus vs Influenza in Adults Hospitalized With Acute](#)

# Respiratory Illness From a Prospective Multicenter Study

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Affiliations expand

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- PMCID: [PMC10250013](#)
- DOI: [10.1093/cid/ciad031](#)

**Free PMC article**

## Abstract

**Background:** Current understanding of severe respiratory syncytial virus (RSV) infections in adults is limited by clinical underrecognition. We compared the prevalence, clinical characteristics, and outcomes of RSV infections vs influenza in adults hospitalized with acute respiratory illnesses (ARIs) in a prospective national surveillance network.

**Methods:** Hospitalized adults who met a standardized ARI case definition were prospectively enrolled across 3 respiratory seasons from hospitals participating across all sites of the US Hospitalized Adult Influenza Vaccine Effectiveness Network (2016-2019). All participants were tested for RSV and influenza using real-time reverse-transcription polymerase chain reaction assay. Multivariable logistic regression was used to test associations between laboratory-confirmed infection and characteristics and clinical outcomes.

**Results:** Among 10 311 hospitalized adults, 6% tested positive for RSV (n = 622), 18.8% for influenza (n = 1940), and 75.1% negative for RSV and influenza (n = 7749). Congestive heart failure (CHF) or chronic obstructive pulmonary disease (COPD) was more frequent with RSV than influenza (CHF: 37.3% vs 28.8%, P < .0001; COPD: 47.6% vs 35.8%, P < .0001). Patients with RSV more frequently had longer admissions (odds ratio [OR], 1.38; 95% confidence interval [CI], 1.06-1.80) for stays >1 week) and mechanical ventilation (OR,

1.45; 95% CI, 1.09-1.93) compared with influenza but not compared with the influenza-negative group (OR, 1.03; 95% CI, .82-1.28 and OR, 1.17; 95% CI, .91-1.49, respectively).

**Conclusions:** The prevalence of RSV across 3 seasons was considerable. Our findings suggest that those with RSV have worse outcomes compared with influenza and frequently have cardiopulmonary conditions. This study informs future vaccination strategies and underscores a need for RSV surveillance among adults with severe ARI.

**Keywords:** adults; hospitalization; influenza; respiratory syncytial virus.

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## Conflict of interest statement

Potential conflicts of interest. L. E. L. reports grant support paid to institution from the CDC and funding from Janssen Scientific Affairs paid to institution. E. T. M. reports institutional grant support from the CDC, CDC-Abt Associates, and Merck and grants or contracts unrelated to this work from the NIH, Merck, and FluLab. A. N. M reports a role as member of the Society of Healthcare Epidemiology of America Board of Trustees. F. P. S. reports a research grant paid to institution and unrelated to this work from Ansun and payment to author for honoraria for lectures, presentations, speakers bureaus, manuscript writing, or education events from Janssen. M. J. G. reports institutional grant support or contracts from the CDC; funding from the CDC, CDC-Abt Associates, MedImmune, Janssen, and Pfizer; and a role as co-chair of the Infectious Diseases and Immunization Committee and as chair of the Texas RSV Taskforce for the Texas Pediatric Society, Texas Chapter of American Academy of Pediatrics. A. S. L. reports grants or contracts unrelated to this work from the CDC, Burroughs Wellcome Fund, and National Institute of Allergy and Infectious Diseases (NIAID) and consulting fees from Sanofi and from Roche as a paid member of the baloxavir trial steering committee. R. K. Z. reports a research grant to their university from Sanofi Pasteur. D. B. M. reports consulting fees (advisory group payment to author) from Moderna, Seqirus, Sanofi Pasteur, Novavax, and Valneva and lecture payment to author from Merck and Pfizer. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

SUPPLEMENTARY INFO

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

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J Gerontol B Psychol Sci Soc Sci

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. 2023 Jun 9;gbad087.

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## Chronic Stress and Latent Virus Reactivation: Effects on Immune Aging, Chronic Disease Morbidity, and Mortality

[Eric T Klopak](#)<sup>1</sup>

Affiliations expand

- PMID: 37294880
- DOI: [10.1093/geronb/gbad087](https://doi.org/10.1093/geronb/gbad087)

### Abstract

**Objectives:** Social stress has been shown to affect immune functioning. Past research has found that chronic social stress and latent viral infections accelerate immune aging, leading to chronic disease morbidity and mortality. Chronic stress may also reactivate latent viral infections, like cytomegalovirus (CMV), accelerating the aging of the immune system.

**Method:** Utilizing panel survey data from 8995 US adults aged 56 or older from the Health and Retirement Study (HRS), this study investigates whether chronic stress interacts with CMV positivity to drive aging of the immune system, multi-morbidity, and mortality.

**Results:** Results of moderated mediation analysis indicate that the effect of CMV positivity on morbidity and mortality as mediated by immune aging indicators is amplified by chronic stress.

**Discussion:** These findings suggest that immune aging is a biological pathway underlying the stress process and help explain past findings in the literature on stress and health.

**Keywords:** Cytomegalovirus; Health and Retirement Study; Immunosenescence.

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BMC Pulm Med

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. 2023 Jun 8;23(1):200.

doi: 10.1186/s12890-023-02497-2.

## [Incidence and risk factors of pneumococcal pneumonia in adults: a population-based study](#)

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- PMID: 37291502
- DOI: [10.1186/s12890-023-02497-2](#)

# Abstract

**Background:** Infection caused by *Streptococcus pneumoniae*, mainly invasive pneumococcal disease (IPD) and pneumococcal pneumonia (PP), are a major public health problem worldwide. This study investigated population-based incidence and risk of PP among Catalanian persons  $\geq 50$  years-old with and without specific underlying conditions/comorbidities, examining the influence of single and multi-comorbidities in the risk of suffering PP.

**Methods:** Population-based cohort study involving 2,059,645 persons  $\geq 50$  years-old in Catalonia, Spain, who were retrospectively followed between 01/01/2017-31/12/2018. The Catalanian information system for development of research in primary care (SIDIAP) was used to establish baseline characteristics of the cohort (comorbidities/underlying conditions), and PP cases were collected from discharge codes (ICD-10: J13) of the 68 referral Catalanian hospitals.

**Results:** Global incidence rate (IR) was 90.7 PP cases per 100,000 person-years, with a 7.6% (272/3592) case-fatality rate (CFR). Maximum IRs emerged among persons with history of previous IPD or all-cause pneumonia, followed by haematological neoplasia (475.0), HIV-infection (423.7), renal disease (384.9), chronic respiratory disease (314.7), liver disease (232.5), heart disease (221.4), alcoholism (204.8), solid cancer (186.2) and diabetes (159.6). IRs were 42.1, 89.9, 201.1, 350.9, 594.3 and 761.2 in persons with 0, 1, 2, 3, 4 and  $\geq 5$  comorbidities, respectively. In multivariable analyses, HIV-infection (hazard ratio [HR]: 5.16; 95% CI: 3.57-7.46), prior all-cause pneumonia (HR: 3.96; 95% CI: 3.45-4.55), haematological neoplasia (HR: 2.71; 95% CI: 2.06-3.57), chronic respiratory disease (HR: 2.66; 95% CI: 2.47-2.86) and prior IPD (HR: 2.56; 95% CI: 2.03-3.24) were major predictors for PP.

**Conclusion:** Apart of increasing age and immunocompromising conditions (classically recognised as high-risk conditions), history of prior IPD/pneumonia, presence of chronic pulmonary/respiratory disease and/or co-existing multi-comorbidity (i.e., two or more underlying conditions) are major risk factors for PP in adults, with an excess risk near to immunocompromised subjects. Redefining risk categories for PP, including all the above-mentioned conditions into the high-risk category, could be necessary to improve prevention strategies in middle-aged and older adults.

**Keywords:** Adults; Incidence; Multimorbidity; Pneumococcal pneumonia; Risk factors.

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. 2023 Jun 8.

doi: 10.1038/s41432-023-00903-6. Online ahead of print.

# Is periodontitis associated with the risk of immune-mediated systemic conditions?

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Affiliations [expand](#)

- PMID: 37291451
- DOI: [10.1038/s41432-023-00903-6](https://doi.org/10.1038/s41432-023-00903-6)

## Abstract

**Aim:** This study evaluates the long-term risk of immune-mediated systemic conditions in individuals with periodontitis compared to those without.

**Data sources:** A structured online search was conducted in Medline, Cochrane library, and EMBASE using MeSH terms. All the databases were explored from initiation to June 2022. Reference lists of the eligible studies were hand searched as well.

**Study selection:** Peer-reviewed longitudinal retrospective/prospective cohorts and randomized controlled trials comparing incident metabolic/autoimmune/inflammatory diseases in periodontitis to healthy individuals were deemed eligible. Only studies with a minimum follow-up of one year were included.

**Data extraction and synthesis:** The authors checked demographics, data source, exclusion/inclusion criteria, total follow-up duration, disease outcome, and limitations to determine the eligible studies. After assessing the risk of bias for the included studies using the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool, the authors used the following measures to quantify the disease outcome: relative risk (RR), odds ratio (OR), and hazard ratio (HR). Systemic conditions were categorized as immune-mediated via disrupted metabolic networks (diabetes, kidney disease, liver disease, metabolic syndrome) or chronic inflammation (inflammatory bowel disease, osteoporosis, RA, psoriasis, Sjogren's syndrome), hence recognized as metabolic or autoimmune/inflammatory diseases, respectively. A random effect meta-analysis was used to synthesize the risk of developing each disease. The authors performed subgroup analysis for periodontitis diagnosis type (self-report/clinically diagnosed) and severity. They also conducted a sensitivity analysis to assess the effect of removing studies that did not adjust for smoking status.

**Results:** From 3354 studies, 166 full texts were screened. Finally, 30 studies were deemed eligible for the systematic review, of which 27 made it to the meta-analysis. The risks of diabetes, rheumatoid arthritis (RA) and osteoporosis were increased in individuals with periodontitis compared to those without periodontitis (diabetes-relative risk [RR]: 1.22, 95% CI: 1.13-1.33; RA-RR: 1.27, 95% CI: 1.07-1.52; osteoporosis-RR: 1.40, 95% CI: 1.12-1.75). The risk of diabetes showed a gradient increase by periodontitis severity (moderate-RR = 1.20, 95% CI = 1.11-1.31; severe-RR = 1.34, 95% CI = 1.10-1.63).

**Conclusions:** People with moderate-to-severe periodontitis have the highest risk of developing diabetes. In contrast, the effect of periodontal severity on the risk of other immune-mediated systemic conditions requires further investigation. More homologous evidence is needed to assess the periodontitis-multimorbidity association further.

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Int Arch Allergy Immunol

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. 2023 Jun 8;1-11.

doi: 10.1159/000530842. Online ahead of print.

# Analysis of Multimorbidity of Moderate to Severe Allergic Rhinitis in Children: A Real-World Study

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Affiliations expand

- PMID: 37290409
- DOI: [10.1159/000530842](https://doi.org/10.1159/000530842)

## Abstract

**Introduction:** Allergic rhinitis (AR) in children is associated with various comorbidities, posing challenges for treatment and management. There have been few investigations of these multimorbidities in Chinese children with AR. Here, we investigated the prevalence of multimorbidities in children with moderate to severe AR and analyzed the influencing factors using real-world data.

**Methods:** In total, 600 children who visited the outpatient clinic of our hospital and were diagnosed with moderate-severe AR were prospectively enrolled. All children underwent allergen detection and electronic nasopharyngoscopy. Parents or guardians completed a questionnaire that included age, sex, mode of delivery, feeding pattern, and familial history of allergy. The multimorbidities investigated included atopic dermatitis (AD), asthma, allergic conjunctivitis (AC), chronic rhinosinusitis (CRS), adenoid hypertrophy (AH), tonsil hypertrophy (TH), recurrent epistaxis, and recurrent respiratory tract infections (RRTIs).

**Results:** The AR multimorbidities reported in children were as follows: recurrent epistaxis (46.5%), AC (46.3%), AD (40.7%), asthma (22.5%), RRTIs (21.3%), CRS (20.5%), AH (19.7%),

and TH (12.5%). In univariate logistic regression analysis, age ( $\leq 6$  years), birth mode, familial history of allergy, and single dust mite allergy were associated with AR multimorbidity ( $p < 0.05$ ). Multivariate logistic regression revealed that a familial history of allergy was an independent risk factor for AC (odds ratio [OR] = 1.539, 95% confidence interval [CI]: 1.104-2.145) and AH (OR = 1.506, 95% CI: 1.000-2.267) ( $p < 0.05$ ). Age ( $\leq 6$  years) was independently associated with the risk of AD (OR = 1.405, 95% CI: 1.003-1.969) and RRTIs (OR = 1.869, 95% CI: 1.250-2.793) ( $p < 0.05$ ), cesarean section with AR and CRS risk (OR = 1.678, 95% CI: 1.100-2.561), and single dust mite allergy with asthma (OR = 1.590, 95% CI: 1.040-2.432) and CRS (OR = 1.600, 95% CI: 1.018-2.515) risk ( $p < 0.05$ ). Further, non-dust mite allergy was independently associated with AR and CRS (OR = 2.056, 95% CI: 1.084-3.899).

**Conclusion:** AR was found to be accompanied by different comorbidities, including both allergic and non-allergic comorbidities, complicating disease treatment. These findings demonstrated that age ( $\leq 6$  years), familial history of allergy, types of allergens, and cesarean section were risk factors for different multimorbidities associated with AR.

**Keywords:** Allergic rhinitis; Child; Multimorbidity; Prevalence; Risk factor.

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. 2023 Jun 8;32(11):S15-S21.

doi: 10.12968/bjon.2023.32.11.S15.

# Co-designing health services for people living with HIV who have multimorbidity: a feasibility study

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Affiliations expand

- PMID: 37289710
- DOI: [10.12968/bjon.2023.32.11.S15](https://doi.org/10.12968/bjon.2023.32.11.S15)

## Abstract

This study explored the feasibility of using an experience-based co-design service improvement methodology to develop a new approach to managing multimorbidity in people living with HIV. Patients with HIV and multimorbidity and staff were recruited from five hospital departments and general practice. Staff and patient experiences were gathered through semi-structured interviews, filmed patient interviews, non-participant observation and patient diaries. A composite film developed from interviews illustrated the touchpoints in the patient journey, and priorities for service improvement were identified by staff and patients in focus groups. Twenty-two people living with HIV and 14 staff took part. Four patients completed a diary and 10 a filmed interview. Analysis identified eight touchpoints, and group work pinpointed three improvement priorities: medical records and information sharing; appointment management; and care co-ordination and streamlining. This study demonstrates that experience-based co-design is feasible in the context of HIV and can inform healthcare improvement for people with multimorbidity.

**Keywords:** Experience-based co-design; HIV; Healthcare improvement; Multimorbidity.

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# What can death records tell us about multimorbidity?

[Mohammad Reza Baneshi](#)<sup>1</sup>, [James Eynstone-Hinkins](#)<sup>2</sup>, [Paul McElwee](#)<sup>1</sup>, [Gita D Mishra](#)<sup>1</sup>, [Lauren Moran](#)<sup>2</sup>, [Michael Waller](#)<sup>1</sup>, [Annette Dobson](#)<sup>3</sup>

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- PMID: 37286346
- DOI: [10.1136/jech-2023-220654](https://doi.org/10.1136/jech-2023-220654)

## Abstract

**Background:** Multimorbidity has been measured from many data sources which show that prevalence increases with age and is usually greater among women than men and in more recent periods. Analyses of multiple cause of death data have shown different patterns of multimorbidity associated with demographic and other characteristics.

**Methods:** Deaths in Australia among over 1.7 million decedents aged 55+ were stratified into three types: medically certified deaths, coroner-referred deaths with natural underlying causes and coroner-referred deaths with external underlying causes. Multimorbidity was measured by prevalence of  $\geq 2$  causes and analysed over three periods based on administrative changes: 2006-2012, 2013-2016 and 2017-2018. Poisson regression was used to examine the influence of gender, age and period.

**Results:** The prevalence of deaths with multimorbidity was 81.0% for medically certified deaths, 61.1% for coroner-referred deaths with natural underlying causes and 82.4% for coroner-referred deaths with external underlying causes. For medically certified deaths, multimorbidity increased with age: incidence rate ratio (IRR 1.070, 95% CI 1.068, 1.072) was lower for women than men (0.954, 95% CI 0.952, 0.956) and changed little over time. For coroner-referred deaths with natural underlying causes, multimorbidity showed the expected pattern increasing with age (1.066, 95% CI 1.062, 1.070) and being higher for

women than men (1.025, 95% CI 1.015, 1.035) and in more recent periods. For coroner-referred deaths with external underlying causes, there were marked increases over time that differed by age group due to changes in coding processes.

**Conclusion:** Death records can be used to examine multimorbidity in national populations but, like other data sources, how the data were collected and coded impacts the conclusions.

**Keywords:** DEATH; DEATH CERTIFICATES; MORBIDITY.

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## Conflict of interest statement

Competing interests: None declared.

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J Am Geriatr Soc

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. 2023 Jun 7.

doi: 10.1111/jgs.18465. Online ahead of print.

## [Overtreatment and associated risk factors among multimorbid older patients with diabetes](#)

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Affiliations [expand](#)

- PMID: 37286338
- DOI: [10.1111/jgs.18465](https://doi.org/10.1111/jgs.18465)

## Abstract

**Background:** In multimorbid older patients with type 2 diabetes mellitus (T2DM), the intensity of glucose-lowering medication (GLM) should be focused on attaining a suitable level of glycated hemoglobin (HbA<sub>1c</sub>) while avoiding side effects. We aimed at identifying patients with overtreatment of T2DM as well as associated risk factors.

**Methods:** In a secondary analysis of a multicenter study of multimorbid older patients, we evaluated HbA<sub>1c</sub> levels among patients with T2DM. Patients were aged  $\geq 70$  years, with multimorbidity ( $\geq 3$  chronic diagnoses) and polypharmacy ( $\geq 5$  chronic medications), enrolled in four university medical centers across Europe (Belgium, Ireland, Netherlands, and Switzerland). We defined overtreatment as HbA<sub>1c</sub>  $< 7.5\%$  with  $\geq 1$  GLM other than metformin, as suggested by Choosing Wisely and used prevalence ratios (PRs) to evaluate risk factors of overtreatment in age- and sex-adjusted analyses.

**Results:** Among the 564 patients with T2DM (median age 78 years, 39% women), mean  $\pm$  standard deviation HbA<sub>1c</sub> was  $7.2 \pm 1.2\%$ . Metformin (prevalence 51%) was the most frequently prescribed GLM and 199 (35%) patients were overtreated. The presence of severe renal impairment (PR 1.36, 1.21-1.53) and outpatient physician (other than general practitioner [GP], i.e. specialist) or emergency department visits (PR 1.22, 1.03-1.46 for 1-2 visits, and PR 1.35, 1.19-1.54 for  $\geq 3$  visits versus no visits) were associated with overtreatment. These factors remained associated with overtreatment in multivariable analyses.

**Conclusions:** In this multicountry study of multimorbid older patients with T2DM, more than one third were overtreated, highlighting the high prevalence of this problem. Careful balancing of benefits and risks in the choice of GLM may improve patient care, especially in the context of comorbidities such as severe renal impairment, and frequent non-GP healthcare contacts.

**Keywords:** HbA<sub>1c</sub>; glucose-lowering medication; multimorbidity; polypharmacy; type 2 diabetes mellitus.

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. 2023 Jun 7;18(6):e0286401.

doi: 10.1371/journal.pone.0286401. eCollection 2023.

# [Geographical specific association between lifestyles and multimorbidity among adults in China](#)

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Affiliations expand

- PMID: 37285342
- PMCID: [PMC10246811](#)

- DOI: [10.1371/journal.pone.0286401](https://doi.org/10.1371/journal.pone.0286401)

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## Abstract

The relationship between lifestyles and multimorbidity is well established, but previous studies have often neglected the role of spatial heterogeneity. Thus, this study is the first to explore this association in Chinese adults from a spatial perspective using a geographically weighted logistic regression (GWLR) model and describe the geographical characteristics across different regions. According to 2018 China Health and Retirement Longitudinal Study (CHARLS) database, a total of 7101 subjects were finally included, with 124 prefecture-level administrative regions in China. Non-spatial and GWLR model were used for analysis, and gender stratification analysis was also performed. Data were visualized through ArcGIS 10.7. The results showed that a total prevalence of approximately 5.13% of multimorbidity, and among participants with multimorbidity, the separate prevalence of hypertension, diabetes or high blood sugar, heart disease, and stroke were 4.45%, 2.32%, 3.02%, and 1.41%, respectively. The GWLR model indicated that current (OR: 1.202-1.220) and former smokers (OR: 1.168-1.206) may be important risk factors for multimorbidity in adults, especially in north and west among male. Past drinkers (OR: 1.233-1.240), especially in eastern China, contribute to the development of the multimorbidity in men but not in women. Vigorous-intensity activities (OR: 0.761-0.799) were negatively associated with multimorbidity in the west, with no gender difference. Depression (OR: 1.266-1.293) appeared to increase the risk for multimorbidity, with the weakest effects in central China and no gender difference. There was an interaction between light activities and gender ( $P = 0.024$ ). The prevalence of multimorbidity differed across various areas of the province. The role of geographical variations in lifestyles and multimorbidity may provide valuable information for developing site-specific intervention strategies.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

- [39 references](#)
- [11 figures](#)

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Cancer Med



. 2023 Jun 7.

doi: 10.1002/cam4.6204. Online ahead of print.

# [Financial well-being as a mediator of the relationship between multimorbidity and health-related quality of life in people with cancer](#)

[Winnie K W So](#)<sup>1</sup>, [Doreen W H Au](#)<sup>1,2</sup>, [Dorothy N S Chan](#)<sup>1</sup>, [Marques S N Ng](#)<sup>1</sup>, [Kai Chow Choi](#)<sup>1</sup>, [Weijie Xing](#)<sup>3</sup>, [Mandy Chan](#)<sup>4</sup>, [Suzanne S S Mak](#)<sup>4</sup>, [Pui Shan Ho](#)<sup>5</sup>, [Man Tong](#)<sup>5</sup>, [Cecilia Au](#)<sup>6</sup>, [Wai Man Ling](#)<sup>6</sup>, [Maggie Chan](#)<sup>7</sup>, [Raymond J Chan](#)<sup>8</sup>

Affiliations expand

- PMID: 37283252
- DOI: [10.1002/cam4.6204](https://doi.org/10.1002/cam4.6204)

**Free article**

## Abstract

**Background:** It is unknown whether financial well-being mediates the impact of multimorbidity on the health-related quality of life (HRQoL) of cancer patients.

**Methods:** Participants were recruited from three outpatient oncology clinics of Hong Kong public hospitals. Multimorbidity was assessed using the Charlson Comorbidity Index. Financial well-being, the mediator of the association between multimorbidity and HRQoL outcomes, was assessed using the Comprehensive Score for Financial Toxicity Functional Assessment of Chronic Illness Therapy. The HRQoL outcomes were assessed using the Functional Assessment of Cancer Therapy - General (FACT-G) and its four sub-dimensions. Mediation analyses were conducted using SPSS PROCESS v4.1.

**Results:** Six-hundred and forty cancer patients participated in the study. Multimorbidity had a direct effect on FACT-G scores independent of financial well-being ( $\beta$  for path  $c'$  = -0.752,  $p < 0.001$ ). In addition, multimorbidity had an indirect effect on FACT-G scores through its effect on financial well-being ( $\beta$  for path  $a$  = -0.517,  $p < 0.05$ ;  $\beta$  for path  $b$  = 0.785,  $p < 0.001$ ). Even after adjustments were made for the covariates, the indirect effect of multimorbidity on FACT-G via financial well-being remained significant, accounting for 38.0% of the overall effect, indicating partial mediation. Although there were no statistically significant associations between multimorbidity, social well-being, and emotional well-being, the indirect effects of multimorbidity on physical and functional well-being through financial well-being remained significant.

**Conclusions:** Poor financial well-being attributable to multimorbidity partially mediates the direct impact of chronic conditions on HRQoL in Chinese cancer patients, particularly their physical and functional well-being.

**Keywords:** cancer patients; financial well-being; multimorbidity; quality of life.

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Geriatr Gerontol Int

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. 2023 Jun 7.

doi: 10.1111/ggi.14616. Online ahead of print.

# Effect of drugs on nutritional status and drug-nutrition interactions in older patients

[Masafumi Kuzuya](#)<sup>1</sup>

Affiliations expand

- PMID: 37282980
- DOI: [10.1111/ggi.14616](https://doi.org/10.1111/ggi.14616)

## Abstract

Older patients are prone to multimorbidity or related polypharmacy, which may cause various adverse drug reactions (ADRs) and a high incidence of drug-related health problems. Although not often noted, ADRs include nutrition-related adverse reactions. Aging, multiple illnesses, mental and psychological problems, declining physical function, and environmental factors can lead to decreased food intake and increased metabolic stress in older people, resulting in energy imbalances that cause malnutrition. ADRs can lead to appetite loss, followed by decreased food intake, which in turn causes malnutrition and deficiencies of various nutrients. However, these nutrition-related ADRs have received less attention. This review article describes drug-nutrition interactions, with a particular focus on older patients. Geriatr Gerontol Int 2023; ••: ••-••.

**Keywords:** adverse drug reactions; appetite; drug-nutrition interactions; medications; older patients.

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Pharmacol Rep

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. 2023 Jun 6;1-16.

doi: 10.1007/s43440-023-00501-4. Online ahead of print.

# [Polypharmacology: promises and new drugs in 2022](#)

[Piotr Ryszkiewicz](#)<sup>1</sup>, [Barbara Malinowska](#)<sup>2</sup>, [Eberhard Schlicker](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 37278927

- PMCID: [PMC10243259](#)

- DOI: [10.1007/s43440-023-00501-4](https://doi.org/10.1007/s43440-023-00501-4)

Free PMC article

## Abstract

Polypharmacology is an emerging strategy of design, synthesis, and clinical implementation of pharmaceutical agents that act on multiple targets simultaneously. It should not be mixed up with polytherapy, which is based on the use of multiple selective drugs and is considered a cornerstone of current clinical practice. However, this 'classic' approach, when facing urgent medical challenges, such as multifactorial diseases, increasing resistance to pharmacotherapy, and multimorbidity, seems to be insufficient. The 'novel' polypharmacology concept leads to a more predictable pharmacokinetic profile of multi-target-directed ligands (MTDLs), giving a chance to avoid drug-drug interactions and improve patient compliance due to the simplification of dosing regimens. Plenty of recently marketed drugs interact with multiple biological targets or disease pathways. Many offer a significant additional benefit compared to the standard treatment regimens. In this paper, we will briefly outline the genesis of polypharmacology and its differences to polytherapy. We will also present leading concepts for obtaining MTDLs. Subsequently, we will describe some successfully marketed drugs, the mechanisms of action of which are based on the interaction with multiple targets. To get an idea, of whether MTDLs are indeed important in contemporary pharmacology, we also carefully analyzed drugs approved in 2022 in Germany: 10 out of them were found multi-targeting, including 7 antitumor agents, 1 antidepressant, 1 hypnotic, and 1 drug indicated for eye disease.

**Keywords:** Multi-target drugs; Multi-target-directed ligands; Polypharmacology; Polytherapy; Targeted therapy.

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## Conflict of interest statement

The authors declare that they have no competing interests. All authors read and approved the final manuscript.

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

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. 2023 Jun 5;113(6):8-9.

doi: 10.7196/SAMJ.2023.v113i6.769.

# Behavioural Medicine: Strengthening approaches to address co-morbid chronic physical and mental disorders

[Stephan Rabie](#)<sup>1</sup>, [John A Joska](#)<sup>2</sup>

Affiliations expand

- PMID: 37278265
- DOI: [10.7196/SAMJ.2023.v113i6.769](https://doi.org/10.7196/SAMJ.2023.v113i6.769)

## Abstract

South Africa is confronted with multi-morbid chronic physical and mental disorders. The relationships between these conditions are often multidirectional and result in a variety of adverse mental and physical health outcomes. The risk factors and perpetuating conditions in multi-morbidity are potentially modifiable through effective behaviour change. However, in South Africa, interventions and clinical care that address these co-occurring factors have traditionally functioned in a vacuum, created by a lack of formalised multidisciplinary collaboration. In high-income settings, the field of Behavioural Medicine was established in recognition of the importance of psychosocial factors in illness and assumes that the presence of physical concerns can be influenced by psychological and behavioural factors.

The large body of evidence supporting Behavioural Medicine has afforded the field global recognition. Yet, it remains an emerging field in South Africa and on the African continent. The purpose of this paper is to contextualise the field of Behavioural Medicine in South Africa and present a way forward to establish the field in our context.

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MeSH termsexpand

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Aging Clin Exp Res

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. 2023 Jun 5.

doi: 10.1007/s40520-023-02455-2. Online ahead of print.

# [Dynapenic abdominal obesity and incident multimorbidity: findings from the English longitudinal study on ageing](#)

[Nicola Veronese](#)<sup>1</sup>, [Ai Koyanagi](#)<sup>2</sup>, [Pinar Soysal](#)<sup>3</sup>, [Vitalba Sapienza](#)<sup>4</sup>, [Francesco Saverio Ragusa](#)<sup>4</sup>, [Francesco Bolzetta](#)<sup>5</sup>, [Ligia J Dominguez](#)<sup>4,6</sup>, [Mario Barbagallo](#)<sup>4</sup>, [Lee Smith](#)<sup>7</sup>

Affiliations expand

- PMID: 37273091

- DOI: [10.1007/s40520-023-02455-2](https://doi.org/10.1007/s40520-023-02455-2)

## Abstract

**Background:** Dynapenic abdominal obesity (DAO) (i.e., impairment in muscle strength and high waist circumference) is gaining interest, as it is associated with several important adverse health outcomes. However, the association between DAO and multimorbidity is largely unclear. Thus, the aim of the present study was to investigate the association between DAO at baseline and new onset multimorbidity over ten years of follow-up.

**Methods:** People participating in the English Longitudinal Study of Ageing were included. DAO was defined as waist circumference > 102 cm in men and > 88 cm in women, and a concomitant presence of dynapenia (handgrip strength defined as < 27 kg for men and < 16 kg for women). Multimorbidity was defined as having two or more chronic conditions. The association between DAO and incident multimorbidity was assessed using a multivariable logistic regression analysis, reporting the data as odds ratios (ORs) and their 95% confidence intervals (CIs).

**Results:** Overall, 3302 participants (mean age: 63.4 years, males: 50.3%) without multimorbidity at baseline were followed-up for ten years. After adjusting for several variables, compared to participants without dynapenia nor abdominal obesity, the presence of abdominal obesity (OR = 1.505; 95%CI: 1.272-1.780;  $p < 0.0001$ ) and DAO (OR = 1.671; 95%CI: 1.201-2.325;  $p = 0.002$ ) significantly increased the risk of multimorbidity. Compared to no dynapenia nor abdominal obesity, DAO was associated with significantly higher risk for arthritis and diabetes.

**Conclusions:** DAO was significantly associated with a higher risk of incident multimorbidity, over 10 years of follow-up. The results of our study suggest that addressing DAO can potentially decrease risk for multimorbidity.

**Keywords:** Cohort; Dynapenic abdominal obesity; Multimorbidity; Risk factors.

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- [42 references](#)

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AIDS Care

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. 2023 Jun 5;1-6.

doi: 10.1080/09540121.2023.2218638. Online ahead of print.

# The experiences of individuals living with HIV in Ireland attending out-patient physiotherapy

[Adam McDermott](#)<sup>1</sup>, [Niamh Murphy](#)<sup>1</sup>, [Chiara Reddin](#)<sup>1</sup>, [Colm Bergin](#)<sup>1,2</sup>

Affiliations expand

- PMID: 37272341
- DOI: [10.1080/09540121.2023.2218638](https://doi.org/10.1080/09540121.2023.2218638)

## Abstract

People living with HIV (PLWH) are living longer and are becoming increasingly susceptible to multi-morbidity resulting in disability. Physiotherapy is an important component in the care of PLWH, increasing functional capacity and quality of life. However, few PLWH access physiotherapy services due to a lack of specialised services, relapses in medical conditions and financial barriers. This study aimed to gather feedback from PLWH in a tertiary infection centre in Ireland attending out-patient physiotherapy on their experiences of physiotherapy. Eleven PLWH completed a semi-structured feedback survey focusing on their expectations and experiences of physiotherapy. Participants reported an overall positive experience of physiotherapy especially in terms of improving movement, confidence, physical activity level and sense of control. In addition, participants highlighted the importance of a physiotherapist with specialist knowledge of HIV. Barriers to participation in physiotherapy included potential relapses in other medical conditions, lack of time due to work and lack of flexibility or availability of physiotherapy appointments. This study highlights the important role of physiotherapy in the care of PLWH, several potential barriers to participation in physiotherapy for PLWH and the importance of the participation of PLWH in the co-design of services.

**Keywords:** Physiotherapy; cross-sectional study; patient experience; quality improvement; rehabilitation.

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. 2023 Jun 4.

doi: 10.1111/jocn.16767. Online ahead of print.

# [Informal carer support needs, facilitators and barriers in transitional care for older adults from hospital to home: A scoping review](#)

[Jacqueline Allen](#)<sup>1</sup>, [Marta Woolford](#)<sup>2</sup>, [Patricia M Livingston](#)<sup>3</sup>, [Michelle Lobchuk](#)<sup>4</sup>, [Anne Muldowney](#)<sup>5</sup>, [Alison M Hutchinson](#)<sup>6</sup>

Affiliations expand

- PMID: 37272211
- DOI: [10.1111/jocn.16767](https://doi.org/10.1111/jocn.16767)

# Abstract

**Aim:** To synthesise evidence about informal carers' (carers) experience of their support needs, facilitators and barriers regarding transitional care of older adults with multimorbidity.

**Background:** Carers provide crucial support for older adults during care transitions. Although health practitioners are well positioned to support carers, system factors including limited healthcare resources can compromise the quality of care transitions.

**Design:** Scoping review.

**Methods:** Searches were undertaken of the published literature. Five databases were searched including MEDLINE, CINAHL, EMBASE, PsycINFO and the Cochrane Library. Two reviewers independently screened articles to identify relevant studies. Studies were retrieved from January 2000 to July 2022. Data were extracted and tabulated for study characteristics, support needs, facilitators and barriers. Key themes and patterns were synthesised across the studies.

**Results:** Eighteen studies including N = 3174 participants were retrieved. Most studies (n = 13) employed qualitative designs. Five studies used surveys. Carers reported their need to: be involved in coordinated discharge planning; advocate and be involved in decision-making; and receive community-based follow-up. Carers described facilitators and barriers in four themes: (1) relationships with the older adult and health practitioners, (2) being involved in coordinated discharge planning; (3) communication and information strategies; and (4) community-based follow-up. Synthesis of themes across all studies resulted in the identification of five areas of research: carers' health literacy; community-based care; carers' involvement in transitional care planning; inpatient and community health practitioners' communication skills; and culturally diverse carers' experiences.

**Conclusion and relevance to clinical practice:** The review highlights the importance of quality communication and relationships between carers, older adults, health practitioners and health organisations. Although information and education are important there is a need for further research to examine systems that support communication between carers, older adults and health practitioners and health literacy for all carers including culturally diverse carers.

**Keywords:** discharge and transitional care; family caregivers; informal carers; multimorbidity; older adults; scoping review; unpaid carers.

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- [45 references](#)

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

FULL TEXT LINKS



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EMBO Mol Med



. 2023 Jun 7;15(6):e16928.

doi: 10.15252/emmm.202216928. Epub 2023 May 8.

# Microbial metabolites in chronic heart failure and its common comorbidities

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Affiliations expand

- PMID: 37155563
- PMCID: [PMC10245034](#)
- DOI: [10.15252/emmm.202216928](#)

**Free PMC article**

## Abstract

This study aimed to identify microbial signatures that contribute to the shared etiologies between chronic heart failure (CHF), type 2 diabetes, and chronic kidney disease. The serum levels of 151 microbial metabolites were measured in 260 individuals from the Risk Evaluation and Management of heart failure cohort, and it was found that those metabolites varied by an order of  $10^5$  fold. Out of 96 metabolites associated with the three cardiometabolic diseases, most were validated in two geographically independent cohorts. In all three cohorts, 16 metabolites including imidazole propionate (ImP) consistently showed significant differences. Notably, baseline ImP levels were three times higher in the Chinese compared with the Swedish cohorts and increased by 1.1–1.6 fold with each additional CHF comorbidity in the Chinese population. Cellular experiments further supported a causal link between ImP and distinct CHF relevant phenotypes. Additionally, key microbial metabolite-based risk scores were superior in CHF prognosis than the traditional Framingham or Get with the Guidelines-Heart Failure risk scores. Interactive visualization of these specific metabolite-disease links is available on our omics data server (<https://omicsdata.org/Apps/REM-HF/>).

**Keywords:** biomarkers; chronic heart failure; microbial metabolites; multimorbidity.

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## Conflict of interest statement

The authors declare that they have no conflict of interest.

- [70 references](#)
- [10 figures](#)

### SUPPLEMENTARY INFO

MeSH terms, Grant support[expand](#)

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. 2023 Jun 8;116(6):429-435.

doi: 10.1093/qjmed/hcad050.

# Classifying the unclassifiable—a Delphi study to reach consensus on the fibrotic nature of diseases

[G M Massen](#)<sup>1</sup>, [R J Allen](#)<sup>2,3</sup>, [O C Leavy](#)<sup>2,3</sup>, [N M Selby](#)<sup>4</sup>, [G P Aithal](#)<sup>5</sup>, [N Oliver](#)<sup>6</sup>, [H Parfrey](#)<sup>7</sup>, [L V Wain](#)<sup>2,3</sup>, [G Jenkins](#)<sup>1</sup>, [I Stewart](#)<sup>1</sup>, [J K Quint](#)<sup>1</sup>

Affiliations expand

- PMID: 37004203
- PMCID: [PMC10250078](#)
- DOI: [10.1093/qjmed/hcad050](#)

**Free PMC article**

## Abstract

**Background:** Traditionally, clinical research has focused on individual fibrotic diseases or fibrosis in a particular organ. However, it is possible for people to have multiple fibrotic diseases. While multi-organ fibrosis may suggest shared pathogenic mechanisms, yet there is no consensus on what constitutes a fibrotic disease and therefore fibrotic multimorbidity.

**Aim:** A Delphi study was performed to reach consensus on which diseases may be described as fibrotic.

**Methods:** Participants were asked to rate a list of diseases, sub-grouped according to eight body regions, as 'fibrotic manifestation always present', 'can develop fibrotic manifestations', 'associated with fibrotic manifestations' or 'not fibrotic nor associated'. Classifications of 'fibrotic manifestation always present' and 'can develop fibrotic manifestations' were merged and termed 'fibrotic'. Clinical consensus was defined according to the interquartile range, having met a minimum number of responses. Clinical

agreement was used for classification where diseases did not meet the minimum number of responses (required for consensus measure), were only classified if there was 100% consensus on disease classification.

**Results:** After consulting experts, searching the literature and coding dictionaries, a total of 323 non-overlapping diseases which might be considered fibrotic were identified; 92 clinical specialists responded to the first round of the survey. Over three survey rounds, 240 diseases were categorized as fibrotic via clinical consensus and 25 additional diseases through clinical agreement.

**Conclusion:** Using a robust methodology, an extensive list of diseases was classified. The findings lay the foundations for studies estimating the burden of fibrotic multimorbidity, as well as investigating shared mechanisms and therapies.

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

SUPPLEMENTARY INFO

Grant support[expand](#)

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

1  
PLoS One

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. 2023 Jun 9;18(6):e0286870.

doi: 10.1371/journal.pone.0286870. eCollection 2023.

**Video-based teach-to-goal  
intervention on inhaler technique on**

# adults with asthma and COPD: A randomized controlled trial

[Mohammad Samer Al-Kharouf<sup>1</sup>](#), [Mariam Hantash Abdeljalil<sup>1</sup>](#), [Nathir M Obeidat<sup>2,3</sup>](#), [Khaled Al Oweidat<sup>2,3</sup>](#), [Oriana Awwad<sup>1</sup>](#)

Affiliations expand

- PMID: 37294823
- DOI: [10.1371/journal.pone.0286870](https://doi.org/10.1371/journal.pone.0286870)

## Abstract

**Background:** Incorrect use of inhalers is a problem associated with poor patient outcomes. Despite improvement in the technique after verbal educations, this deteriorates over-time requiring re-enforcement through different educative strategies. This study aimed to assess the impact of a novel video-based teach-to-goal (TTG) educational intervention on: mastery of inhaler technique, disease control, medication adherence and disease-related quality of life (QoL) over-time among asthma and COPD patients.

**Methods:** This prospective, open-label, randomized controlled trial was registered in ClinicalTrials.gov: Identifier [NCT05664347](#). After baseline assessment participants received either a verbal (control group) or a video-based (intervention group) TTG strategy. After 3-month the intervention was assessed for impact on the intended outcomes. Inhaler technique was assessed using standardized checklists, disease control using the Asthma control test and COPD assessment test respectively for asthma and COPD patients while adherence using the Morisky Green Levine scale. For QoL, the mini asthma quality of life questionnaire and the St. George respiratory questionnaire were used for asthmatic and COPD patients, respectively. Differences in outcomes between intervention-control groups were analyzed using either Chi-Square (X<sup>2</sup>)/Fisher Exact or Mann Whitney test. The impact of intervention on outcomes over-time was examined using either McNemar or Wilcoxon test.

**Results:** At baseline, intervention (n = 51) and control (n = 52) groups had comparable demographic/clinical characteristics. At follow-up, inhaler technique improved among intervention group compared to control group (93.4% vs 67%) and to baseline (93.4% to 49.5%), (P<0.05). Similarly, medication adherence ameliorated among the intervention group in comparison to control group (88.2% to 61.5%) and to baseline (88.2% to 66.7%), (P<0.05). In regards to disease control, results showed an amelioration among the intervention group compared to baseline (35.3% to 54.9%) (P<0.05). QoL scores improved



significantly among asthma patients (intervention group) at follow-up vs baseline. Better scores were also observed for COPD patients compared to controls, ( $P < 0.05$ ).

**Conclusion:** Video-based (TTG) was effective in enhancing inhaler technique over time as well as improving disease control, medication adherence, and QoL.

**Trial registration:** ClinicalTrials.gov: [NCT05664347](https://clinicaltrials.gov/ct2/show/NCT05664347).  
<https://clinicaltrials.gov/ct2/show/NCT05664347>.

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## Conflict of interest statement

The authors have declared that no competing interests exist.

### SUPPLEMENTARY INFO

Associated dataexpand

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J Investig Allergol Clin Immunol

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. 2023 Jun 8;0.

doi: 10.18176/jiaci.0905. Online ahead of print.

# REDES study: Mepolizumab is effective in patients with severe asthma and comorbid nasal polyps

[E Arismendi](#)<sup>1,2</sup>, [C Cisneros](#)<sup>3</sup>, [M Blanco-Aparicio](#)<sup>4</sup>, [E Martínez-Moragón](#)<sup>5</sup>, [S Quirce](#)<sup>2,6</sup>, [D Bañas Conejero](#)<sup>7</sup>, [A L Moure](#)<sup>7</sup>, [M G Sánchez-Herrero](#)<sup>7</sup>

Affiliations [expand](#)

- PMID: 37294091
- DOI: [10.18176/jiaci.0905](https://doi.org/10.18176/jiaci.0905)

*No abstract available*

**Keywords:** Eosinophilic Phenotype; Exacerbations; Oral Corticosteroids; Real World Evidence.

FULL TEXT LINKS



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Pediatr Pulmonol

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. 2023 Jun 9.

doi: 10.1002/ppul.26546. Online ahead of print.

## Modified lung ultrasound score for bronchopulmonary dysplasia predicts

# late respiratory outcomes in preterm infants

[Jieru Shen](#)<sup>1</sup>, [Yang Du](#)<sup>2</sup>, [Yinghua Sun](#)<sup>3</sup>, [Xiangyuan Huang](#)<sup>4</sup>, [Jianguo Zhou](#)<sup>1</sup>, [Chao Chen](#)<sup>1</sup>

Affiliations expand

- PMID: 37294069
- DOI: [10.1002/ppul.26546](https://doi.org/10.1002/ppul.26546)

## Abstract

**Objective:** Lung ultrasound (LUS) is a useful and radiation-free diagnostic tool for predicting bronchopulmonary dysplasia, which is a risk factor for late respiratory disease. However, data on the relationship of LUS with late respiratory disease was scarce. This study aims to determine whether LUS is associated with late respiratory disease during early childhood.

**Methods:** This prospective cohort study enrolled preterm infants born before 32 weeks of gestation. LUS was performed at 36 weeks' postmenstrual age. The predictive values of a modified lung ultrasound (mLUS) score based on eight standard sections were assessed to predict late respiratory disease, defined as a physician diagnosis of bronchopulmonary dysplasia deterioration, asthma, reactive airway disease, bronchiolitis, pneumonia, or respiratory-related hospitalization during the first 2 years of life.

**Results:** A total of 94 infants completed follow-up, of whom 74.5% met the late respiratory disease criteria. The mLUS scores were significantly associated with late respiratory disease (adjusted odds ratio: 1.23, CI: 1.10-1.38,  $p < 0.001$ ). The mLUS scores also well predicted late respiratory disease (AUC = 0.820, 95% CI: 0.733-0.907). These scores were superior to the classic lung ultrasound score ( $p = 0.02$ ) and as accurate as the modified NICHD-defined bronchopulmonary dysplasia classification ( $p = 0.91$ ). A mLUS score  $\geq 14$  was the optimal cutoff point for predicting late respiratory disease.

**Conclusion:** The modified lung ultrasound score correlates significantly with late respiratory disease and well predicts it in preterm infants during the first 2 years of life.

**Keywords:** bronchopulmonary dysplasia; late respiratory disease; lung ultrasound; premature.

- [40 references](#)

SUPPLEMENTARY INFO

Grant support[expand](#)

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J Asthma

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. 2023 Jun 9;1-10.

doi: 10.1080/02770903.2023.2220815. Online ahead of print.

# [Effect of long-term medium to high-dose inhaled budesonide on bone mineral density in children with asthma: a cross-sectional study](#)

[Sumanth H Patil](#)<sup>1</sup>, [Vishal Kumar](#)<sup>1</sup>, [Devki Nandan](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 37294051
- DOI: [10.1080/02770903.2023.2220815](https://doi.org/10.1080/02770903.2023.2220815)

## Abstract

**Objective:** The objective of this study was to examine the impact of long-term medium to high-dose inhaled budesonide on bone mineral density in children with asthma.

**Methods:** We conducted a cross-sectional study in children aged 7-17 years with asthma, who received long-term ( $\geq 2$  years), medium to high-dose inhaled budesonide ( $\geq 400\mu\text{g/day}$  in 6-11 years old;  $\geq 800\mu\text{g/day}$  in  $> 11$  years old). We measured bone mineral density (BMD) using dual-energy X-ray absorptiometry and compared it with reference Indian normative values.

**Results:** Thirty-five children with moderate to severe asthma receiving long-term medium to high-dose inhaled budesonide, were included in the study. We found a significantly low lumbar-spine BMD in the study population compared to reference Indian values (p-value 0.002). Eight cases had short stature. Despite the adjustment for height-age in these short-stature cases, lumbar-spine BMD remained significantly low in the study population (p-value 0.020). No significant difference was found in 25-hydroxy vitamin D levels between subjects with "low BMD" and "BMD z-score  $> -2$ ".

**Conclusion:** The findings of this study suggest that long-term medium to high-dose inhaled budesonide treatment in children with asthma is associated with decreased BMD. However, further investigation with a larger sample size is necessary to confirm this relationship.

**Keywords:** Bone mineral accretion (BMA); Bone mineral content; Dual-energy X-ray absorptiometry (DXA); Inhaled corticosteroids (ICS); Paediatric asthma; Pediatric.

FULL TEXT LINKS



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[Review](#)

Clin Exp Allergy

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. 2023 Jun 9.

# Effectiveness of FeNO-guided treatment in adult asthma patients: A systematic review and meta-analysis

[Daniël A Korevaar](#)<sup>1</sup>, [Johanna A Damen](#)<sup>2,3</sup>, [Pauline Heus](#)<sup>2,3</sup>, [Maaïke J Moen](#)<sup>4</sup>, [René Spijker](#)<sup>2,5</sup>, [Ilonka H van Veen](#)<sup>6</sup>, [Els J Weersink](#)<sup>1</sup>, [Geert-Jan van Kemenade](#)<sup>4</sup>, [Peter Th W van Hal](#)<sup>4,7</sup>, [Lotty Hooft](#)<sup>2,3</sup>

Affiliations expand

- PMID: 37293870
- DOI: [10.1111/cea.14359](https://doi.org/10.1111/cea.14359)

## Abstract

**Objective:** Asthma control is generally monitored by assessing symptoms and lung function. However, optimal treatment is also dependent on the type and extent of airway inflammation. Fraction of exhaled Nitric Oxide (FeNO) is a noninvasive biomarker of type 2 airway inflammation, but its effectiveness in guiding asthma treatment remains disputed. We performed a systematic review and meta-analysis to obtain summary estimates of the effectiveness of FeNO-guided asthma treatment.

**Design:** We updated a Cochrane systematic review from 2016. Cochrane Risk of Bias tool was used to assess risk of bias. Inverse-variance random-effects meta-analysis was performed. Certainty of evidence was assessed using GRADE. Subgroup analyses were performed based on asthma severity, asthma control, allergy/atopy, pregnancy and obesity.

**Data sources:** The Cochrane Airways Group Trials Register was searched on 9 May 2023.

**Eligibility criteria:** We included randomized controlled trials (RCTs) comparing the effectiveness of a FeNO-guided treatment versus usual (symptom-guided) treatment in adult asthma patients.

**Results:** We included 12 RCTs (2,116 patients), all showing high or unclear risk of bias in at least one domain. Five RCTs reported support from a FeNO manufacturer. FeNO-guided treatment probably reduces the number of patients having  $\geq 1$  exacerbation (OR = 0.61; 95%CI 0.44 to 0.83; six RCTs; GRADE moderate certainty) and exacerbation rate (RR = 0.67; 95%CI 0.54 to 0.82; six RCTs; moderate certainty), and may slightly improve Asthma

Control Questionnaire score (MD = -0.10; 95%CI -0.18 to -0.02, six RCTs; low certainty), however, this change is unlikely to be clinically important. An effect on severe exacerbations, quality of life, FEV1, treatment dosage and FeNO values could not be demonstrated. There were no indications that effectiveness is different in subgroups of patients, although evidence for subgroup analysis was limited.

**Conclusions:** FeNO-guided asthma treatment probably results in fewer exacerbations but may not have clinically important effects on other asthma outcomes.

**Keywords:** Fraction of exhaled Nitric Oxide; asthma; eosinophils; meta-analysis; systematic review.

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- [40 references](#)

#### SUPPLEMENTARY INFO

Publication types, Grant support[expand](#)

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Int J Mol Med

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. 2023 Jul;52(1):63.

doi: 10.3892/ijmm.2023.5266. Epub 2023 Jun 9.

## Obesity alters inflammatory response in the pathology of asthma (Review)

[Ziwen Qin](#)<sup>1</sup>, [Hong Yang](#)<sup>2</sup>, [Junli Liu](#)<sup>3</sup>, [Dongxiao Li](#)<sup>4</sup>, [Yue Wang](#)<sup>1</sup>, [Yujuan Chen](#)<sup>4</sup>, [Chuanjun Huang](#)<sup>5</sup>

Affiliations expand

- PMID: 37293862
- DOI: [10.3892/ijmm.2023.5266](https://doi.org/10.3892/ijmm.2023.5266)

## Abstract

Obesity is one of the comorbidities in patients with asthma and obese patients with asthma present with a distinct phenotype with more severe disease outcomes and reduced responsiveness to standard therapies. Although the full mechanisms of obesity-related asthma are still not completely understood, abnormal immune responses have been demonstrated to have a critical role in asthma pathogenesis. The present review summarizes the data from clinical, epidemiological and animal studies to provide an updated understanding of the immune responses in obesity-related asthma, as well as the effect of various factors, such as oxidative stress, mitochondrial dysfunction, genetics and epigenetics, on asthmatic inflammation. Further studies on the in-depth mechanisms are still required to develop novel preventive and therapeutic strategies for patients with asthma combined with obesity.

**Keywords:** T helper 2; airway hyperresponsiveness; airway inflammation; body mass index; high-fat diet; immune response; nitric oxide; obesity-related asthma; reactive oxygen species.

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. 2023 Jun 8;10(1):370.

doi: 10.1038/s41597-023-02241-9.



# Home monitoring with connected mobile devices for asthma attack prediction with machine learning

[Kevin C H Tsang](#)<sup>1,2</sup>, [Hilary Pinnock](#)<sup>3</sup>, [Andrew M Wilson](#)<sup>3,4,5</sup>, [Dario Salvi](#)<sup>6</sup>, [Syed Ahmar Shah](#)<sup>7,8</sup>

Affiliations expand

- PMID: 37291158
- DOI: [10.1038/s41597-023-02241-9](https://doi.org/10.1038/s41597-023-02241-9)

## Abstract

Monitoring asthma is essential for self-management. However, traditional monitoring methods require high levels of active engagement, and some patients may find this tedious. Passive monitoring with mobile-health devices, especially when combined with machine-learning, provides an avenue to reduce management burden. Data for developing machine-learning algorithms are scarce, and gathering new data is expensive. A few datasets, such as the Asthma Mobile Health Study, are publicly available, but they only consist of self-reported diaries and lack any objective and passively collected data. To fill this gap, we carried out a 2-phase, 7-month AAMOS-00 observational study to monitor asthma using three smart-monitoring devices (smart-peak-flow-meter/smart-inhaler/smartwatch), and daily symptom questionnaires. Combined with localised weather, pollen, and air-quality reports, we collected a rich longitudinal dataset to explore the feasibility of passive monitoring and asthma attack prediction. This valuable anonymised dataset for phase-2 of the study (device monitoring) has been made publicly available. Between June-2021 and June-2022, in the midst of UK's COVID-19 lockdowns, 22 participants across the UK provided 2,054 unique patient-days of data.

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- [52 references](#)

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Respir Med

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. 2023 Jun 6;107285.

doi: 10.1016/j.rmed.2023.107285. Online ahead of print.

# Real-world effectiveness of benralizumab in US subspecialist-treated adults with severe asthma: Findings from CHRONICLE

[Reynold A Panettieri](#)<sup>1</sup>, [Njira Lugogo](#)<sup>2</sup>, [Wendy C Moore](#)<sup>3</sup>, [Bradley E Chipps](#)<sup>4</sup>, [Brett Jepson](#)<sup>5</sup>, [Wenjiong Zhou](#)<sup>6</sup>, [Christopher S Ambrose](#)<sup>7</sup>, [Eduardo Genofre](#)<sup>8</sup>, [Donna D Carstens](#)<sup>9</sup>

Affiliations expand

- PMID: 37290579
- DOI: [10.1016/j.rmed.2023.107285](https://doi.org/10.1016/j.rmed.2023.107285)

## Abstract

**Background:** Patients with eosinophilic severe asthma (SA) have an increased risk of asthma exacerbations. Benralizumab is approved for eosinophilic SA, and there is great value in understanding real-world effectiveness.

**Objective:** The aim of this analysis was to examine the effectiveness of benralizumab in a real-world cohort of subspecialist-treated US patients with eosinophilic SA.

**Methods:** CHRONICLE is an ongoing, noninterventional study of subspecialist-treated US adults with SA receiving biologics, maintenance systemic corticosteroids, or those persistently uncontrolled by high-dose inhaled corticosteroids with additional controllers. For this analysis, eligible patients enrolled from February 2018 to February 2021, had received  $\geq 1$  dose of benralizumab, and had study data for  $\geq 3$  months before and after benralizumab initiation. The primary analysis included patients with prior exacerbations reported and 12 months of outcomes data before and after initiation. Patient outcomes occurring 6-12 months before and after initiation were also evaluated.

**Results:** A total of 317 patients had  $\geq 3$  months of follow-up before and after first benralizumab dose. For patients with 12 months ( $n = 107$ ) and 6-12 months ( $n = 166$ ) of data, significant reductions were observed in annualized rates of exacerbations (62%;  $P < 0.001$  and 65%;  $P < 0.001$ , respectively), with similar reductions in the rates of hospitalizations and emergency department visits. Benralizumab recipients with blood eosinophil counts (BEC) of  $\geq 300/\mu\text{L}$  and  $< 300/\mu\text{L}$  at baseline and 12 months of data also had significant reductions in exacerbations (68%;  $P < 0.001$ , 61%;  $P < 0.001$ ).

**Conclusion:** This real-world, noninterventional analysis reinforces the clinical value of benralizumab in the management of patients with eosinophilic SA.

**Keywords:** Clinical use; Exacerbations; Noninterventional; Patient outcomes; Severe eosinophilic asthma.

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## Conflict of interest statement

Declaration of competing interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests RA Panettieri Jr.: Advisory boards and grant support — AstraZeneca, Sanofi, Genentech, Regeneron, Novartis. N Lugogo: Received consulting fees — Amgen, AstraZeneca, Avillion, Genentech, GlaxoSmithKline, Novartis, Regeneron, Sanofi, and Teva; honoraria for non-speakers bureau presentations — GlaxoSmithKline and AstraZeneca; travel support — AstraZeneca; her institution received research support — Amgen, AstraZeneca, Avillion, Evidera, Gossamer Bio, Genentech, GlaxoSmithKline, Regeneron, Sanofi, Novartis and Teva; honorary faculty member — Observational and Pragmatic Research Institute (OPRI) but does not receive compensation for this role. WC Moore: Advisory boards — AstraZeneca, Sanofi, Genentech, GlaxoSmithKline, Regeneron. BE Chipps: Advisory boards, consultant, and speaker — AstraZeneca, Boehringer Ingelheim, Genentech, Novartis, Regeneron, Sanofi Genzyme. B Jepson: Employee — Cytel, on assignment to AstraZeneca. W Zhou: Employee — ClinChoice. CS Ambrose: Employee and shareholder — AstraZeneca. E Genofre: at the time of this study, was an employee and shareholder — AstraZeneca. D Carstens: Employee and shareholder — AstraZeneca.

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Hosp Pediatr

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. 2023 Jun 8;e2023007167.

doi: 10.1542/hpeds.2023-007167. Online ahead of print.

# [The Role of Hospitalists in Reducing Childhood Asthma Disparities: Time to Step-up?](#)

[Katherine Pumphrey](#)<sup>1,2</sup>, [Jessica Hart](#)<sup>1,2</sup>, [Chén C Kenyon](#)<sup>1,3,2</sup>

Affiliations expand

- PMID: 37288507
- DOI: [10.1542/hpeds.2023-007167](https://doi.org/10.1542/hpeds.2023-007167)

*No abstract available*

## Conflict of interest statement

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

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Published Erratum

Eur Respir Rev

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. 2023 Jun 7;32(168):225202.

doi: 10.1183/16000617.5202-2022. Print 2023 Jun 30.

**"Strength of association between comorbidities and asthma: a meta-analysis" Paola Rogliani, Rossella Laitano, Josuel Ora, Richard Beasley and Luigino Calzetta. *Eur Respir Rev* 2023; 32: 220202**

*No authors listed*

- PMID: 37286222
- PMCID: [PMC10245130](#)
- DOI: [10.1183/16000617.5202-2022](#)

**Free PMC article**

*No abstract available*

## Erratum for

- [Strength of association between comorbidities and asthma: a meta-analysis.](#)  
Rogliani P, Laitano R, Ora J, Beasley R, Calzetta L. *Eur Respir Rev.* 2023 Mar 8;32(167):220202. doi: 10.1183/16000617.0202-2022. Print 2023 Mar 31. PMID: 36889783 **Free PMC article.** Review.

SUPPLEMENTARY INFO

Publication types [expand](#)

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Review

Eur Respir Rev

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. 2023 Jun 7;32(168):230019.

doi: 10.1183/16000617.0019-2023. Print 2023 Jun 30.

## [Extreme weather and asthma: a systematic review and meta-analysis](#)

[Firdian Makrufardi](#)<sup>1,2</sup>, [Amja Manullang](#)<sup>1</sup>, [Desy Rusmawatiningtyas](#)<sup>2</sup>, [Kian Fan Chung](#)<sup>3</sup>, [Sheng-Chieh Lin](#)<sup>4,5</sup>, [Hsiao-Chi Chuang](#)<sup>6,7,8,9</sup>

Affiliations [expand](#)

- PMID: 37286218

- PMCID: [PMC10245140](#)
- DOI: [10.1183/16000617.0019-2023](#)

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## Abstract

**Background:** Climate change's influence on extreme weather events poses a significant threat to the morbidity and mortality of asthma patients. The aim of this study was to examine associations between extreme weather events and asthma-related outcomes.

**Methods:** A systematic literature search for relevant studies was performed using the PubMed, EMBASE, Web of Science and ProQuest databases. Fixed-effects and random-effects models were applied to estimate the effects of extreme weather events on asthma-related outcomes.

**Results:** We observed that extreme weather events were associated with increasing risks of general asthma outcomes with relative risks of 1.18-fold for asthma events (95% CI 1.13-1.24), 1.10-fold for asthma symptoms (95% CI 1.03-1.18) and 1.09-fold for asthma diagnoses (95% CI 1.00-1.19). Extreme weather events were associated with increased risks of acute asthma exacerbation with risk ratios of asthma emergency department visits of 1.25-fold (95% CI 1.14-1.37), of asthma hospital admissions of 1.10-fold (95% CI 1.04-1.17), of asthma outpatient visits of 1.19-fold (95% CI 1.06-1.34) and of asthma mortality of 2.10-fold (95% CI 1.35-3.27). Additionally, an increase in extreme weather events increased risk ratios of asthma events by 1.19-fold in children and 1.29-fold in females (95% CI 1.08-1.32 and 95% CI 0.98-1.69, respectively). Thunderstorms increased the risk ratio of asthma events by 1.24-fold (95% CI 1.13-1.36).

**Conclusions:** Our study showed that extreme weather events more prominently increased the risk of asthma morbidity and mortality in children and females. Climate change is a critical concern for asthma control.

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## Conflict of interest statement

Conflict of interest: All authors have nothing to disclose.

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

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Eur J Pediatr

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. 2023 Jun 7.

doi: 10.1007/s00431-023-05047-4. Online ahead of print.

# Evaluation of the possible effect of inspiratory muscle training on inflammation markers and oxidative stress in childhood asthma

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Affiliations expand

- PMID: 37285069
- DOI: [10.1007/s00431-023-05047-4](https://doi.org/10.1007/s00431-023-05047-4)

## Abstract



Airway inflammation characterized as asthma is one of the most common chronic diseases in the world. The aim of this study was to evaluate the possible effect of inspiratory muscle training on inflammation markers and oxidative stress levels in childhood asthma. A total of 105 children (age range 8-17 years), including 70 asthmatics and 35 healthy children, participated in the study. The 70 asthma patients were randomly assigned to the inspiratory muscle training (IMT) group (n = 35) and control group (n = 35), and healthy children were assigned to the healthy group (n = 35). The IMT group was treated with the threshold IMT device for 7 days/6 weeks at 30% of maximum inspiratory pressure. Respiratory muscle strength was evaluated with a mouth pressure measuring device, and respiratory function was evaluated with a spirometer. In addition, CRP, periostin, TGF- $\beta$ , and oxidative stress levels were analyzed. The evaluation was performed only once in the healthy group and twice (at the beginning and end of 6 weeks) in asthma patients. In the study, there were significant differences between asthma patients and the healthy group in terms of MIP and MEP values, respiratory function, oxidative stress level, periostin, and TGF- $\beta$ . Post-treatment, differences were observed in the oxidative stress level, periostin, and TGF- $\beta$  of the IMT group ( $p < .05$ ).

**Conclusion:** After 6 weeks of training, IMT positively contributed to reducing the inflammation level and oxidative stress. This suggests that IMT should be used as an alternative therapy to reduce inflammation and oxidative stress. (Trial Registration: The clinical trial protocol number is [NCT05296707](https://clinicaltrials.gov/ct2/show/study/NCT05296707)).

**What is known:** • It is known that adjunctive therapies given in addition to pharmacological treatment contribute to improving symptom control and quality of life in individuals with asthma.

**What is new:** • There are no studies about the effect of respiratory physiotherapy on biomarkers in asthmatic children. The sub-mechanism of improvement in individuals has not been elucidated. • In this context, inspiratory muscle training has a positive effect on inflammation and oxidative stress levels in children with asthma and IMT should be used as an alternative treatment for childhood asthma.

**Keywords:** Children asthma; Inflammation; Inspiratory muscle training; Oxidative stress.

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- [65 references](#)

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Curr Allergy Asthma Rep

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. 2023 Jun 7.

doi: 10.1007/s11882-023-01093-y. Online ahead of print.

# The Impact of Climate Change on Asthma and Allergic-Immunologic Disease

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Affiliations expand

- PMID: 37284923
- DOI: [10.1007/s11882-023-01093-y](https://doi.org/10.1007/s11882-023-01093-y)

## Abstract

**Purpose of review:** This review discusses climate change-related impacts on asthma and allergic-immunologic disease, relevant US public health efforts, and healthcare professional resources.

**Recent findings:** Climate change can impact people with asthma and allergic-immunologic disease through various pathways, including increased exposure to asthma triggers (e.g., aeroallergens, ground-level ozone). Climate change-related disasters (e.g., wildfires, floods) disrupting healthcare access can complicate management of any allergic-immunologic disease. Climate change disproportionately affects some communities, which can exacerbate disparities in climate-sensitive diseases like asthma. Public health efforts include implementing a national strategic framework to help communities track, prevent, and respond to climate change-related health threats. Healthcare professionals can use resources or tools to help patients with asthma and allergic-immunologic disease prevent climate change-related health impacts. Climate change can affect people with asthma and allergic-immunologic disease and exacerbate health disparities. Resources and tools are available to help prevent climate change-related health impacts at the community and individual level.

**Keywords:** Allergy; Asthma; Climate change; Health equity; Public health; Race/ethnicity.

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- [100 references](#)

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Diabetes Obes Metab

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. 2023 Jun 7.

doi: 10.1111/dom.15154. Online ahead of print.

# Weight change and risk of obesity-related complications: A retrospective population-based cohort study of a UK primary care database

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Affiliations expand

- PMID: 37283064
- DOI: [10.1111/dom.15154](https://doi.org/10.1111/dom.15154)

## Abstract

**Aims:** To examine associations between weight loss/gain and risk of developing 13 obesity-related complications (ORCs), stratified by baseline body mass index (BMI).

**Materials and methods:** In this retrospective cohort study, we included adults with obesity ( $>30 \text{ kg/m}^2$ ) from the UK Clinical Practice Research Datalink GOLD database with weight change ( $-50\%$  to  $+50\%$ ) between Years 1 and 4 ( $N = 418\,774$  [median follow-up: 7 years]). Associations between weight change, baseline BMI and risk of developing ORCs during follow-up were assessed using Cox proportional hazard models.

**Results:** The impact of weight change on ORCs was generally dependent on baseline BMI. Four clear patterns were seen across the 13 outcomes. Pattern 1 showed greatest weight loss benefit for people with low baseline BMI (type 2 diabetes, sleep apnoea, hypertension and dyslipidaemia); Pattern 2 showed most weight loss benefit at lower baseline BMI but no significant weight loss effect at higher baseline BMI (asthma, hip/knee osteoarthritis and polycystic ovary syndrome); Pattern 3 showed benefit in most cardiovascular diseases with weight loss (chronic kidney disease, heart failure, atrial fibrillation and venous thromboembolism), but no additional benefit with  $>10\%$  weight loss; Pattern 4 showed no clear relationship between weight change and unstable angina/myocardial infarction and depression. We found similar but opposite patterns for weight gain.

**Conclusions:** Weight loss benefit is dependent on weight loss magnitude and initial BMI, and weight gain is associated with a similar risk increase. Four patterns of association were identified between degree of weight change, baseline BMI and 13 ORCs.

**Keywords:** body composition; cohort study; population study; real-world evidence; weight control.

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BMC Pulm Med

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. 2023 Jun 6;23(1):196.

doi: 10.1186/s12890-023-02479-4.

# [Increasing the accuracy of the asthma diagnosis using an operational definition for asthma and a machine learning method](#)

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Affiliations expand

- PMID: 37280559

- PMID: [PMC10245465](#)
- DOI: [10.1186/s12890-023-02479-4](#)

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## Abstract

**Introduction:** Analysis of the National Health Insurance data has been actively carried out for the purpose of academic research and establishing scientific evidences for health care service policy in asthma. However, there has been a limitation for the accuracy of the data extracted through conventional operational definition. In this study, we verified the accuracy of conventional operational definition of asthma, by applying it to a real hospital setting. And by using a machine learning technique, we established an appropriate operational definition that predicts asthma more accurately.

**Methods:** We extracted asthma patients using the conventional operational definition of asthma at Seoul St. Mary's hospital and St. Paul's hospital at the Catholic University of Korea between January 2017 and January 2018. Among these extracted patients of asthma, 10% of patients were randomly sampled. We verified the accuracy of the conventional operational definition for asthma by matching actual diagnosis through medical chart review. And then we operated machine learning approaches to predict asthma more accurately.

**Results:** A total of 4,235 patients with asthma were identified using a conventional asthma definition during the study period. Of these, 353 patients were collected. The patients of asthma were 56% of study population, 44% of patients were not asthma. The use of machine learning techniques improved the overall accuracy. The XGBoost prediction model for asthma diagnosis showed an accuracy of 87.1%, an AUC of 93.0%, sensitivity of 82.5%, and specificity of 97.9%. Major explanatory variable were ICS/LABA, LAMA and LTRA for proper diagnosis of asthma.

**Conclusions:** The conventional operational definition of asthma has limitation to extract true asthma patients in real world. Therefore, it is necessary to establish an accurate standardized operational definition of asthma. In this study, machine learning approach could be a good option for building a relevant operational definition in research using claims data.

**Keywords:** Asthma; Conventional operational definition; Machine learning.

## Conflict of interest statement

The authors declare no competing interests.

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

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MeSH terms, Grant support[expand](#)

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Am J Physiol Lung Cell Mol Physiol

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. 2023 Jun 6.

doi: 10.1152/ajplung.00058.2023. Online ahead of print.

# Baseline reticular basement membrane morphology is related to subsequent spirometry deterioration in pediatric chronic airway inflammation: A follow-up study

[Václav Koucký](#)<sup>1,2</sup>, [Jiří Uhlík](#)<sup>2</sup>, [Lenka Hoňková](#)<sup>1,2</sup>, [Arnošt Komárek](#)<sup>3</sup>, [Petr Pohunek](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 37280505
- DOI: [10.1152/ajplung.00058.2023](https://doi.org/10.1152/ajplung.00058.2023)

## Abstract

Reticular basement membrane (RBM) thickening may occur in children with allergic bronchial asthma (BA), cystic fibrosis (CF), and primary ciliary dyskinesia (PCD). Its functional consequences remain unknown. We investigated the relationship between baseline RBM thickness and subsequent spirometry. In our cohort follow-up study, patients aged 3-18 years with BA, CF, and PCD and controls underwent baseline lung clearance index (LCI) measurement, spirometry, and endobronchial biopsy sampling. Total RBM and collagen IV-positive layer thickness were measured. Trends in forced vital capacity (FVC), forced expired volume in 1 second (FEV<sub>1</sub>), and FEV<sub>1</sub>/FVC were analyzed during follow-up, and their relationship to baseline characteristics was studied using univariate analysis and multiple regression models. Complete baseline data were available in 19 BA, 30 CF, 25 PCD patients, and 19 controls. The RBM was thicker in BA ( $6.33 \pm 1.22 \mu\text{m}$ ), CF ( $5.60 \pm 1.39 \mu\text{m}$ ), and PCD ( $6.50 \pm 1.87 \mu\text{m}$ ) than in controls ( $3.29 \pm 0.55 \mu\text{m}$ ) (all  $p < 0.001$ ). The LCI was higher in CF ( $15.32 \pm 4.58$ ,  $p < 0.001$ ) and PCD ( $10.97 \pm 2.46$ ,  $p = 0.002$ ) than in controls ( $7.44 \pm 0.43$ ). The median follow-up times were 3.6, 4.8, 5.7, and 1.9 years in BA, CF, PCD, and controls respectively. The Z-scores of FEV<sub>1</sub> and FEV<sub>1</sub>/FVC deteriorated significantly in all groups except in controls. In CF and PCD, trends in FEV<sub>1</sub> z-scores correlated with baseline LCI and RBM; in BA, it correlated with collagen IV. In multiple regression models, RBM morphology and ventilation inhomogeneity could predict up to 84.4% of variability in spirometry trends. In conclusion, baseline LCI value and RBM morphology may predict trends in subsequent spirometry.

**Keywords:** airway remodeling; pediatric chronic airway inflammation; respiratory function tests; reticular basement membrane.

SUPPLEMENTARY INFO

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Adv Ther

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. 2023 Jun 7;1-17.

doi: 10.1007/s12325-023-02543-9. Online ahead of print.

# SABAs as Reliever Medications in Asthma Management: Evidence-Based Science

[Israel Amirav](#)<sup>1</sup>, [Gabriel Garcia](#)<sup>2</sup>, [Bao Khac Le](#)<sup>3</sup>, [Paulina Barria](#)<sup>4</sup>, [Gur Levy](#)<sup>5</sup>, [Bhumika Aggarwal](#)<sup>6</sup>, [Kyle Fahrback](#)<sup>7</sup>, [Amber Martin](#)<sup>7</sup>, [Abhay Phansalkar](#)<sup>8</sup>, [Thitiwat Sriprasart](#)<sup>9</sup>

Affiliations expand

- PMID: 37280414
- PMCID: [PMC10244083](#)
- DOI: [10.1007/s12325-023-02543-9](#)

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## Abstract

The role of as-needed inhaled short-acting  $\beta_2$ -agonists (SABAs) in the management of asthma has become a subject of debate due to differing opinions in the professional community relating to the use of SABAs. In this article, we summarize the current position of SABAs when used as reliever medications and examine the challenges to appropriate use including a critique of the data that have led to the condemnation of SABA used as a reliever. We consider the evidence for the appropriate use of SABA as a reliever together with practical solutions to ensure such use, including identifying patients at risk of misusing their SABA relievers and managing issues of inhaler technique and treatment adherence. We conclude that inhaled corticosteroid (ICS)-based maintenance treatment

with SABA used as-needed as a reliever is an effective and safe treatment for patients with asthma, with no scientific evidence of a causal link between SABA use as a reliever and mortality or serious adverse events (including exacerbations). Increased SABA use warns of a deterioration in asthma control, and patients at risk of misusing their ICS and SABA medication should be rapidly identified to ensure they are receiving adequate ICS-based controller therapy. Appropriate use of ICS-based controller therapy and as-needed SABA should be encouraged and promoted with educational activities.

**Keywords:** As-needed reliever; Asthma management; SABA; Scientific evidence; Short-acting  $\beta$ 2-agonists.

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## Conflict of interest statement

Israel Amirav has no competing interests to declare. Gabriel Garcia has received advisory board consulting fees from Chiesi, GSK, Novartis and Sanofi; and has received support to attend conferences from GSK, Novartis and Sanofi. Le Khac Bao has received honoraria for lectures, presentations, speakers' bureaus or educational events from Abbott, AstraZeneca, Boehringer Ingelheim, GSK, Pfizer and Novartis; honoraria for providing expert advice in advisory boards from Boehringer Ingelheim, GSK and Pfizer; and support for travel/attending meetings from AstraZeneca, Boehringer Ingelheim and Pfizer. Paulina Barria has received honoraria for lecture presentations from GSK and Sanofi-Aventis; honoraria for providing expert advice in advisory boards/expert forums from AstraZeneca, GSK and Novartis; and support for travel/attending meetings from GSK and Sanofi-Aventis. Thitiwat Sriprasart has no competing interests to declare. Gur Levy, Bhumika Aggarwal, Abhay Phansalkar and Peter Daley-Yates are GSK employees and hold GSK shares. Kyle Fahrbach and Amber Martin are employees of Evidera who provided statistical and intellectual support for this manuscript, funded by GSK.

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# Impact of Post-Visit Outreach on Inhaled Corticosteroid Refill Persistence in Children and Young Adults With Asthma

[Kelly C Patrick](#)<sup>1</sup>, [Beverly J Spray](#)<sup>2</sup>, [Matthew C Pertzborn](#)<sup>3</sup>

Affiliations expand

- PMID: 37280076
- DOI: [10.4187/respcare.10534](https://doi.org/10.4187/respcare.10534)

## Abstract

**Background:** Inhaled corticosteroids (ICSs) are a fundamental pillar of most regimens for long-term control of persistent asthma. Poor adherence to ICS medication is a common problem in the asthma population that can lead to poor asthma control. We hypothesized that conducting a follow-up telephone call after general pediatric clinic visits for asthma would improve refill persistence.

**Methods:** We conducted a prospective cohort analysis of pediatric and young adult subjects followed in our pediatric primary care clinic for asthma on ICS medication found to have poor ICS refill persistence. This cohort received a follow-up telephone outreach call 5-8 weeks after the clinic visit. The primary outcome measure was refill persistence with regard to ICS therapy.

**Results:** There were 289 subjects who met the inclusion criteria and did not meet any exclusion criteria for the study ( $n = 131$  in the primary cohort,  $n = 158$  in the post-COVID cohort). The mean ICS refill persistence increased significantly for subjects in the primary cohort ( $39.4 \pm 30.8\%$  post intervention vs  $32.4 \pm 19.7\%$  pre intervention) ( $P = .02$ ) but not in the post-COVID cohort ( $36.4 \pm 25.6\%$  post intervention vs  $38.9 \pm 21.0\%$  pre intervention)

( $P = .26$ ). There was not a statistically significant change in hospitalizations after the intervention in either the primary or the post-COVID cohorts ( $P = .08$  and  $.07$ , respectively). Systemic corticosteroid courses and emergency department visits decreased significantly post intervention ( $P = .01$  and  $P = .004$ , respectively) in the primary group but not in the post-COVID group ( $P = .75$  and  $P = .16$ , respectively).

**Conclusions:** These results suggest that telephone outreach after out-patient clinic visits for asthma may have short-term benefit in ICS refill persistence; however, the effect size was small.

**Keywords:** chronic disease; glucocorticoids; inhalation administration; lung diseases; medication adherence; pediatrics.

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Respir Med

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. 2023 Jun 4;107301.

doi: 10.1016/j.rmed.2023.107301. Online ahead of print.

## [Obesity associates with increased all-cause and cardiovascular mortality in adults with asthma](#)

[Axel Stureson](#)<sup>1</sup>, [Linnea Hedman](#)<sup>2</sup>, [Caroline Stridsman](#)<sup>3</sup>, [Anne Lindberg](#)<sup>3</sup>, [Eva Rönmark](#)<sup>2</sup>, [Helena Backman](#)<sup>2</sup>

Affiliations expand

- PMID: 37279801

- DOI: [10.1016/j.rmed.2023.107301](https://doi.org/10.1016/j.rmed.2023.107301)

## Abstract

**Background:** Asthma and obesity are prevalent conditions that are increasing worldwide. Asthma is characterized by airway inflammation and bronchial variability, while obesity is a complex metabolic disorder that poses significant morbidity and mortality risks. Obesity is a risk factor for asthma and a plethora of other non-communicable diseases.

**Objective:** To compare all-cause and cause-specific mortality between obese, overweight and normal weight adults with asthma in a cohort with long-term follow-up.

**Methods:** Individuals from a population-based adult asthma cohort recruited in Norrbotten county, Sweden, were clinically examined between 1986 and 2001 and grouped into body mass index (BMI) categories. Underlying causes of death until December 31st 2020 were categorized as cardiovascular, respiratory, cancer and other mortality by linking cohort data to the Swedish National Board of Health and Welfare's National Cause of Death register. Hazard ratios (HR) with 95% confidence intervals (CI) for all-cause and cause-specific mortality associated with overweight and obesity were calculated via Cox proportional hazard models.

**Results:** In total, 940 individuals were normal weight, 689 overweight and 328 obese while only 13 were underweight. Obesity increased the hazard for all-cause (HR 1.26, 95% CI 1.03-1.54) and cardiovascular mortality (HR 1.43, 95% CI 1.03-1.97). Obesity was not significantly associated with respiratory or cancer mortality. Overweight did not increase the hazard of all-cause or any cause-specific mortality category.

**Conclusion:** Obesity, but not overweight, was significantly associated with increased hazard of all-cause and cardiovascular mortality in adults with asthma. Neither obesity nor overweight were associated with increased hazard of respiratory mortality.

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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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Review

J Occup Environ Hyg

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. 2023 Jun 6;1-19.

doi: 10.1080/15459624.2023.2221712. Online ahead of print.

# Exposure frequency, intensity, and duration: What we know about work-related asthma risks for healthcare workers from cleaning and disinfection

[Amanda M Wilson](#)<sup>1</sup>, [Olusola Ogunseye](#)<sup>1</sup>, [Tina Finges](#)<sup>1</sup>, [D Jean McClelland](#)<sup>1</sup>, [Lynn B Gerald](#)<sup>2</sup>, [Philip Harber](#)<sup>1</sup>, [Paloma I Beamer](#)<sup>1</sup>, [Rachael M Jones](#)<sup>3</sup>

Affiliations expand

- PMID: 37279493
- DOI: [10.1080/15459624.2023.2221712](https://doi.org/10.1080/15459624.2023.2221712)

## Abstract

The objective of this review was to scope the current evidence base related to three exposure assessment concepts: frequency, intensity, and duration (latency) for cleaning and disinfection exposures in healthcare and subsequent work-related asthma risks. A

search strategy was developed addressing intersections of four main concepts: 1) work-related asthma, 2) occupation (healthcare workers/nurses), 3) cleaning and disinfection, and 4) exposure. Three databases were searched: Embase, PubMed, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database. Data were extracted related to three main components of risk assessment: 1) exposure frequency, 2) exposure intensity, 3) exposure duration. Latency data were analyzed using an exponential distribution fit, and extracted concentration data were compared to occupational exposure limits. The final number of included sources from which data were extracted was 133. Latency periods for occupational asthma were exponentially distributed, with a mean waiting time ( $1/\lambda$ ) of 4.55 years. No extracted concentration data were above OELs except for some formaldehyde and glutaraldehyde concentrations. Data from included sources also indicated some evidence for a dose-response relationship regarding increased frequency yielding increased risk, but this relationship is unclear due to potential confounders (differences in role/task and associated exposure) and the healthy worker effect. Data priority needs include linking concentration data to health outcomes, as most current literature does not include both types of measurements in a single study, leading to uncertainty in dose-response relationships.

**Keywords:** Chemical; hygiene; inhalation; latency; occupational health; respiratory; review.

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Am J Respir Crit Care Med

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. 2023 Jun 6.

doi: 10.1164/rccm.202305-0792LE. Online ahead of print.

# [Brusselle and Riemann Reply to: Disconnect for Tezepelumab on Exacerbations, Symptoms and Quality of Life in Type 2 Low Asthma](#)

[Guy Brusselle](#)<sup>1,2</sup>, [Sebastian Riemann MD](#)<sup>3,4</sup>

Affiliations expand

- PMID: 37279365
- DOI: [10.1164/rccm.202305-0792LE](https://doi.org/10.1164/rccm.202305-0792LE)

*No abstract available*

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Am J Respir Crit Care Med

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. 2023 Jun 6.

doi: [10.1164/rccm.202304-0746LE](https://doi.org/10.1164/rccm.202304-0746LE). Online ahead of print.

# [Disconnect for Tezepelumab on Exacerbations, Symptoms and Quality of Life in Type 2 Low Asthma](#)



[Brian Lipworth](#)<sup>1</sup>, [Rory Chan](#)<sup>2</sup>

Affiliations expand

- PMID: 37279364
- DOI: [10.1164/rccm.202304-0746LE](https://doi.org/10.1164/rccm.202304-0746LE)

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Meta-Analysis

PLoS Med

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. 2023 Jun 6;20(6):e1004176.

doi: 10.1371/journal.pmed.1004176. eCollection 2023 Jun.

# Treatment effect modification due to comorbidity: Individual participant data meta-analyses of 120 randomised controlled trials

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Affiliations expand

- PMID: 37279199
- PMCID: [PMC10243630](#)
- DOI: [10.1371/journal.pmed.1004176](#)

**Free PMC article**

## Abstract

**Background:** People with comorbidities are underrepresented in clinical trials. Empirical estimates of treatment effect modification by comorbidity are lacking, leading to uncertainty in treatment recommendations. We aimed to produce estimates of treatment effect modification by comorbidity using individual participant data (IPD).

**Methods and findings:** We obtained IPD for 120 industry-sponsored phase 3/4 trials across 22 index conditions (n = 128,331). Trials had to be registered between 1990 and 2017 and have recruited  $\geq 300$  people. Included trials were multicentre and international. For each index condition, we analysed the outcome most frequently reported in the included trials. We performed a two-stage IPD meta-analysis to estimate modification of treatment effect by comorbidity. First, for each trial, we modelled the interaction between comorbidity and treatment arm adjusted for age and sex. Second, for each treatment within each index condition, we meta-analysed the comorbidity-treatment interaction terms from each trial. We estimated the effect of comorbidity measured in 3 ways: (i) the number of comorbidities (in addition to the index condition); (ii) presence or absence of the 6 commonest comorbid diseases for each index condition; and (iii) using continuous markers of underlying conditions (e.g., estimated glomerular filtration rate (eGFR)). Treatment effects were modelled on the usual scale for the type of outcome (absolute scale for numerical outcomes, relative scale for binary outcomes). Mean age in the trials ranged from 37.1 (allergic rhinitis trials) to 73.0 (dementia trials) and percentage of male participants range from 4.4% (osteoporosis trials) to 100% (benign prostatic hypertrophy trials). The percentage of participants with 3 or more comorbidities ranged from 2.3% (allergic rhinitis trials) to 57% (systemic lupus erythematosus trials). We found no evidence of modification of treatment efficacy by comorbidity, for any of the 3 measures of comorbidity. This was the case for 20 conditions for which the outcome variable was continuous (e.g., change in glycosylated haemoglobin in diabetes) and for 3 conditions in which the outcomes were discrete events (e.g., number of headaches in migraine). Although all were null, estimates of treatment effect modification were more precise in some cases (e.g., sodium-glucose co-transporter-2 (SGLT2) inhibitors for type 2 diabetes-interaction term for comorbidity count 0.004, 95% CI -0.01 to 0.02) while for others

credible intervals were wide (e.g., corticosteroids for asthma-interaction term -0.22, 95% CI -1.07 to 0.54). The main limitation is that these trials were not designed or powered to assess variation in treatment effect by comorbidity, and relatively few trial participants had >3 comorbidities.

**Conclusions:** Assessments of treatment effect modification rarely consider comorbidity. Our findings demonstrate that for trials included in this analysis, there was no empirical evidence of treatment effect modification by comorbidity. The standard assumption used in evidence syntheses is that efficacy is constant across subgroups, although this is often criticised. Our findings suggest that for modest levels of comorbidities, this assumption is reasonable. Thus, trial efficacy findings can be combined with data on natural history and competing risks to assess the likely overall benefit of treatments in the context of comorbidity.

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## Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: SD received fees from the Association of the British Pharmaceutical Industry (ABPI) for delivery of a Masterclass (unrelated to this work). The other authors have declared that no competing interests exist.

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

### SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant support[expand](#)

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J Behav Med

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. 2023 Jun 6.

doi: 10.1007/s10865-023-00424-8. Online ahead of print.

# Assessing the interrelationship between asthma and obesity self-management behaviors

[Nikita Agrawal](#)<sup>1</sup>, [Jenny L Lin](#)<sup>2</sup>, [Jyoti Ankam](#)<sup>2</sup>, [Fernando Holguin](#)<sup>3</sup>, [Juan P Wisnivesky](#)<sup>4,2</sup>, [Alex Federman](#)<sup>2</sup>

Affiliations expand

- PMID: 37278861
- DOI: [10.1007/s10865-023-00424-8](https://doi.org/10.1007/s10865-023-00424-8)

## Abstract

Asthma and obesity are common coexisting conditions with increasing prevalence and substantial morbidity. This study examines the inter-relationship between illness and treatment beliefs in asthma and obesity and how they influence self-management behaviors. Overweight and obese adults  $\geq 18$  years with asthma were recruited from primary care and pulmonary practices in New York, NY and Denver, CO ( $n = 219$ ). Path analysis was used to examine the relationship between asthma, weight and exercise-related illness and medication beliefs and SMB. Necessity beliefs about asthma medications and diet were associated with better medication adherence and healthier dietary behaviors ( $\beta = 0.276$ ,  $p = < 0.001$ ,  $\beta = 0.148$ ,  $p = 0.018$  respectively) whereas concerns about these self-care activities were associated with poorer adherence and worse dietary behaviors ( $\beta = -0.282$ ,  $p < 0.001$ ,  $\beta = -0.188$ ,  $p = 0.003$  respectively). We found no statistically significant association of exercise behaviors with any other weight or asthma illness or treatment beliefs. Our study demonstrates that necessity and concerns about treatment are associated with adherence in asthma and obesity. The lack of association of exercise behaviors with any asthma or weight related beliefs may reflect limited awareness of the impact of weight on asthma and warrants additional research.

**Keywords:** Adherence; Asthma; Illness beliefs; Medication beliefs; Obesity; Self-management.

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- [45 references](#)

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Int J Nurs Pract

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. 2023 Jun 4;e13171.

doi: 10.1111/ijn.13171. Online ahead of print.

# [Study of the emotional adjustment of the caregiver-patient dyad to bronchial asthma in adolescence](#)

[Selene Valero-Moreno](#)<sup>1</sup>, [Inmaculada Montoya-Castilla](#)<sup>1</sup>, [Marián Pérez-Marín](#)<sup>1</sup>

Affiliations expand

- PMID: 37271579
- DOI: [10.1111/ijn.13171](https://doi.org/10.1111/ijn.13171)

# Abstract

**Aim:** This study aimed to investigate the impact of bronchial asthma-related factors on the emotional well-being of adolescents with bronchial asthma and their primary caregivers.

**Background:** Bronchial asthma is a common chronic disease in childhood and adolescence that can have a psychological impact on both patients and their primary caregivers.

**Methods:** The study used a cross-sectional design and included 150 patient-caregiver dyads diagnosed with bronchial asthma, aged between 12 and 16 years and collected between 2018 and 2020. It assessed the emotional adjustment of both patients and caregivers and recorded variables related to the disease. Qualitative and quantitative analyses were conducted to perform statistical analyses.

**Results:** Caregivers had higher anxiety and depression scores than patients. Good adherence to treatment was necessary for the emotional adjustment of the dyad. Controlled asthma, good adherence to treatment and a reduction in medical treatment were the primary predictors of emotional adjustment.

**Conclusions:** The study highlights the importance of assessing anxiety and depression levels in both patients and caregivers because the presence of these symptoms can lead to the misuse of medication, inadequate inhalation techniques, the omission of medication and reduced confidence in controlling asthma symptoms.

**Keywords:** adolescence; anxiety; bronchial asthma; caregivers; depression; nurses.

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- [40 references](#)

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. 2023 Jun 9;1-15.

doi: 10.1080/14737167.2023.2221435. Online ahead of print.

# Economic evaluation of biological treatments in patients with severe asthma: a systematic review

[Sara Alves](#)<sup>1</sup>, [João Cavaleiro Rufo](#)<sup>2,3</sup>, [José Crispim](#)<sup>4</sup>

Affiliations expand

- PMID: 37265078
- DOI: [10.1080/14737167.2023.2221435](https://doi.org/10.1080/14737167.2023.2221435)

## Abstract

**Background:** Asthma is a highly prevalent disease, one of the chronic diseases with the highest economic costs; thus, it imposes a high economic burden on society, the healthcare system, patients, and third-party payers. Contrary to this study, until now, systematic reviews of economic evaluations (EEs) of treatments for severe asthma have not been exclusively focused on biological treatments, and have included a small number of studies and only model-based EEs.

**Methods:** This study systematically reviews EEs of biological therapies for severe asthma published until December 2022 using PRISMA guidelines. The review analyzes the cost-effectiveness of biologicals in comparison to SOC, or SOC plus OCS. The quality of the EEs is assessed using Consensus on Health Economics Checklist extended (CHEC-extended).

**Results:** Thirty-nine studies were eligible: 15 based on a Markov model, and 19 trial-based; eight adopting societal and NHS perspectives, and seven the payer's perspective. The

reviewed EEs addressed cost-effectiveness, cost-utility, and incremental costs and outcomes comparison. Their findings were mainly expressed through ICER-incremental cost-effectiveness ratio (24 studies: 13 concluded that biological were cost-effective) and cost comparison analysis (14 studies: 6 concluded that biological were cost-effective), and were sensitive to a wide variety of factors (e.g. medication cost, treatment response, time horizon, utility benefits, mortality, exacerbation rate, discount rate, etc.).

**Conclusions:** There has been some ambiguity concerning the EE of biological therapies due to variation in choice of study design and contradictory results. Nevertheless, it can be concluded that biological treatments improve health outcomes, in many contexts at a high cost.

**Keywords:** Asthma; Biological therapies; Cost-effectiveness; Economic evaluation; Quality of life.

SUPPLEMENTARY INFO

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. 2023 Jun 5;1-9.

doi: 10.1080/14737167.2023.2220966. Online ahead of print.

## [Cost-effectiveness of Arg16Gly in ADRB2 pharmacogenomic-guided treatment for pediatric asthma](#)



[Xinyan Li](#)<sup>1</sup>, [Yunyun Cao](#)<sup>2</sup>

Affiliations expand

- PMID: 37256257
- DOI: [10.1080/14737167.2023.2220966](https://doi.org/10.1080/14737167.2023.2220966)

## Abstract

**Objectives:** To assess the cost-effectiveness of Arg16Gly *ADRB2* pharmacogenomic testing compared with no Arg16Gly *ADRB2* testing to guide the use of long-acting  $\beta_2$  receptor agonist (LABA) in asthma patients aged 1 to 5 years in China.

**Methods:** This economic evaluation developed a Markov model with four health states (no exacerbation, mild exacerbation, moderate-to-severe exacerbation, and death). Transition probabilities were estimated from the rate of exacerbations, the case-fatality rate of patients hospitalized for exacerbations, and natural mortality. Costs included drug costs and exacerbation management costs. Cost inputs and utilities for each health state were gained from public databases and the literatures. Costs and quality-adjusted life years (QALYs) were estimated for ten years. Deterministic and probabilistic sensitivity analyses were performed.

**Results:** In the base case analysis, in contrast to the group without the genotype test, the incremental total cost was -¥334.7, and the incremental QALY was 0.001 in the Arg16Gly *ADRB2* genotyping group. Therefore, the Arg16Gly *ADRB2* test group was the dominant strategy for children with asthma in China. The sensitivity analyses showed that the model was relatively stable.

**Conclusion:** Arg16Gly *ADRB2* testing before using LABA is a cost-effective approach compared with no gene testing for pediatric asthma.

**Keywords:** Arg16gly *ADRB2* pharmacogenomic test; Cost-effectiveness analysis; LABA; pediatric asthma; quality-adjusted life years.

FULL TEXT LINKS



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J Asthma

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. 2023 Jun 7;1-9.

doi: 10.1080/02770903.2023.2214921. Online ahead of print.

# Association between adult food insecurity and self-reported asthma in the United States: NHANES 2003–2018

[Kejie Ni](#)<sup>1</sup>, [Yufeng Wan](#)<sup>1</sup>, [Yulong Zheng](#)<sup>1</sup>

Affiliations expand

- PMID: 37255268
- DOI: [10.1080/02770903.2023.2214921](https://doi.org/10.1080/02770903.2023.2214921)

## Abstract

**Objective:** Asthma is a chronic disease of the lungs. The development of asthma is related to various risk factors. Food insecurity is a critical social determinant of health, although there is little information on the association between adult food insecurity and asthma. The purpose of this study is to explore the potential correlation in US adults.

**Methods:** The study population data were extracted from NHANES 2003–2018. Food insecurity was measured using the USDA FSSM and categorized as full, marginal, low, or very low food security. The assessment of self-reported asthma was determined by self-report questionnaires. The self-reported positive outcomes were that participants had asthma and a history of asthma attacks and asthma-related ER visits in the past year. We developed two multivariate logistic regression models. Stratified analyses were performed by gender and age.

**Results:** A total of 38,077 participants were considered in our final analysis. Compared to participants with FFS, the ORs (95% CIs) for asthma were 1.16 (1.00–1.33), 1.42 (1.23–1.64), and 1.56 (1.34–1.80) for participants with MFS, LFS, and VLFS, respectively (Model II).

Additionally, after full adjustment, individuals with VLFS had 49% greater risks of asthma attacks (OR = 1.49; 95% CI 1.13-1.97). The ORs (95% CIs) for asthma-related ER visits were 1.59 (1.14-2.23) and 1.98 (1.36-2.87) for participants with LFS and VLFS, respectively (Model II). The positive correlations remained robust when stratified by gender and age.

**Conclusion:** Our research showed that food insecurity among US adults was associated with asthma, asthma attacks, and asthma-related ER visits.

**Keywords:** FSSM; Food insecurity; NHANES; asthma; cross-sectional study.

FULL TEXT LINKS



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Review

J Exp Med

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. 2023 Jun 5;220(6):e20221094.

doi: 10.1084/jem.20221094. Epub 2023 May 10.

## T helper 2 cells in asthma

[James A Harker](#)<sup>1</sup>, [Clare M Lloyd](#)<sup>1</sup>

Affiliations expand

- PMID: 37163370

- PMCID: [PMC10174188](#)

- DOI: [10.1084/jem.20221094](https://doi.org/10.1084/jem.20221094)

**Free PMC article**

## Abstract

Allergic asthma is among the most common immune-mediated diseases across the world, and type 2 immune responses are thought to be central to pathogenesis. The importance of T helper 2 (Th2) cells as central regulators of type 2 responses in asthma has, however, become less clear with the discovery of other potent innate sources of type 2 cytokines and innate mediators of inflammation such as the alarmins. This review provides an update of our current understanding of Th2 cells in human asthma, highlighting their many guises and functions in asthma, both pathogenic and regulatory, and how these are influenced by the tissue location and disease stage and severity. It also explores how biologics targeting type 2 immune pathways are impacting asthma, and how these have the potential to reveal hitherto underappreciated roles for Th2 cell in lung inflammation.

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## Conflict of interest statement

Disclosures: the authors declare no competing interests exist.

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

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Publication types, MeSH terms, Substances [expand](#)

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Eur J Med Chem

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. 2023 Jun 5;254:115331.

doi: 10.1016/j.ejmech.2023.115331. Epub 2023 Apr 7.

# Application of an "inhalation by design" approach to the identification and in-vitro evaluation of novel purine based PI3K $\delta$ inhibitors

[Roberta Mazzucato](#)<sup>1</sup>, [Marinella Roberti](#)<sup>2</sup>, [Anna Maria Capelli](#)<sup>3</sup>, [Fabio Rancati](#)<sup>4</sup>, [Matteo Biagetti](#)<sup>5</sup>, [Claudio Fiorelli](#)<sup>4</sup>, [Paolo Bruno](#)<sup>4</sup>, [Paolo Ronchi](#)<sup>4</sup>, [Serena Bertolini](#)<sup>6</sup>, [Mauro Corsi](#)<sup>7</sup>, [Daniele Pala](#)<sup>8</sup>

Affiliations expand

- PMID: 37094451
- DOI: [10.1016/j.ejmech.2023.115331](https://doi.org/10.1016/j.ejmech.2023.115331)

## Abstract

PI3K $\delta$  is a lipid kinase which plays a key role in airway inflammatory conditions. Accordingly, the inhibition of PI3K $\delta$  can be considered a valuable strategy for the treatment of chronic respiratory diseases such as Asthma and Chronic obstructive pulmonary disease (COPD). In this work, we describe our efforts to identify new PI3K $\delta$  inhibitors following an "inhalation by design" strategy. Starting from the identification of a purine scaffold, we carried out a preliminary SAR expansion which led to the identification of a new hit characterized by a high enzymatic potency and moderate PI3K $\delta$  selectivity. A subsequent optimization led to novel purine based derivatives with favorable in vitro ADME profiles, which might represent promising starting points for future development of new inhaled drug candidates.

**Keywords:** Asthma; Chronic obstructive pulmonary disease (COPD); Chronic respiratory diseases; Inhalation by design; PI3-kinases (PI3Ks); PI3K $\delta$ .

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## Conflict of interest statement

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

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Randomized Controlled Trial

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. 2023 Jun 5;48(6):660-666.

doi: 10.1093/ced/llad098.

# Topical tacrolimus versus corticosteroids in childhood moderate-to-severe atopic dermatitis and the impact on airway inflammation: a long-term randomized open-label study

[Miia Perälä<sup>1</sup>](#), [Alexander Salava<sup>1</sup>](#), [Pekka Malmberg<sup>1</sup>](#), [Anna S Pelkonen<sup>1</sup>](#), [Mika J Mäkelä<sup>1</sup>](#), [Anita Remitz<sup>1</sup>](#)

Affiliations expand

- PMID: 36916653
- DOI: [10.1093/ced/llad098](https://doi.org/10.1093/ced/llad098)

## Abstract

**Background:** Childhood atopic dermatitis (AD) is often followed by other atopic comorbidities such as asthma.

**Aim:** To compare the effectiveness of topical tacrolimus (TAC) and topical corticosteroids (TCSs) and their impact on airway inflammation and bronchial hyperresponsiveness in patients with paediatric AD.

**Methods:** This was a 3-year randomized open-label comparative follow-up study of 152 1-3-year-old children with moderate-to-severe AD (trial registration: EudraCT2012-002412-95). Frequent study visits including clinical examinations, laboratory investigations (total IgE, specific IgEs, blood eosinophils), skin prick and respiratory function tests to assess airway inflammation and bronchial hyperresponsiveness (exhaled nitric oxide, airway responsiveness to exercise and methacholine) were performed.

**Results:** Changes in eczema parameters at 36 months were similar in the TCS and TAC groups for mean body surface area (BSA) difference 1.4 [95% confidence interval (CI) -1.48 to 4.19;  $P = 0.12$ ], mean Eczema Area and Severity Index (EASI) difference 0.2 (95% CI -1.38 to 1.82;  $P = 0.2$ ), mean Investigator's Global Assessment (IGA) difference, 0.3 (95% CI -0.12 to 0.67;  $P = 0.12$ ) and mean transepidermal water loss (TEWL) difference at the eczema site, -0.3 (95% CI -4.93 to 4.30;  $P = 0.96$ ) and at the control site, 1.4 (95% CI -0.96 to 3.60,  $P = 0.19$ ). The control-site TEWL increased more towards the end of follow-up in the TCS vs. TAC group (mean change difference -4.2, 95% CI -8.14 to -0.29;  $P = 0.04$ ). No significant impact on development of airway inflammation or bronchial hyperresponsiveness occurred in early effective eczema-treatment responders vs. others ('early' vs. 'other' response was defined as the difference in treatment response to airway outcomes in BSA, EASI or IGA at 3 months).

**Conclusion:** Children with moderate-to-severe AD benefit from long-term treatment with TCS or TAC. There were no significant differences in treatment efficacy. No differences in the impact on airways occurred between early effective treatment responders vs. others.

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## Conflict of interest statement

Conflicts of interest Outside the submitted work, A.R. has served as primary investigator, consultant and lecturer for AbbVie, Eli Lilly, Leo Pharma, Novartis, Roche and Regeneron-Sanofi. The other authors declare they have no conflicts of interest.

#### SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Ann Work Expo Health

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. 2023 Jun 6;67(5):553-558.

doi: 10.1093/annweh/wxad007.

## Total Reactive Isocyanate Group (TRIG) Measurement: A Commentary

[Glen McConnachie](#)<sup>1</sup>, [Paul Johnson](#)<sup>1</sup>

Affiliations expand

- PMID: 36866423
- PMCID: [PMC10243925](#)
- DOI: [10.1093/annweh/wxad007](#)



## Abstract

Exposure to airborne isocyanates has, for decades, been a leading cause of occupational asthma. As respiratory sensitizers, isocyanates can induce allergic respiratory diseases with symptoms persisting even without further exposure. As this cause of occupational asthma is recognized it should be almost entirely preventable. In several countries isocyanates are assigned occupational exposure limits based on the total of reactive isocyanate groups (TRIG). The measurement of TRIG has some significant advantages over the measurement of individual isocyanate compounds. This exposure metric is explicit, simplifying calculations, and comparisons across published data. It reduces the risk of underestimating exposure by 'missing' important isocyanate compounds that may be present but are not the target analytes. It allows for quantification of exposure to complex mixtures of isocyanates, di-isocyanates monomers, prepolymers, polyisocyanates, oligomers, and/or intermediate forms. This is becoming increasingly important as more complex isocyanate products are being used in the workplace. There are many methods and techniques for measuring air concentrations/potential exposure to isocyanates. Several established methods have been standardized and published as International Organization for Standardization (ISO) methods. While some may be applied directly for determination of TRIG, others (developed for determination of individual isocyanates), require modification. This commentary aims to highlight the relative merits and limitations of those methods capable of determining TRIG and also considers potential future developments.

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## Conflict of interest statement

The authors declare no conflict of interest relating to the material presented in this article.

- [60 references](#)

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS



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

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Lakartidningen

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. 2023 Jun 9;120:23041.

## [Allergic rhinitis in children and adults – international recommendations adapted to the clinical situation in Sweden]

[Article in Swedish]

[Mats Holmström](#)<sup>1</sup>, [Åke Davidsson](#)<sup>2</sup>, [Björn Stridh](#)<sup>3</sup>, [Erik Melén](#)<sup>4</sup>, [Marit Westman](#)<sup>5</sup>, [Adrian Brunkhorst](#)<sup>6</sup>, [Ulla Nyström](#)<sup>7</sup>

Affiliations expand

- PMID: 37293752

### Abstract

Allergic rhinitis is the most common chronic disease in Sweden, with impact on quality of life and with a heavy economic burden for the society. More than 20 years have passed since national recommendations were launched, and meanwhile both ARIA (Allergic rhinitis and its impact of asthma) and EUFOREA (The European Forum for Research and Education in Allergy and Airway Diseases) have presented international guidelines which in this article have been adapted to the clinical situation in Sweden. Visual analogue scale (VAS) is recommended for symptom evaluation, and the importance of correct allergen analysis and examination for coexisting asthma is emphasized. Treatment is recommended according to EUFOREA. Follow-up is important, and if VAS is  $\geq 5$  the disease is regarded as uncontrolled and must lead to a change of treatment. Since self-treatment is common in allergic rhinitis the importance of patient cooperation and information is underlined.

SUPPLEMENTARY INFO

Publication typesexpand

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Int Arch Allergy Immunol

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. 2023 Jun 8;1-11.

doi: 10.1159/000530842. Online ahead of print.

# [Analysis of Multimorbidity of Moderate to Severe Allergic Rhinitis in Children: A Real-World Study](#)

[Zheng Gu](#)<sup>1</sup>, [Ping Wei](#)<sup>2</sup>, [Wei Kou](#)<sup>2</sup>, [Xin-Ye Tang](#)<sup>2</sup>, [Hong-Bing Yao](#)<sup>2</sup>, [En-Mei Liu](#)<sup>2</sup>

Affiliations expand

- PMID: 37290409
- DOI: [10.1159/000530842](https://doi.org/10.1159/000530842)

## Abstract

**Introduction:** Allergic rhinitis (AR) in children is associated with various comorbidities, posing challenges for treatment and management. There have been few investigations of these multimorbidities in Chinese children with AR. Here, we investigated the prevalence of multimorbidities in children with moderate to severe AR and analyzed the influencing factors using real-world data.

**Methods:** In total, 600 children who visited the outpatient clinic of our hospital and were diagnosed with moderate-severe AR were prospectively enrolled. All children underwent allergen detection and electronic nasopharyngoscopy. Parents or guardians completed a

questionnaire that included age, sex, mode of delivery, feeding pattern, and familial history of allergy. The multimorbidities investigated included atopic dermatitis (AD), asthma, allergic conjunctivitis (AC), chronic rhinosinusitis (CRS), adenoid hypertrophy (AH), tonsil hypertrophy (TH), recurrent epistaxis, and recurrent respiratory tract infections (RRTIs).

**Results:** The AR multimorbidities reported in children were as follows: recurrent epistaxis (46.5%), AC (46.3%), AD (40.7%), asthma (22.5%), RRTIs (21.3%), CRS (20.5%), AH (19.7%), and TH (12.5%). In univariate logistic regression analysis, age ( $\leq 6$  years), birth mode, familial history of allergy, and single dust mite allergy were associated with AR multimorbidity ( $p \leq 0.05$ ). Multivariate logistic regression revealed that a familial history of allergy was an independent risk factor for AC (odds ratio [OR] = 1.539, 95% confidence interval [CI]: 1.104-2.145) and AH (OR = 1.506, 95% CI: 1.000-2.267) ( $p \leq 0.05$ ). Age ( $\leq 6$  years) was independently associated with the risk of AD (OR = 1.405, 95% CI: 1.003-1.969) and RRTIs (OR = 1.869, 95% CI: 1.250-2.793) ( $p \leq 0.05$ ), cesarean section with AR and CRS risk (OR = 1.678, 95% CI: 1.100-2.561), and single dust mite allergy with asthma (OR = 1.590, 95% CI: 1.040-2.432) and CRS (OR = 1.600, 95% CI: 1.018-2.515) risk ( $p \leq 0.05$ ). Further, non-dust mite allergy was independently associated with AR and CRS (OR = 2.056, 95% CI: 1.084-3.899).

**Conclusion:** AR was found to be accompanied by different comorbidities, including both allergic and non-allergic comorbidities, complicating disease treatment. These findings demonstrated that age ( $\leq 6$  years), familial history of allergy, types of allergens, and cesarean section were risk factors for different multimorbidities associated with AR.

**Keywords:** Allergic rhinitis; Child; Multimorbidity; Prevalence; Risk factor.

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Clin Exp Med

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. 2023 Jun 7.

# Association of serum CD14 level and functional polymorphism C-159T in the promoter region of CD14 gene with allergic rhinitis

[Mai A Kamel](#)<sup>1</sup>, [Elham S Selim](#)<sup>1</sup>, [Enas A Tantawy](#)<sup>1</sup>, [Aya Elgendy](#)<sup>2</sup>, [Alsayed Abdulmageed](#)<sup>3</sup>, [Reham H Anis](#)<sup>1</sup>

Affiliations expand

- PMID: 37286630
- DOI: [10.1007/s10238-023-01097-y](https://doi.org/10.1007/s10238-023-01097-y)

## Abstract

Allergic rhinitis (AR) is an inflammatory disease of the upper respiratory tract affecting a significant number of the world's population. It occurs as an IgE-mediated immune response of the nasal mucosa to inhaled allergens. The human Cluster of Differentiation 14 (CD14) is a glycosyl-phosphatidylinositol-anchored molecule expressed on the surface of monocytes and macrophages and functions as a receptor to lipopolysaccharides and inhaled endotoxins that may stimulate interleukins production by antigen-presenting cells. Consequently, CD14 plays a substantial role in allergic diseases and may become one of their etiological causes. Allergic rhinitis (AR) is an inflammatory disease of the upper respiratory tract affecting a significant number of the world's population. It occurs as an IgE-mediated immune response of the nasal mucosa to inhaled allergens. The human Cluster of Differentiation 14 (CD14) is a glycosyl-phosphatidylinositol-anchored molecule expressed on the surface of monocytes and macrophages and functions as a receptor to lipopolysaccharides and inhaled endotoxins that may stimulate interleukins production by antigen-presenting cells. Consequently, CD14 plays a substantial role in allergic diseases and may become one of their etiological causes. This study aimed to determine the association between C-159T polymorphism in the CD14 gene promoter region and serum CD14 levels and the risk of Allergic rhinitis Egyptian patients and to test the validity of serum CD14 level measurement in predicting AR. This case-control study included 45 patients with AR referred to Allergy and Immunology Unit, Zagazig University Hospital, Zagazig, Egypt, and 45 healthy subjects as controls. Serum CD14 levels were measured by ELISA. The polymerase chain reaction-restriction fragment length polymorphism technique was used to detect C-159T gene polymorphism in the CD14 promoter region. This case-

control study included 45 patients with AR referred to Allergy and Immunology Unit, Zagazig University Hospital, Zagazig, Egypt, and 45 healthy subjects as controls. Serum CD14 levels were measured by ELISA. The polymerase chain reaction-restriction fragment length polymorphism technique was used to detect C-159T gene polymorphism in the CD14 promoter region. There was a significant association between CD14 serum levels and AR incidence ( $P < 0.001$ ), with patients having higher serum CD14 levels than controls. In addition, a significant association ( $P < 0.001$ ) was detected between serum CD14 levels and the severity of AR, as well as elevated serum CD14 levels in severe and the most severe cases. On the molecular level, there was a statistically significant relationship between patients and the control group regarding the CD14 genotype ( $P < 0.001$ ), where CT and TT genotypes and T allele were primarily associated with the cases group, indicating that the risk of AR was significantly associated with the inheritance of the TT genotype. Additionally, a statistically significant association was found between the severity of AR and CD14 genotype ( $P < 0.001$ ), where TT genotypes were mainly associated with severe and the most severe cases. In the studied groups, there was a statistically significant difference ( $P < 0.05$ ) between the CD14 genotype and serum CD14 levels, with TT genotypes being associated with higher CD14 levels. The results obtained in this study revealed that serum CD14 level is a potential biomarker for the diagnosis of AR and, at the genetic level, a potential predictor of disease.

**Keywords:** Allergic rhinitis; C-159T; CD14; Polymorphism.

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- [34 references](#)

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Meta-Analysis

PLoS Med

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. 2023 Jun 6;20(6):e1004176.

doi: 10.1371/journal.pmed.1004176. eCollection 2023 Jun.

# Treatment effect modification due to comorbidity: Individual participant data meta-analyses of 120 randomised controlled trials

[Peter Hanlon](#)<sup>1</sup>, [Elaine W Butterly](#)<sup>1</sup>, [Anoop Sv Shah](#)<sup>2</sup>, [Laurie J Hannigan](#)<sup>3 4 5</sup>, [Jim Lewsey](#)<sup>1</sup>, [Frances S Mair](#)<sup>1</sup>, [David M Kent](#)<sup>6</sup>, [Bruce Guthrie](#)<sup>7</sup>, [Sarah H Wild](#)<sup>7</sup>, [Nicky J Welton](#)<sup>4</sup>, [Sofia Dias](#)<sup>8</sup>, [David A McAllister](#)<sup>1</sup>

Affiliations expand

- PMID: 37279199
- PMCID: [PMC10243630](#)
- DOI: [10.1371/journal.pmed.1004176](#)

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## Abstract

**Background:** People with comorbidities are underrepresented in clinical trials. Empirical estimates of treatment effect modification by comorbidity are lacking, leading to uncertainty in treatment recommendations. We aimed to produce estimates of treatment effect modification by comorbidity using individual participant data (IPD).

**Methods and findings:** We obtained IPD for 120 industry-sponsored phase 3/4 trials across 22 index conditions (n = 128,331). Trials had to be registered between 1990 and 2017 and have recruited ≥300 people. Included trials were multicentre and international. For each index condition, we analysed the outcome most frequently reported in the included trials. We performed a two-stage IPD meta-analysis to estimate modification of treatment effect by comorbidity. First, for each trial, we modelled the interaction between comorbidity and treatment arm adjusted for age and sex. Second, for each treatment within each index condition, we meta-analysed the comorbidity-treatment interaction

terms from each trial. We estimated the effect of comorbidity measured in 3 ways: (i) the number of comorbidities (in addition to the index condition); (ii) presence or absence of the 6 commonest comorbid diseases for each index condition; and (iii) using continuous markers of underlying conditions (e.g., estimated glomerular filtration rate (eGFR)). Treatment effects were modelled on the usual scale for the type of outcome (absolute scale for numerical outcomes, relative scale for binary outcomes). Mean age in the trials ranged from 37.1 (allergic rhinitis trials) to 73.0 (dementia trials) and percentage of male participants range from 4.4% (osteoporosis trials) to 100% (benign prostatic hypertrophy trials). The percentage of participants with 3 or more comorbidities ranged from 2.3% (allergic rhinitis trials) to 57% (systemic lupus erythematosus trials). We found no evidence of modification of treatment efficacy by comorbidity, for any of the 3 measures of comorbidity. This was the case for 20 conditions for which the outcome variable was continuous (e.g., change in glycosylated haemoglobin in diabetes) and for 3 conditions in which the outcomes were discrete events (e.g., number of headaches in migraine). Although all were null, estimates of treatment effect modification were more precise in some cases (e.g., sodium-glucose co-transporter-2 (SGLT2) inhibitors for type 2 diabetes-interaction term for comorbidity count 0.004, 95% CI -0.01 to 0.02) while for others credible intervals were wide (e.g., corticosteroids for asthma-interaction term -0.22, 95% CI -1.07 to 0.54). The main limitation is that these trials were not designed or powered to assess variation in treatment effect by comorbidity, and relatively few trial participants had >3 comorbidities.

**Conclusions:** Assessments of treatment effect modification rarely consider comorbidity. Our findings demonstrate that for trials included in this analysis, there was no empirical evidence of treatment effect modification by comorbidity. The standard assumption used in evidence syntheses is that efficacy is constant across subgroups, although this is often criticised. Our findings suggest that for modest levels of comorbidities, this assumption is reasonable. Thus, trial efficacy findings can be combined with data on natural history and competing risks to assess the likely overall benefit of treatments in the context of comorbidity.

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## Conflict of interest statement

I have read the journal's policy and the authors of this manuscript have the following competing interests: SD received fees from the Association of the British Pharmaceutical Industry (ABPI) for delivery of a Masterclass (unrelated to this work). The other authors have declared that no competing interests exist.

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



## SUPPLEMENTARY INFO

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Eur Arch Otorhinolaryngol

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. 2023 Jun 5.

doi: 10.1007/s00405-023-08006-9. Online ahead of print.

# [Azelastine/fluticasone and allergic rhinitis in clinical practice](#)

[Desiderio Passali](#)<sup>1</sup>, [Giulio Cesare Passali](#)<sup>2</sup>, [Valerio Damiani](#)<sup>3</sup>, [Giorgio Ciprandi](#)<sup>4</sup>

Affiliations expand

- PMID: 37277684
- DOI: [10.1007/s00405-023-08006-9](https://doi.org/10.1007/s00405-023-08006-9)

*No abstract available*

## Comment on

- [Therapeutic management of allergic rhinitis: a survey of otolaryngology and allergology specialists.](#)  
Colás C, Álvarez-Suárez ME, Benedito-Palos L, Alobid I. Eur Arch Otorhinolaryngol. 2023 Jul;280(7):3469-3474. doi: 10.1007/s00405-023-07955-5. Epub 2023 Apr 5. PMID: 37020046
- [5 references](#)

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Ann Otol Rhinol Laryngol

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. 2023 Jun 4;34894231176327.

doi: 10.1177/00034894231176327. Online ahead of print.

# [Intranasal Schirmer Test in Allergic Rhinitis: Relationship to Symptom Scores and Role in Determining Response to Treatment](#)

[Ozlem Onerci Celebi](#)<sup>1</sup>, [Ela Araz Server](#)<sup>1</sup>, [Tolga Kirgezen](#)<sup>1</sup>, [Ozgur Yigit](#)<sup>1</sup>, [Ecem Sevim Aki](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 37271974

- DOI: [10.1177/00034894231176327](https://doi.org/10.1177/00034894231176327)

## Abstract

**Objectives:** The Intranasal Schirmer test (INS) is an easy to administer test that can yield objective measurement of the quantity of nasal secretion and has been studied in patients with various nasal and systemic pathologies; however, the role of INS in patients with allergic rhinitis remains unclear. Our aim was to determine the relationship between various allergic symptoms and the Intranasal Schirmer Test (INS) score and to evaluate the utility of INS in determining treatment effect in patients with allergic rhinitis.

**Methods:** This prospective study included patients with allergic rhinitis who were randomly divided into 3 treatment groups (nasal steroid only, oral antihistamine only, nasal steroid and oral antihistamine). For all patients, Total Nasal Symptom Score (TNSS) was used to measure symptom severity and INS was administered before and after treatment. Pre-treatment and post treatment TNSS and INS scores were compared between different treatment groups and within each group.

**Results:** The study included 120 patients, with 40 patients in each group. There were significant differences both in pre-treatment and post-treatment symptom severity score with changes of INS scores between treatment groups ( $P < .001$  and  $P = .002$ , respectively). There was a significant difference between pre-treatment and post-treatment symptom severity scores and the INS score in each treatment group ( $P < .001$ ). There was also a significant positive correlation between INS score and TNSS ( $r = .591$  and  $P < .001$ ).

**Conclusion:** The Intranasal Schirmer Test can be used as an objective tool for patients with allergic rhinitis as an adjunct to subjective patient symptom reports and can also be used to determine the response to treatment.

**Keywords:** Intranasal Schirmer test; allergic rhinitis; nasal steroids; oral antihistamines.

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

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Indian J Pediatr

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. 2023 Jun 8.

doi: 10.1007/s12098-023-04632-7. Online ahead of print.

# Evaluation of Chronic Cough in Children Using Management Algorithm: A Prospective Cohort Study

[Nikhil Rajvanshi](#)<sup>1</sup>, [Prawin Kumar](#)<sup>1</sup>, [Jagdish Prasad Goyal](#)<sup>2</sup>

Affiliations expand

- PMID: 37289310
- DOI: [10.1007/s12098-023-04632-7](https://doi.org/10.1007/s12098-023-04632-7)

## Abstract

**Objective:** To assess the use of a standardized evaluation algorithm [American College of Chest Physician (ACCP) 2006] in children with chronic cough.

**Methods:** In this prospective cohort study, children with chronic cough were evaluated as per the ACCP 2006 diagnostic algorithm. All children were followed regularly at an interval of 2-4 wk. The study's endpoint was for the patient being cough free for four weeks either following treatment or naturally.

**Results:** The mean age of the 87 studied children (52 male, 35 female) was  $11.9 \pm 3$  y. Forty children (45.9%) had specific cough pointers on history and examination. Radiograph showed abnormalities in 12 (13.8%) children, and spirometry showed a reversible obstructive pattern on spirometry in 6 (6.9%) among 47 (54%) children without specific cough pointers. After a detailed evaluation, 16 (18.3%) children had no remarkable findings and were reviewed after two weeks. Spontaneous resolution of cough occurred in 6 children. A trial of inhalational corticosteroids (ICS) (9 children) or antibiotics (1 child) was given to the rest of the ten children. Specific underlying diagnoses could be established in

80 (91.9%) children. The most common etiology identified in the study was asthma and asthma-like illnesses (n = 52; 59.8%), followed by upper airway cough syndrome (n = 13; 14.9%) and tuberculosis (n = 9; 10.4%). Eighty-four (96.5%) children had complete resolution of cough during follow-up. The mean time to resolution in the study was  $33.6 \pm 16.8$  d.

**Conclusions:** This study demonstrated that the ACCP 2006 algorithm is effective in establishing the underlying etiology and managing children with chronic cough.

**Keywords:** ACCP algorithm; Chronic cough; Management.

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Review

Curr Hypertens Rep

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. 2023 Jun 7.

doi: 10.1007/s11906-023-01248-2. Online ahead of print.

## [ACE-Inhibitors in Hypertension: A Historical Perspective and Current Insights](#)

[Stacey Cutrell](#)<sup>1</sup>, [Ibrahim S Alhomoud](#)<sup>1,2</sup>, [Anurag Mehta](#)<sup>3</sup>, [Azita H Talasaz](#)<sup>1</sup>, [Benjamin Van Tassel](#)<sup>1</sup>, [Dave L Dixon](#)<sup>4</sup>

Affiliations expand

- PMID: 37284934
- DOI: [10.1007/s11906-023-01248-2](https://doi.org/10.1007/s11906-023-01248-2)

## Abstract

**Purpose of review:** This review describes the discovery and development of ACE inhibitors as antihypertensive agents, compares their efficacy, tolerability, and safety to ARBs, and highlights the contemporary issues surrounding ACE inhibitor use for HTN.

**Recent findings:** Angiotensin-converting enzyme (ACE) inhibitors are commonly prescribed medications for the management of hypertension (HTN) and other chronic conditions including heart failure and chronic kidney disease. These agents inhibit ACE, the enzyme that is responsible for converting angiotensin (AT) I to AT II. Inhibiting the synthesis of AT II causes arterial and venous vasodilation, natriuresis, and a decrease in sympathetic activity, resulting in the reduction of blood pressure. ACE inhibitors are first-line therapy in HTN management along with thiazide diuretics, calcium channel blockers, and angiotensin receptor blockers (ARB). Along with inhibiting AT II synthesis, inhibition of ACE causes accumulation of bradykinin, increasing the risk of bradykinin-mediated side effects like angioedema and cough. Since ARBs do not work on ACE in the renin-angiotensin system, the risk of angioedema and cough are lower with ARBs. Recent evidence has also suggested ARBs may have neuroprotective effects compared to other antihypertensives, including ACE inhibitors; however, this warrants further study. Currently, ACE inhibitors and ARBs have an equal class of recommendation for first-line treatment for the management of HTN. Recent evidence has shown ARBs to be just as effective as ACE inhibitors for HTN but with improved tolerability.

**Keywords:** Angiotensin II; Angiotensin II receptor blockers; Angiotensin-converting enzyme inhibitors; Hypertension; Renin-angiotensin.

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- [56 references](#)

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# Cystic Fibrosis: A Review

[Thida Ong](#)<sup>1</sup>, [Bonnie W Ramsey](#)<sup>1</sup>

Affiliations [expand](#)

- PMID: 37278811
- DOI: [10.1001/jama.2023.8120](https://doi.org/10.1001/jama.2023.8120)

## Abstract

**Importance:** Cystic fibrosis, a genetic disorder defined by variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, affects more than 30 000 individuals in the US and approximately 89 000 worldwide. Absent or decreased function of the CFTR protein is associated with multiorgan dysfunction and shortened life expectancy.

**Observations:** CFTR is an anion channel in the apical membrane of epithelial cells. Loss of function leads to obstructed exocrine glands. Of people with cystic fibrosis in the US, approximately 85.5% have the gene variant F508del. Manifestations of cystic fibrosis in patients with the F508del gene variant begin in infancy with steatorrhea, poor weight gain, and respiratory symptoms (coughing, wheezing). As people with cystic fibrosis age, chronic respiratory bacterial infections cause loss of lung function and bronchiectasis. With the availability of universal newborn screening in multiple countries including the US, many people with cystic fibrosis are asymptomatic at diagnosis. With multidisciplinary care teams that included dietitians, respiratory therapists, and social workers, treatment of cystic fibrosis can slow disease progression. Median survival has improved from 36.3 years (95% CI, 35.1-37.9) in 2006 to 53.1 years (95% CI, 51.6-54.7) in 2021. Pulmonary therapies for patients with cystic fibrosis consist of mucolytics (eg, dornase alfa), anti-inflammatories (eg, azithromycin), and antibiotics (such as tobramycin delivered by a nebulizer). Four small molecular therapies, termed CFTR modulators, that facilitate CFTR production and/or function have received regulatory approval. Examples are ivacaftor and elexacaftor-tezacaftor-ivacaftor. For example, in patients with 1 F508del variant, the combination of ivacaftor, tezacaftor, and elexacaftor improved lung function from -0.2% in the placebo group to 13.6% (difference, 13.8%; 95% CI, 12.1%-15.4%) and decreased the annualized estimated rate of pulmonary exacerbations from 0.98 to 0.37 (rate ratio, 0.37; 95% CI, 0.25-0.55). Improved respiratory function and symptoms have lasted up to 144 weeks in

postapproval observational studies. An additional 177 variants are eligible for treatment with the elexacaftor-tezacaftor-ivacaftor combination.

**Conclusion:** Cystic fibrosis affects approximately 89 000 people worldwide and is associated with a spectrum of disease related to exocrine dysfunction, including chronic respiratory bacterial infections and reduced life expectancy. First-line pulmonary therapies consist of mucolytics, anti-inflammatories, and antibiotics, and approximately 90% of people with cystic fibrosis who are 2 years or older may benefit from a combination of ivacaftor, tezacaftor, and elexacaftor.

#### SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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#### JAMA

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. 2023 Jun 6;329(21):1859-1871.

doi: 10.1001/jama.2023.8120.

[Thida Ong](#)<sup>1</sup>, [Bonnie W Ramsey](#)<sup>1</sup>

Affiliations expand

- PMID: 37278811
- DOI: [10.1001/jama.2023.8120](https://doi.org/10.1001/jama.2023.8120)

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#### SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

#### FULL TEXT LINKS



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

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Eur Respir Rev

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. 2023 Jun 7;32(168):230015.

doi: 10.1183/16000617.0015-2023. Print 2023 Jun 30.

## Basic, translational and clinical aspects of bronchiectasis in adults

[James D Chalmers](#)<sup>1</sup>, [Stuart Elborn](#)<sup>2</sup>, [Catherine M Greene](#)<sup>3</sup>

Affiliations expand

- PMID: 37286220
- PMCID: [PMC10245133](#)
- DOI: [10.1183/16000617.0015-2023](#)

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## Abstract

Bronchiectasis is a common progressive respiratory disease with recognisable radiological abnormalities and a clinical syndrome of cough, sputum production and recurrent respiratory infections. Inflammatory cell infiltration into the lung, in particular neutrophils, is central to the pathophysiology of bronchiectasis. Herein we explore the roles and relationships between infection, inflammation and mucociliary clearance dysfunction in the establishment and progression of bronchiectasis. Microbial and host-mediated damage are important processes underpinning bronchiectasis and the relative contribution of proteases, cytokines and inflammatory mediators to the propagation of inflammation is presented. We also discuss the emerging concept of inflammatory endotypes, defined by the presence of neutrophilic and eosinophilic inflammation, and explore the role of inflammation as a treatable trait. Current treatment for bronchiectasis focuses on

treatment of underlying causes, enhancing mucociliary clearance, controlling infection and preventing and treating complications. Data on airway clearance approaches *via* exercise and mucoactive drugs, pharmacotherapy with macrolides to decrease exacerbations and the usefulness of inhaled antibiotics and bronchodilators are discussed, finishing with a look to the future where new therapies targeting host-mediated immune dysfunction hold promise.

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## Conflict of interest statement

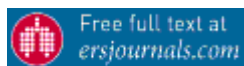
Conflict of interest: J.D. Chalmers reports grants or contracts from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Gilead Sciences, Grifols, Novartis and Insmmed, outside the submitted work; consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Insmmed, Janssen, Novartis, Pfizer and Zambon, outside the submitted work. Conflict of interest: 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 Viartis Inc.; and has been a paid speaker for many pharmaceutical companies over 30 years in respiratory medicine. Conflict of interest: C.M. Greene reports grants or contracts from NIH and Vertex, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Vertex, outside the submitted work; support for attending meetings and/or travel from European Respiratory Society, outside the submitted work; and was Head of ERS Assembly 3 2019–2022, outside the submitted work.

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# Clinical course and risk factors for development and progression of interstitial lung disease in primary Sjögren's syndrome

[Kyung-Ann Lee](#)<sup>#1</sup>, [Bo Da Nam](#)<sup>#2</sup>, [Jung Hwa Hwang](#)<sup>2</sup>, [Hyun-Sook Kim](#)<sup>3</sup>

Affiliations [expand](#)

- PMID: 37280251
- PMCID: [PMC10244322](#)
- DOI: [10.1038/s41598-023-35608-4](#)

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## Abstract

This single-center, retrospective study aimed to investigate the course and prognostic factors of patients with primary Sjögren syndrome-associated interstitial lung disease (pSS-ILD). We included 120 pSS patients who underwent at least two high-resolution computed tomography (HRCT) scans between 2013 and 2021. Clinical symptoms, laboratory data, HRCT findings, and pulmonary function test results were collected. Two thoracic radiologists reviewed the HRCT findings. In patients with pSS without ILD at baseline (n = 81), no development of ILD was found on follow-up (median, 2.8 years). In patients with pSS-ILD (n = 39), total disease extent, extent of coarse reticulation, and traction bronchiectasis increased on HRCT, whereas the extent of ground glass opacity (GGO) decreased at follow-up (median, 3.2 years) (each  $p < 0.001$ ). In progressive group of pSS-ILD (48.7%), the extent of coarse reticulation and coarseness score of fibrosis were increased at follow-up ( $p < 0.05$ ). Usual interstitial pneumonia pattern on CT (OR, 15.237)

and follow-up duration (OR, 1.403) were independent risk factors for disease progression in patients with pSS-ILD. In both progressive and non-progressive pSS-ILD, GGO decreased, whereas the extent of fibrosis increased even after treatment with glucocorticoid and/or immunosuppressants. In conclusion, progression occurred in approximately half of the pSS-ILD patients with slow gradual deterioration. Our study identified a definite group of progressive pSS-ILD who did not respond to current anti-inflammatory treatment.

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# Conflict of interest statement

The authors declare no competing interests.

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

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JAMA

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- . 2023 Jun 6;329(21):1859-1871.  
doi: 10.1001/jama.2023.8120.

# Cystic Fibrosis: A Review

[Thida Ong](#)<sup>1</sup>, [Bonnie W Ramsey](#)<sup>1</sup>

Affiliations expand

- PMID: 37278811
- DOI: [10.1001/jama.2023.8120](https://doi.org/10.1001/jama.2023.8120)

## Abstract

**Importance:** Cystic fibrosis, a genetic disorder defined by variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, affects more than 30 000 individuals in the US and approximately 89 000 worldwide. Absent or decreased function of the CFTR protein is associated with multiorgan dysfunction and shortened life expectancy.

**Observations:** CFTR is an anion channel in the apical membrane of epithelial cells. Loss of function leads to obstructed exocrine glands. Of people with cystic fibrosis in the US, approximately 85.5% have the gene variant F508del. Manifestations of cystic fibrosis in patients with the F508del gene variant begin in infancy with steatorrhea, poor weight gain, and respiratory symptoms (coughing, wheezing). As people with cystic fibrosis age, chronic respiratory bacterial infections cause loss of lung function and bronchiectasis. With the availability of universal newborn screening in multiple countries including the US, many people with cystic fibrosis are asymptomatic at diagnosis. With multidisciplinary care teams that included dietitians, respiratory therapists, and social workers, treatment of cystic fibrosis can slow disease progression. Median survival has improved from 36.3 years (95% CI, 35.1-37.9) in 2006 to 53.1 years (95% CI, 51.6-54.7) in 2021. Pulmonary therapies for patients with cystic fibrosis consist of mucolytics (eg, dornase alfa), anti-inflammatories (eg, azithromycin), and antibiotics (such as tobramycin delivered by a nebulizer). Four small molecular therapies, termed CFTR modulators, that facilitate CFTR production and/or function have received regulatory approval. Examples are ivacaftor and elexacaftor-tezacaftor-ivacaftor. For example, in patients with 1 F508del variant, the combination of ivacaftor, tezacaftor, and elexacaftor improved lung function from -0.2% in the placebo group to 13.6% (difference, 13.8%; 95% CI, 12.1%-15.4%) and decreased the annualized estimated rate of pulmonary exacerbations from 0.98 to 0.37 (rate ratio, 0.37; 95% CI, 0.25-0.55). Improved respiratory function and symptoms have lasted up to 144 weeks in postapproval observational studies. An additional 177 variants are eligible for treatment with the elexacaftor-tezacaftor-ivacaftor combination.

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consist of mucolytics, anti-inflammatories, and antibiotics, and approximately 90% of people with cystic fibrosis who are 2 years or older may benefit from a combination of ivacaftor, tezacaftor, and elexacaftor.

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Editorial

Pediatr Pulmonol

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. 2023 Jun 6.

doi: 10.1002/ppul.26529. Online ahead of print.

## [Primary ciliary dyskinesia as a common cause of bronchiectasis in the Canadian Inuit population](#)

[Deborah J Morris-Rosendahl](#)<sup>1,2</sup>

Affiliations expand

- PMID: 37278553

- DOI: [10.1002/ppul.26529](https://doi.org/10.1002/ppul.26529)

*No abstract available*

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