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

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Heart

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. 2023 Jul 6;heartjnl-2023-322881.

doi: 10.1136/heartjnl-2023-322881. Online ahead of print.

## [Updated definition of pulmonary hypertension and outcome after transcatheter aortic valve implantation](#)

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- PMID: 37414524

- DOI: [10.1136/heartjnl-2023-322881](https://doi.org/10.1136/heartjnl-2023-322881)

## Abstract

**Objective:** The European Society of Cardiology guidelines have recently defined new cut-offs for pulmonary hypertension (PH) and pulmonary vasculature resistance (PVR; median pulmonary artery pressure (mPAP) >20 instead of 25 mm Hg and PVR >2 instead of 3 Wood unit). The prognostic value of this updated classification after transcatheter aortic valve implantation (TAVI) is unknown.

**Methods:** 579 consecutive patients treated by TAVI with preprocedural right heart catheterisation evaluation were included. Patients were grouped as: (1) no PH, (2) isolated precapillary/combined (I-PreC/Co) PH and (3) isolated postcapillary PH (I-PoC). All-cause death, cardiovascular death and hospitalisations for heart failure (HF) were evaluated at follow-up. We also analysed the prognostic role of residual postprocedural PH.

**Results:** Out of 579 patients, 299 (52%) had PH according to the new criteria compared with 185 (32%) according to the previous ones. Overall median age was 82 years, while 55.3% patients were male. Patients with PH were more frequently diagnosed with chronic obstructive pulmonary disease and atrial fibrillation and were characterised by higher surgical risk as compared with patients without PH. At a median follow-up of 2.9 years, the presence of PH according to previous definition was associated with worse survival ( $p < 0.001$ ) and HF hospitalisation ( $p = 0.002$ ) rates, irrespective of PVR values. With newer cut-offs, PH was associated with worse outcomes only in patients with increased PVR, while no differences were found between patients with PH and normal PVR values and those without PH. Postprocedural mPAP normalisation was observed in 45% of the cases, but it was associated with improved long-term survival only in the I-PoC PH group.

**Conclusions:** New ESC PH cut-offs increased the number of PH diagnoses. The presence of PH, particularly in the setting of increased PVR, identify patients at higher risk for postprocedural mortality and rehospitalisation. Normalisation of PH was associated with better survival only in I-PoC group.

**Keywords:** aortic stenosis; transcatheter aortic valve replacement.

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## Conflict of interest statement

Competing interests: GT reported honoraria for lectures/consulting from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, GADA. The remaining authors have nothing to disclose.

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. 2023 Jul 6;2300883.

doi: 10.1183/13993003.00883-2023. Online ahead of print.

# Single-inhaler triple *versus* dual bronchodilator therapy for GOLD E and other exacerbating patients with COPD: Real-world comparative effectiveness and safety

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Affiliations expand

- PMID: 37414423
- DOI: [10.1183/13993003.00883-2023](https://doi.org/10.1183/13993003.00883-2023)

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. 2023 Jul 6;2300463.

doi: 10.1183/13993003.00463-2023. Online ahead of print.

# Mechanisms of hypoxaemia in severe pulmonary hypertension associated with COPD

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- PMID: 37414421
- DOI: [10.1183/13993003.00463-2023](https://doi.org/10.1183/13993003.00463-2023)

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. 2023 Jul 6;2300442.

doi: 10.1183/13993003.00442-2023. Online ahead of print.

# European Respiratory Society statement on frailty in adults with chronic lung disease

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- PMID: 37414420
- DOI: [10.1183/13993003.00442-2023](https://doi.org/10.1183/13993003.00442-2023)

## Abstract

Frailty is a complex, multidimensional syndrome characterised by a loss of physiological reserves that increases a person's susceptibility to adverse health outcomes. Most knowledge regarding frailty originates from geriatric medicine, however, awareness of its importance as a treatable trait for people with chronic respiratory disease (including asthma, COPD and interstitial lung disease) is emerging. A clearer understanding of frailty and its impact in chronic respiratory disease is a pre-requisite to optimise clinical management in the future. This unmet need underpins the rationale for undertaking the present work. This European Respiratory Society Statement synthesises current evidence and clinical insights from international experts and people affected by chronic respiratory conditions regarding frailty in adults with chronic respiratory disease. The scope includes coverage of frailty within international respiratory guidelines, prevalence and risk factors, review of clinical management options (including comprehensive geriatric care, rehabilitation, nutrition, pharmacological and psychological therapies), and identification of evidence gaps to inform future priority areas of research. Frailty is under-represented in international respiratory guidelines, despite being common and related to increased hospitalisation and mortality. Validated screening instruments can detect frailty to prompt comprehensive assessment and personalised clinical management. Clinical trials targeting people with chronic respiratory disease and frailty are needed.

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. 2023 Jul 4;102231.

doi: 10.1016/j.pupt.2023.102231. Online ahead of print.

# [Assessing the relationship between cardiovascular and small airway disease and acute events in COPD: The ARCADIA study protocol](#)

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- PMID: 37414133
- DOI: [10.1016/j.pupt.2023.102231](https://doi.org/10.1016/j.pupt.2023.102231)

## Abstract

The initial alterations of chronic obstructive pulmonary disease (COPD) involve the small airways. Small airway disease (SAD) is related to lung hyperinflation and air trapping. Several lung function tests may detect the presence of SAD, namely forced mid-expiratory flows, residual volume (RV), RV/total lung capacity (TLC) ratio, functional residual capacity, airway resistances obtained with body-plethysmography and oscillometry, and the single-breath nitrogen washout test. Additionally, high-resolution computed tomography can detect SAD. In addition to SAD, COPD is related to cardiovascular disease (CVD) such as heart failure, peripheral vascular disease, and ischemic heart disease. No studies have assessed the relationship between CVD, COPD, and SAD. Therefore, the main objective of the Assessing the Relationship between Cardiovascular and small Airway Disease and Acute events in COPD (ARCADIA) study is to assess the risk of CVD in COPD patients according to SAD in a real-life setting. The correlation between CVD, mortality, and acute

exacerbation of COPD (AECOPD) is also evaluated. ARCADIA is a 52-week prospective, multicentre, pilot, observational, cohort study conducted in  $\geq 22$  pulmonary centres in Italy and that enrolls  $\geq 500$  COPD patients, regardless of disease severity (protocol registration: ISRCTN49392136). SAD is evaluated at baseline, after that CVD, mortality, and AECOPD are recorded at 6 and 12 months. Bayesian inference is used to quantify the risk and correlation of the investigated outcomes in COPD patients according to SAD. The ARCADIA study provides relevant findings in the daily clinical management of COPD patients.

**Keywords:** Bayesian inference; COPD; Cardiovascular disease; Exacerbation; Mortality; Respiratory pharmacology; Small airway disease.

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## Conflict of interest statement

Declaration of competing interest The authors declare no conflict of interest.

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Am J Respir Crit Care Med

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. 2023 Jul 6.

doi: 10.1164/rccm.202303-0458OC. Online ahead of print.

## Icenticaftor, a CFTR Potentiator, in COPD: A Multicenter, Parallel-Group, Double-Blind Clinical Trial

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- PMID: 37411039
- DOI: [10.1164/rccm.202303-0458OC](https://doi.org/10.1164/rccm.202303-0458OC)

## Abstract

**Rationale:** CF transmembrane conductance regulator (CFTR) dysfunction is associated with mucus accumulation and worsening COPD symptoms. This Phase 2b dose-finding study compared a CFTR potentiator, icenticaftor (QBW251), with placebo in patients with COPD and chronic bronchitis.

**Methods:** COPD patients on triple therapy for at least three months were randomized to six treatment arms (icenticaftor 450, 300, 150, 75, or 25mg or placebo b.i.d.) in a 24-week, multicenter, parallel-group, double-blind study. The primary endpoint was change from baseline in trough FEV<sub>1</sub> after 12 weeks. Secondary endpoints included change from baseline in trough FEV<sub>1</sub>, Evaluating Respiratory Symptoms in COPD (E-RS) total and cough and sputum scores after 24 weeks. Multiple Comparison Procedure-Modelling characterized dose-response. Rescue medication use, exacerbations, and change in serum fibrinogen levels after 24 weeks were exploratory and post-hoc analyses, respectively. Measurements and Main Results: 974 patients were randomized. After 12 weeks of icenticaftor treatment, no dose-response for change from baseline in trough FEV<sub>1</sub> was observed; however, it was observed for E-RS cough and sputum score. A dose-response was observed after 24 weeks for trough FEV<sub>1</sub>, E-RS cough and sputum and total scores, rescue medication use and fibrinogen. 300mg b.i.d. was consistently the most effective dose. Improvements for 300mg b.i.d. versus placebo were also seen in pairwise comparisons of these endpoints. All treatments were well tolerated.

**Conclusions:** The primary endpoint was negative as icenticaftor did not improve trough FEV<sub>1</sub> over 12 weeks. Although the findings must be interpreted with caution, icenticaftor improved trough FEV<sub>1</sub>, cough, sputum, rescue medication use and lowered fibrinogen levels at 24 weeks. Clinical trial registration available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**Clinical trials:** gov, ID: [NCT04072887](https://clinicaltrials.gov/ct2/show/study/NCT04072887).

**Keywords:** CFTR dysfunction; CFTR potentiator; COPD; Chronic Bronchitis; icenticaftor.

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. 2023 Jul 5.

doi: 10.15326/jcopdf.2023.0395. Online ahead of print.

# Disparities in Guideline Concordant Statin Treatment in Individuals with Chronic Obstructive Pulmonary Disease

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- PMID: 37410623
- DOI: [10.15326/jcopdf.2023.0395](https://doi.org/10.15326/jcopdf.2023.0395)

## Abstract

**Rationale:** Cardiovascular disease (CVD) affects prognosis in chronic obstructive pulmonary disease (COPD). Black women with COPD have a disproportionate risk of CVD-related mortality, yet disparities in CVD prevention in COPD are unknown.

**Objectives:** We aimed to identify race-sex differences in the receipt of statin treatment for CVD prevention, and whether these differences were explained by factors influencing healthcare utilization in the REasons for Geographic And Racial Differences in Stroke (REGARDS) COPD sub-cohort.

**Methods:** We conducted a cross-sectional analysis among REGARDS Medicare beneficiaries with COPD. Our primary outcome was the presence of statin on in-home pill bottle review among individuals with an indication. Prevalence ratios (PR) for statin

treatment among race-sex groups compared to White men were estimated using Poisson regression with robust variance. We then adjusted for covariates previously shown to impact healthcare utilization.

**Results:** Of the 2,032 members within the COPD sub-cohort with sufficient data, 1,435 participants (19% Black women, 14% Black men, 28% White women, and 39% White men) had a statin indication. All race-sex groups were less likely to receive statins than White men in unadjusted models. After adjusting for covariates that influence healthcare utilization, Black women (PR 0.76, 95% CI 0.67-0.86) and White women (PR 0.84 95% CI 0.76-0.91) remained less likely to be treated compared to White men.

**Conclusions:** All race-sex groups were less likely to receive statin treatment in the REGARDS COPD sub-cohort compared to White men. This difference persisted in women after controlling for individual healthcare utilization factors, suggesting structural interventions are needed.

**Keywords:** COPD; cardiovascular disease; comorbidity; health delivery.

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. 2023 Jul 3;107347.

doi: 10.1016/j.rmed.2023.107347. Online ahead of print.

## [Underdiagnosis and misclassification of COPD in Sweden – A Nordic Epilung study](#)

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- PMID: 37406781
- DOI: [10.1016/j.rmed.2023.107347](https://doi.org/10.1016/j.rmed.2023.107347)

## Abstract

**Introduction:** The prevalence of COPD tends to level off in populations with decreasing prevalence of smoking but the extent of underdiagnosis in such populations needs further investigation.

**Aim:** To investigate underdiagnosis and misclassification of COPD with a focus on socio-economy, lifestyle determinants and healthcare utilization.

**Method:** The 1839 participants were selected from two ongoing large-scale epidemiological research programs: The Obstructive Lung Disease in Northern Sweden Studies and the West Sweden Asthma Study. COPD<sub>GOLD</sub> was defined according to the fixed post-bronchodilator spirometric criteria FEV1/FVC < 0.70 in combination with respiratory symptoms.

**Results:** Among the 128 participants who fulfilled the criteria for COPD<sub>GOLD</sub>, the underdiagnosis was 83.6% (n = 107) of which 57.9% were men. The undiagnosed participants were younger, had higher FEV1% of predicted and less frequently a family history of bronchitis. One in four of the undiagnosed had utilized healthcare and had more frequently utilized healthcare due to a burden of respiratory symptoms than the general population without COPD. Underdiagnosis was not related to educational level. Misclassification of COPD was characterized by being a woman with low education, ever smoker, having respiratory symptoms and having a previous asthma diagnosis.

**Conclusion:** In the high income country Sweden, the underdiagnosis of COPD was highly prevalent. Reduced underdiagnosis can contribute to risk factor modification, medical treatment and self-management strategies in early stages of the disease, which may prevent disease progression and improve the quality of life among those affected. Therefore, there is a need to increase the use of spirometry in primary care to improve the diagnostic accuracy.

**Keywords:** COPD; Epidemiology; Misclassification; Population study; Underdiagnosis.

## Conflict of interest statement

Declaration of competing interest Malin Axelsson declares no conflicts of interest. Helena Backman reports personal fees for scientific lectures from Boehringer Ingelheim, AstraZeneca and GlaxoSmithKline, outside the submitted work. Bright I. Nwaru reports personal fees for scientific consulting from DBV Technologies, outside the submitted work. Caroline Stridsman declares no conflicts of interest. Lowie Vanfleteren declares no conflicts of interest related to this manuscript. Outside the submitted work: payment for lectures or advisory boards from GSK, AstraZeneca, Chiesi, Boehringer, Novartis, Pulmonx. Linnea Hedman declares no conflicts of interest. Juuso Jalasto declares no conflicts of interest. Päivi Piirilä declares no conflicts of interest. Arnulf Langhammer reports fees for lectures and consulting from AstraZeneca, Boehringer-Ingelheim, GSK, and Diagnostica Ltb, outside the submitted work. Hannu Kankaanranta reports fees for lectures and consulting from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma and SanofiGenzyme, outside the submitted work. Madeleine Rådinger declares no conflicts of interest. Linda Ekerljung declares no conflicts of interest. Eva Rönmark declares no conflicts of interest. Anne Lindberg reports personal fees for advisory board work for AstraZeneca, GlaxoSmithKline, Novartis and Boehringer Ingelhem, as well as personal fees for scientific lectures for Boehringer Ingelheim and Novartis, both outside the submitted work.

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Am J Respir Crit Care Med

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. 2023 Jul 5.

doi: 10.1164/rccm.202303-0534OC. Online ahead of print.

## [A Single-Cell Atlas of Small Airway Disease in Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study](#)

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- PMID: 37406359
- DOI: [10.1164/rccm.202303-0534OC](https://doi.org/10.1164/rccm.202303-0534OC)

## Abstract

**Rationale:** Emerging data demonstrate that the smallest conducting airways, terminal bronchioles (TBs), are reduced by 41% by the time someone is diagnosed with mild (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage1) COPD.

**Objectives:** To understand the structural, cellular and extracellular matrix alterations underlying TB loss in COPD and how they might be targeted for therapeutic intervention.

**Methods:** This cross-sectional study of 34 ex-smokers with normal lung function (n=10), GOLD1 (n=10), GOLD2 (n=8), and GOLD4 (n=6) COPD used micro-computed tomography, and non-linear optical microscopy imaging to assess the morphology and extracellular matrix of TBs in 262 lung samples. A subset of 57 TBs across all groups was assessed using imaging mass spectrometry to generate a single-cell atlas of TB pathology.

**Measurements and main results:** Compared to ex-smokers the TB airway wall in all GOLD stages was homogenously thickened, but the TB lumen was progressively narrowed with disease severity ( $p < 0.05$ ). Progressive loss of radial tethering due to reduced numbers of alveolar attachments/TB perimeter ( $p < 0.05$ ), was associated with degradation and fragmentation of radial elastic fibers and accumulation of disorganized fibrillar collagen ( $p < 0.05$ ). Single-cell imaging identified adaptive immune cells within the TB wall and M1-like macrophage aggregates and neutrophils in alveolar attachments. TB pathology was associated with the upregulation of genes involved in innate and adaptive immune responses, the interferon response and the degranulation of neutrophils.

**Conclusion:** Loss of TB alveolar attachments through degradation of elastin, is an important feature of small airway obstruction in mild/moderate COPD, emphasizing the need for early diagnosis and treatment.

**Keywords:** COPD; Elastin; Imaging Mass Spectrometry; microCT; small airways disease.

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. 2023 Jul 3;9(4):00148-2023.

doi: 10.1183/23120541.00148-2023. eCollection 2023 Jul.

# Patients' acceptance of outcome and experience measurements during hospitalisation for COPD exacerbations: a CICERO Clinical Research Collaboration-European Lung Foundation online patient survey

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- PMID: 37404845
- PMCID: [PMC10316033](#)
- DOI: [10.1183/23120541.00148-2023](#)

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## Abstract

**Background:** The lack of standardised outcome assessments during hospitalisation and follow-up for acute COPD exacerbations has hampered scientific progress and clinical proficiency. The objective of the present study was to evaluate patients' acceptance of selected outcome and experience measurements during hospitalisations for COPD exacerbations and follow-up.

**Methods:** An online survey was held amongst COPD patients in France, Belgium, The Netherlands, Germany and the UK. The European Lung Foundation COPD Patient Advisory Group was involved in the conceptualisation, development and dissemination of the survey. The survey was complementary to a previously obtained expert consensus. We assessed patients' views and acceptance of selected patient-reported outcomes or experiences and corresponding measurement instruments (for dyspnoea, frequent productive cough, health status and hospitalisation experience), and of selected clinical investigations (blood draw, pulmonary function test, 6-min walk test, chest computed tomography, echocardiography).

**Findings:** 200 patients completed the survey. All selected outcomes and experiences were deemed important, and acceptance of their methods of assessment was high. The modified Medical Research Council scale and a numerical rating scale to address dyspnoea, the COPD Assessment Test for quality of life and frequent productive cough, and the Hospital Consumer Assessment of Healthcare Providers and Systems for hospital experiences were the instruments preferred by patients. Consensus on importance of blood draw and spirometry was higher compared with the other investigations.

**Interpretation:** The survey results endorse the use of the selected outcome and experience measurements during hospitalisations for COPD exacerbations. They can be used to optimise standardised and patient-centred care and facilitate multicentric data collection.

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## Conflict of interest statement

Conflicts of interest: An ICMJE Conflict of Interest form has been collected from all authors. I. Gyselinck reports grants from Research Foundation Flanders (FWO). S. Ramakrishnan reports grants from the National Institute of Health Research UK and AstraZeneca paid to his institution; and honoraria for speaker's fees from AstraZeneca. C. Coleman reports funding from the CICERO CRC budget for coordinating patient involvement in the project paid to the ERS; and is an employee of the European Lung Foundation. T. Greulich reports grants from Grifols paid to his institution; consulting fees from AstraZeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, CSL-Behring, Grifols, GSK, Mundipharma, Novartis and Takeda; honoraria for speaker's fees from AstraZeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, CSL-Behring, Grifols, GSK, Mundipharma and Takeda; travel support from AstraZeneca, Berlin-Chemie, Chiesi, CSL-Behring, Grifols, GSK and Takeda; DSMB and/or advisory board participation for AstraZeneca, Berlin-Chemie, Boehringer-Ingelheim, Chiesi,

CSL-Behring, Grifols, GSK, Mundipharma, Novartis, Takeda; and membership of Alpha-1-Deutschland. F. Franssen reports grants from AstraZeneca; consulting fees from MSD; honoraria for speaker's fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Chiesi and Novartis; and travel support from Chiesi. P.R. Burgel reports grants from GSK and Vertex paid to his institution; consulting fees from AstraZeneca, Chiesi, Insmed, Viatrix, Vertex, Zambon and Boehringer Ingelheim; travel support from Chiesi and Zambon. M. Bafadhel reports grants from AstraZeneca and Roche paid to her institution; honoraria for speaker's fees from AstraZeneca, Chiesi, Cipla, GlaxoSmithKline and Boehringer Ingelheim, paid to her institution; travel support from Boehringer Ingelheim; DSMB and/or advisory board participation for AstraZeneca, Sanofi/Regeneron, GlaxoSmithKline, Albus Health and ProAxis; unpaid leadership roles in the BTS research and scientific faculty and NIHR TRC. W. Janssens reports grants from FWO, AstraZeneca and Chiesi, paid to the institution; honoraria for speaker's fees from AstraZeneca, Chiesi and GlaxoSmithKline; and nonfinancial support from ArtiQ. K. Vermeersch, A. Halner, H. Pott, F. Dobbels, P. Collis and H. Watz report no conflicts of interest.

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. 2023 Jul 5;1410768231184162.

doi: 10.1177/01410768231184162. Online ahead of print.

## [Impact of SARS-CoV-2 infective exacerbation of chronic obstructive pulmonary disease on clinical outcomes in a prospective cohort study of hospitalised adults](#)



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Affiliations expand

- PMID: 37404021
- DOI: [10.1177/01410768231184162](https://doi.org/10.1177/01410768231184162)

## Abstract

**Objectives:** To determine whether acute exacerbations of chronic obstructive pulmonary disease (AECOPD) triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have worse outcomes than AECOPD caused by other infectious agents or non-infective AECOPD (NI-COPD).

**Design:** A two-hospital prospective cohort study of adults hospitalised with acute respiratory disease. We compared outcomes with AECOPD and a positive test for SARS-CoV-2 (n = 816), AECOPD triggered by other infections (n = 3038) and NI-COPD (n = 994). We used multivariable modelling to adjust for potential confounders and assessed variation by seasons associated with different SARS-CoV-2 variants.

**Setting:** Bristol UK, August 2020-May 2022.

**Participants:** Adults (≥18 y) hospitalised with AECOPD.

**Main outcome measures:** We determined the risk of positive pressure support, longer hospital admission and mortality following hospitalisation with AECOPD due to non-SARS-CoV-2 infection compared with SARS-CoV-2 AECOPD and NI-COPD.

**Results:** Patients with SARS-CoV-2 AECOPD, in comparison to non-SARS-CoV-2 infective AECOPD or NI-COPD, more frequently required positive pressure support (18.5% and 7.5% vs. 11.7%, respectively), longer hospital stays (median [interquartile range, IQR]: 7 [3-15] and 5 [2-10] vs. 4 [2-9] days, respectively) and had higher 30-day mortality (16.9% and 11.1% vs. 5.9%, respectively) (all  $p < 0.001$ ). In adjusted analyses, SARS-CoV-2 AECOPD was associated with a 55% (95% confidence interval [95% CI]: 24-93), 26% (95% CI: 15-37) and 35% (95% CI: 10-65) increase in the risk of positive pressure support, hospitalisation length and 30-day mortality, respectively, relative to non-SARS-CoV-2 infective AECOPD. The difference in risk remained similar during periods of wild-type, Alpha and Delta SARS-CoV-2 strain dominance, but diminished during Omicron dominance.

**Conclusions:** SARS-CoV-2-related AECOPD had worse patient outcomes compared with non-SARS-CoV-2 AECOPD or NI-AECOPD, although the difference in risks was less pronounced during Omicron dominance.

**Keywords:** COPD; COVID-19; SARS-CoV-2; acute exacerbation of COPD; airways disease.

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. 2023 Jul 4;23(1):243.

doi: 10.1186/s12890-023-02502-8.

## [Assessing the genetic relationship between gastroesophageal reflux disease and chronic respiratory diseases: a mendelian randomization study](#)

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Affiliations [expand](#)

- PMID: 37403021
- PMCID: [PMC10318641](#)
- DOI: [10.1186/s12890-023-02502-8](#)

## Abstract

**Background:** Previous observational studies have found an association between gastroesophageal reflux disease (GERD) and chronic respiratory diseases, but it remains uncertain whether GERD causally influences these diseases. In this study, we aimed to estimate the causal associations between GERD and 5 chronic respiratory diseases.

**Methods:** 88 GERD-associated single nucleotide polymorphisms (SNPs) identified by the latest genome-wide association study were included as instrumental variables. Individual-level genetic summary data of participants were obtained from corresponding studies and the FinnGen consortium. We applied the inverse-variance weighted method to estimate the causality between genetically predicted GERD and 5 chronic respiratory diseases. Furthermore, the associations between GERD and common risk factors were investigated, and mediation analyses were conducted using multivariable MR. Various sensitivity analyses were also performed to verify the robustness of the findings.

**Results:** Our study demonstrated that genetically predicted GERD was causally associated with an increased risk of asthma (OR 1.39, 95%CI 1.25-1.56,  $P < 0.001$ ), idiopathic pulmonary fibrosis (IPF) (OR 1.43, 95%CI 1.05-1.95,  $P = 0.022$ ), chronic obstructive disease (COPD) (OR 1.64, 95%CI 1.41-1.93,  $P < 0.001$ ), chronic bronchitis (OR 1.77, 95%CI 1.15-2.74,  $P = 0.009$ ), while no correlation was observed for bronchiectasis (OR 0.93, 95%CI 0.68-1.27,  $P = 0.645$ ). Additionally, GERD was associated with 12 common risk factors for chronic respiratory diseases. Nevertheless, no significant mediators were discovered.

**Conclusions:** Our study suggested that GERD was a causal factor in the development of asthma, IPF, COPD and chronic bronchitis, indicating that GERD-associated micro-aspiration of gastric contents process might play a role in the development of pulmonary fibrosis in these diseases.

**Keywords:** Causality; Chronic respiratory diseases; Gastroesophageal reflux disease; Genetic; Mendelian randomization.

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## Conflict of interest statement

The authors declare no competing interests.

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

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. 2023 Jul 4.

doi: 10.1007/s00063-023-01036-5. Online ahead of print.

# Prognostic value of early warning scores in patients presenting to the emergency department with exacerbation of COPD

[Nurettin Özgür Doğan](#)<sup>1</sup>, [İbrahim Ulaş Özturan](#)<sup>2</sup>, [Murat Pekdemir](#)<sup>2</sup>, [Elif Yaka](#)<sup>2</sup>, [Serkan Yılmaz](#)<sup>2</sup>

Affiliations expand

- PMID: 37401954
- DOI: [10.1007/s00063-023-01036-5](https://doi.org/10.1007/s00063-023-01036-5)

## Abstract

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

**Objective:** Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a condition that frequently presents to the emergency department (ED) and its prognosis is not very well understood. Risk tools that can be used rapidly in the ED are needed to predict the prognosis of these patients.

**Methods:** This study comprised a retrospective cohort of AECOPD patients presenting to a single center between 2015 and 2022. The prognostic accuracy of several clinical early warning scoring systems, Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), NEWS-2, Systemic Inflammatory Response Syndrome (SIRS) and the quick Sepsis-related Organ Failure Assessment (qSOFA), were compared. The outcome variable was determined as one-month mortality.

**Results:** Of the 598 patients, 63 (10.5%) had died within 1 month after presenting to the ED. Patients who died had more often congestive heart failure, altered mental status, and admission to intensive care, and they were older. Although the MEWS, NEWS, NEWS-2, and qSOFA scores of those who died were higher than those who survived, there was no difference between the SIRS scores of these two groups. The score with the highest positive likelihood ratio for mortality estimation was qSOFA (8.5, 95% confidence interval [CI] 3.7-19.6). The negative likelihood ratios of the scores were similar, the NEWS score had a negative likelihood ratio of 0.4 (95% CI 0.2-0.8) with the highest negative predictive value of 96.0%.

**Conclusion:** In AECOPD patients, most of the early warning scores that are frequently used in the ED were found to have a moderate ability to exclude mortality and a low ability to predict mortality.

**Keywords:** Chronic obstructive pulmonary disease; Early warning score; Hospital emergency services; Lung diseases, obstructive; Mortality.

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. 2023 Jul 4.

doi: 10.1002/ejhf.2962. Online ahead of print.

# Impact of comorbidities on health status measured using the Kansas City Cardiomyopathy Questionnaire in patients with HFrEF and HFpEF

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Affiliations expand

- PMID: 37401511
- DOI: [10.1002/ejhf.2962](https://doi.org/10.1002/ejhf.2962)

## Abstract

**Background:** Patients with heart failure (HF) often suffer from a range of comorbidities, which may affect their health status.

**Objectives:** To assess the impact of different comorbidities on health status in patients with HF and reduced and preserved ejection fraction (HFrEF and HFpEF).

**Methods:** Using individual patient data from HFrEF (ATMOSPHERE, PARADIGM-HF, DAPA-HF) and HFpEF (TOPCAT, PARAGON-HF) trials, we examined the Kansas City Cardiomyopathy Questionnaire (KCCQ) domain scores and Overall Summary Score (KCCQ-OSS) across a range of cardio-respiratory (angina, AF, stroke, COPD) and other comorbidities (obesity, DM, CKD, anaemia).

**Results:** Of patients with HFrEF (n=20,159), 36.2% had AF, 33.9% CKD, 33.9% diabetes, 31.4% obesity, 25.5% angina, 12.2% COPD, 8.4% stroke, and 4.4% anaemia; the corresponding proportions in HFpEF (n=6,563) were: 54.0% AF, 48.7% CKD, 43.4% diabetes, 53.3% obesity, 28.6% angina, 14.7% COPD, 10.2% stroke, and 6.5% anaemia. HFpEF patients had lower KCCQ domain scores and KCCQ-OSS (67.8 vs. 71.3) than HFrEF patients. Physical limitations, social limitations and quality of life domains were reduced more than symptom frequency and symptom burden domains. In both HFrEF and HFpEF, COPD, angina, anaemia, and obesity were associated with the lowest scores. An increasing number of comorbidities was associated with decreasing scores e.g., KCCQ-OSS 0 vs. ≥4 comorbidities: HFrEF 76.8 vs. 66.4; HFpEF 73.7 vs. 65.2.

**Conclusions:** Cardiac and non-cardiac comorbidities are common in both HFrEF and HFpEF patients and most are associated with reductions in health status although the impact varied among comorbidities, by the number of comorbidities, and by HF phenotype. Treating/correcting comorbidity is a therapeutic approach that may improve the health status of patients with HF. This article is protected by copyright. All rights reserved.

**Keywords:** Kansas City Cardiomyopathy Questionnaire; comorbidity; heart failure; natriuretic peptides; quality of life; symptoms.

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. 2023 Jul 3;23(1):241.

doi: 10.1186/s12890-023-02535-z.

## [Epicardial adipose tissue in patients with chronic obstructive pulmonary disease: systematic review with meta-analysis and trial sequential analysis](#)

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[Affiliations expand](#)

- PMID: 37400821

- PMID: [PMC10318694](#)
- DOI: [10.1186/s12890-023-02535-z](#)

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## Abstract

**Background:** Limited data suggest that chronic obstructive pulmonary disease (COPD) patients have pathologic elevated epicardial adipose tissue (EAT), which is splanchnic fat tissue with anti-inflammatory properties and regulating free fatty acids functions. Therefore, there is a need for meta-analysis to explore the relationship between EAT and COPD.

**Methods:** Online databases were systematically searched for studies about EAT in COPD patients published up to October 5th, 2022. The EAT data of the COPD patient group and the control group were included. Trial sequential analysis (TSA) and meta-analysis were applied to assess the difference in EAT between patients with and without COPD. TSA software and Stata 12.0 were used in all statistical analyses.

**Results:** The final analysis included 5 studies (n = 596 patients). COPD patients had significantly more EAT than control subjects (SMD: 0.0.802; 95% CI: 0.231, 1.372; P = 0.006; TSA-adjusted 95% CI 1.20, 1.80; P < 0.0001). And higher CRP levels in COPD patients than non-COPD patients, whereas triglycerides and LDL were not significantly different between patients with and without COPD.

**Conclusion:** EAT is abnormally elevated in COPD patients, which may be related to systemic inflammatory responses in COPD.

**Prospero number:** CRD42021228273.

**Keywords:** Chronic obstructive pulmonary disease; Epicardial adipose tissue; Meta-analysis.

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## Conflict of interest statement

Not applicable.

- [46 references](#)



- [6 figures](#)

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. 2023 Jul 3;18(7):e0287887.

doi: 10.1371/journal.pone.0287887. eCollection 2023.

# Acceptance of and adherence with long-term positive airway pressure treatment in adults with chronic obstructive pulmonary disease: A systematic review protocol

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Affiliations expand

- PMID: 37399211
- PMCID: [PMC10317229](#)
- DOI: [10.1371/journal.pone.0287887](#)

# Abstract

**Background:** Long-term noninvasive positive airway pressure (PAP) treatment is effective treatment for sleep-related breathing disorders and chronic hypercarbic respiratory failure secondary to chronic obstructive pulmonary disease (COPD). PAP treatment may be delivered as continuous positive airway pressure or noninvasive ventilation. Success in initiating PAP treatment and barriers to its use in adult patients with COPD are largely unknown. This systematic review aims to identify the acceptance of and adherence to PAP treatment prescribed for long-term use in adult patients with COPD and to summarize variables associated with these measures.

**Methods:** Seven online electronic databases will be searched by an experienced medical librarian to identify records containing the concepts "obstructive airways disease" and "noninvasive positive airway pressure" and "acceptance" or "adherence". Randomized and non-randomized studies of interventions will be included. Citation lists from relevant articles will be reviewed, and experts will be contacted regarding unpublished studies. Abstracts from key conferences between 2018-2023 and Google Scholar search results will be reviewed for inclusion. Titles, abstracts and full texts will be reviewed independently for inclusion by two reviewers. Data extraction will be completed by one author using a pre-established form and primary outcomes confirmed by a second author. Methodological quality will be evaluated. If sufficient data are available for meta-analysis, a pooled summary statistic for the primary outcome will be calculated using a random-effects generic inverse-variance meta-analysis, weighted proportion or weighted medians-based approach. Subgroup analysis will explore clinically meaningful sources of heterogeneity. Variables that are associated with acceptance and adherence will be described.

**Discussion:** Long-term PAP treatment is a complex intervention prescribed to patients with COPD for several indications. Synthesis of the evidence on success with PAP treatment and variables associated with acceptance or adherence will inform program and policy development for supporting patients with COPD who are prescribed this therapy.

**Trial registration:** Systematic review registration: This protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on July 13, 2021 (registration number CRD42021259262), with revisions submitted on April 17, 2023.

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## Conflict of interest statement

CRL receives remuneration for the interpretation of home sleep apnea tests by Careica Health. SRP reports an unrestricted grant from Jazz Pharmaceuticals and consulting fees from Paladin Labs, Jazz Pharmaceuticals and the International Centre for Professional Development in Health and Medicine. The other authors have no relevant conflicts of interest to declare. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

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. 2023 Jul 3.

doi: [10.1097/MCP.0000000000000984](https://doi.org/10.1097/MCP.0000000000000984). Online ahead of print.

## [Pulmonary hypertension in interstitial lung disease and in chronic obstructive pulmonary disease: different entities?](#)

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[Affiliations expand](#)

- PMID: 37395513
- DOI: [10.1097/MCP.0000000000000984](https://doi.org/10.1097/MCP.0000000000000984)

# Abstract

**Purpose of review:** Pulmonary hypertension (PH) is a common complication of both chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD), classified as Group 3 PH. To which extent PH presents and behaves similarly in COPD and ILD is unclear. This review examines the similarities and differences in pathogenesis, clinical presentation, natural history and treatment response of PH in COPD and ILD.

**Recent findings:** The latest studies on PH in chronic lung disease have re-evaluated the role of traditionally held etiopathogenetic factors such as tobacco exposure and hypoxia, although new ones such as airborne pollutant and genetic mutations are increasingly recognized. We examine common and diverging factors involved in PH development in COPD and ILD, as well as common and diverging clinical features of presentation, natural history and response to treatment and highlight areas for future research.

**Summary:** The development of PH in lung disease significantly worsens the morbidity and mortality of patients with COPD and ILD. However, recent findings show importance of recognizing distinct patterns and behaviors of pulmonary vascular disease, taking into account the specific underlying lung disease and severity of the hemodynamic involvement. Further studies are needed to build evidence on these aspects, especially in early disease.

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. 2023 Jul 3;23(1):237.

doi: 10.1186/s12890-023-02533-1.

# Smoking cessation after diagnosis of COPD is associated with lower all-cause and cause-specific mortality: a nationwide population-based cohort study of South Korean men

[Jang Ho Doo](#)<sup>1</sup>, [Sung Min Kim](#)<sup>2</sup>, [Young Jun Park](#)<sup>3</sup>, [Kye Hyung Kim](#)<sup>4</sup>, [Yun Hwan Oh](#)<sup>5</sup>, [Ji Soo Kim](#)<sup>6</sup>, [Sang Min Park](#)<sup>7,8</sup>

Affiliations expand

- PMID: 37394482
- PMCID: [PMC10316560](#)
- DOI: [10.1186/s12890-023-02533-1](#)

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## Abstract

**Background:** The most effective way to halt the advancement of COPD is smoking cessation. However, limited data are available on the question of whether quitting smoking within two years after COPD diagnosis reduces the risk of mortality. The goal of our research was to analyze the relationship between quitting smoking after COPD diagnosis and the risks of all-cause and cause-specific mortality, using the Korean National Health Insurance Service (NHIS) database.

**Methods:** This study included 1,740 male COPD patients aged 40 years or more who had been newly diagnosed within the 2003-2014 time period and had smoked prior to their COPD diagnosis. The patients were categorized into two groups according to their smoking status after COPD diagnosis: (i) persistent smokers (ii) quitters (smoking cessation within two years of COPD diagnosis). Multivariate Cox proportional hazard regression was performed to determine the adjusted hazard ratio (HR) and 95% confidence interval (CI) for both all-cause and cause-specific mortality.

**Results:** Among 1,740 patients (mean age, 64.6 years; mean follow-up duration, 7.6 years), 30.5% stopped smoking after COPD diagnosis. Quitters gained a 17% risk reduction in all-

cause mortality (aHR, 0.83; 95% CI, 0.69-1.00) and a 44% risk reduction in cardiovascular mortality (aHR, 0.56; 95% CI, 0.33-0.95) compared with persistent smokers.

**Conclusion:** Our study found that patients who quit smoking within two years after COPD diagnosis had lower risks of all-cause and cardiovascular mortality relative to persistent smokers. These results can be used to encourage newly diagnosed COPD patients to stop smoking.

**Keywords:** COPD; Mortality; Newly diagnosed COPD; Quitting smoking; Smoking cessation.

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## Conflict of interest statement

The authors declare no competing interests.

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

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. 2023 Jul 4;26(5):275-305.

doi: 10.1080/10937404.2023.2208886. Epub 2023 May 14.

# Animal models and mechanisms of tobacco smoke-induced chronic obstructive pulmonary disease (COPD)

[Priya Upadhyay<sup>1</sup>](#), [Ching-Wen Wu<sup>1</sup>](#), [Alexa Pham<sup>1</sup>](#), [Amir A Zeki<sup>2,3</sup>](#), [Christopher M Royer<sup>4</sup>](#), [Urmila P Kodavanti<sup>5</sup>](#), [Minoru Takeuchi<sup>6</sup>](#), [Hasan Bayram<sup>7</sup>](#), [Kent E Pinkerton<sup>1</sup>](#)

Affiliations expand

- PMID: 37183431
- DOI: [10.1080/10937404.2023.2208886](https://doi.org/10.1080/10937404.2023.2208886)

## Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, and its global health burden is increasing. COPD is characterized by emphysema, mucus hypersecretion, and persistent lung inflammation, and clinically by chronic airflow obstruction and symptoms of dyspnea, cough, and fatigue in patients. A cluster of pathologies including chronic bronchitis, emphysema, asthma, and cardiovascular disease in the form of hypertension and atherosclerosis variably coexist in COPD patients. Underlying causes for COPD include primarily tobacco use but may also be driven by exposure to air pollutants, biomass burning, and workplace related fumes and chemicals. While no single animal model might mimic all features of human COPD, a wide variety of published models have collectively helped to improve our understanding of disease processes involved in the genesis and persistence of COPD. In this review, the pathogenesis and associated risk factors of COPD are examined in different mammalian models of the disease. Each animal model included in this review is exclusively created by tobacco smoke (TS) exposure. As animal models continue to aid in defining the pathobiological mechanisms of and possible novel therapeutic interventions for COPD, the advantages and disadvantages of each animal model are discussed.

**Keywords:** animal models; chronic bronchitis; chronic obstructive pulmonary disease (COPD); emphysema; tobacco smoke.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

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# Clinical and prognostic associations of autoantibodies recognizing adrenergic/muscarinic receptors in patients with heart failure

[George Markousis-Mavrogenis<sup>1</sup>](#), [Waldemar B Minich<sup>2,3</sup>](#), [Ali A Al-Mubarak<sup>1</sup>](#), [Stefan D Anker<sup>4</sup>](#), [John G F Cleland<sup>5,6</sup>](#), [Kenneth Dickstein<sup>7</sup>](#), [Chim C Lang<sup>8</sup>](#), [Leong L Ng<sup>9,10</sup>](#), [Nilesh J Samani<sup>7</sup>](#), [Faiez Zannad<sup>11</sup>](#), [Marco Metra<sup>12</sup>](#), [Petra Seemann<sup>2,3</sup>](#), [Antonia Hoeg<sup>2</sup>](#), [Patricio Lopez<sup>2,3</sup>](#), [Dirk J van Veldhuisen<sup>1</sup>](#), [Rudolf A de Boer<sup>1</sup>](#), [Adriaan A Voors<sup>1</sup>](#), [Peter van der Meer<sup>1</sup>](#), [Lutz Schomburg<sup>2</sup>](#), [Nils Bomer<sup>1</sup>](#), [BIOSTAT-CHF Consortium](#)

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- PMID: 36883593
- PMCID: [PMC10325696](#)
- DOI: [10.1093/cvr/cvad042](#)

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## Abstract

**Aims:** The importance of autoantibodies (AABs) against adrenergic/muscarinic receptors in heart failure (HF) is not well-understood. We investigated the prevalence and



clinical/prognostic associations of four AABs recognizing the M2-muscarinic receptor or the  $\beta$ 1-,  $\beta$ 2-, or  $\beta$ 3-adrenergic receptor in a large and well-characterized cohort of patients with HF.

**Methods and results:** Serum samples from 2256 patients with HF from the BIOSTAT-CHF cohort and 299 healthy controls were analysed using newly established chemiluminescence immunoassays. The primary outcome was a composite of all-cause mortality and HF rehospitalization at 2-year follow-up, and each outcome was also separately investigated. Collectively, 382 (16.9%) patients and 37 (12.4%) controls were seropositive for  $\geq 1$  AAB ( $P = 0.045$ ). Seropositivity occurred more frequently only for anti-M2 AABs ( $P = 0.025$ ). Amongst patients with HF, seropositivity was associated with the presence of comorbidities (renal disease, chronic obstructive pulmonary disease, stroke, and atrial fibrillation) and with medication use. Only anti- $\beta$ 1 AAB seropositivity was associated with the primary outcome [hazard ratio (95% confidence interval): 1.37 (1.04-1.81),  $P = 0.024$ ] and HF rehospitalization [1.57 (1.13-2.19),  $P = 0.010$ ] in univariable analyses but remained associated only with HF rehospitalization after multivariable adjustment for the BIOSTAT-CHF risk model [1.47 (1.05-2.07),  $P = 0.030$ ]. Principal component analyses showed considerable overlap in B-lymphocyte activity between seropositive and seronegative patients, based on 31 circulating biomarkers related to B-lymphocyte function.

**Conclusions:** AAB seropositivity was not strongly associated with adverse outcomes in HF and was mostly related to the presence of comorbidities and medication use. Only anti- $\beta$ 1 AABs were independently associated with HF rehospitalization. The exact clinical value of AABs remains to be elucidated.

**Keywords:** Autoimmunity; Beta 1; Beta 2; Beta 3; Immune system; M2.

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## Conflict of interest statement

Conflict of interest: A.A.V. received consultancy fees and/or research grants from AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Cytokinetics, Merck, Novo Nordisk, Novartis, and Roche diagnostics. P.v.d.M. received consultancy fees and/or grants from Novartis, Corvidia, Singulex, Servier, Vifor Pharma, AstraZeneca, Pfizer, and Ionis. R.A.d.B. received grants from AstraZeneca, Abbott, Boehringer Ingelheim, Cardior Pharmaceuticals GmbH, Ionis Pharmaceuticals Inc., Novo Nordisk, and Roche and speaker fees from Abbott, AstraZeneca, Bayer, Novartis, and Roche. F.Z. received personal fees for trial oversight committees, advisory boards, or speakers' bureau from Acceleron, Amgen, Applied Therapeutics, AstraZeneca, Bayer, Boehringer, Cardior, Cereno Scientific, CellProthera, CVRx, G3 Pharmaceuticals, Merck, Merck AG, Novartis, Novo Nordisk, Pfizer, Servier, and Vifor Fresenius and is the co-founder of CardioRenal and CVCT. J.G.F.C. received consultancy fees and/or research grants from Abbott, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cytokinetics, Idorsia, Johnson & Johnson,

Medtronic, MyoKardia, Novartis, NI Medical, Pharmacosmos, Pharma Nord, Philips, Respicardia, Servier, Torrent, Vifor, and Viscardia. M.M. reports fees from Actelion, Amgen, AstraZeneca, LivaNova, Servier, Vifor Pharma, and Windtree Therapeutics as a member of clinical trial committees or advisory boards and from Abbott vascular, Bayer, Boehringer Ingelheim, and Edwards Therapeutics for speeches at sponsored meetings in the last 3 years. W.B.M., P.S., and P.L. are founders of ImmunometriX. W.B.M. and L.S. are listed as inventors on a patent application. All other authors have no relationships to disclose that could be construed as a conflict of interest with regard to this manuscript.

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- [6 figures](#)

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

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. 2023 Jul 6;17423953231187172.

doi: 10.1177/17423953231187172. Online ahead of print.

## Barriers and facilitators of self-management behaviors among patients with chronic obstructive pulmonary disease and chronic comorbidities: A mixed-methods investigation

[Kimberly A Muellers](#)<sup>1,2</sup>, [Rachel O'Connor](#)<sup>3</sup>, [Andrea M Russell](#)<sup>3</sup>, [Guisselle Wismer](#)<sup>3</sup>, [James W Griffith](#)<sup>4</sup>, [Michael S Wolf](#)<sup>3</sup>, [Juan P Wisnivesky](#)<sup>1,5</sup>, [Alex D Federman](#)<sup>1</sup>

Affiliations expand

- PMID: 37415379
- DOI: [10.1177/17423953231187172](https://doi.org/10.1177/17423953231187172)

## Abstract

**Objectives:** We investigated how individuals with chronic obstructive pulmonary disease (COPD) and multi-morbidity (MM) navigate barriers and facilitators to their health management.

**Methods:** We conducted a mixed-methods study using semi-structured interviews and survey assessments of adults with COPD, hypertension, and/or diabetes. We recruited 18 participants with an average age of 65, with 39% being male, 50% Black, and 22% Hispanic/Latino/a. Five investigators used an iterative, hybrid-coding process combining a priori and emergent codes to analyze transcripts and compare quantitative and qualitative data for themes.

**Results:** Participants reported a generalized approach to their health rather than managing MMs separately. Individuals with good or mixed adherence found daily routines facilitated regular medication use, while those with poor adherence experienced complex prescriptions and life stressors as barriers. Walking was viewed as beneficial but challenging due to limited mobility. Most participants viewed diet as important to their MMs, but only two reported high diet quality and many held inaccurate beliefs about healthy diet choices.

**Discussion:** Participants with MM were highly motivated to engage in self-management activities, but some individuals experienced barriers to maintaining them. Emphasizing an individualized clinical approach to assessing and solving patient barriers may improve self-management outcomes in this complex population.

**Keywords:** Multi-morbidity; chronic illness; chronic obstructive pulmonary disease; medication adherence; self-management.

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# Multi-morbidity and its association with common cancer diagnoses: a UK Biobank prospective study

[Megan C Conroy](#)<sup>1</sup>, [Gillian K Reeves](#)<sup>#2</sup>, [Naomi E Allen](#)<sup>#2</sup>

Affiliations expand

- PMID: 37415095

- DOI: [10.1186/s12889-023-16202-9](https://doi.org/10.1186/s12889-023-16202-9)

## Abstract

**Background:** Whilst multi-morbidity is known to be a concern in people with cancer, very little is known about the risk of cancer in multi-morbid patients. This study aims to investigate the risk of being diagnosed with lung, colorectal, breast and prostate cancer associated with multi-morbidity.

**Methods:** We investigated the association between multi-morbidity and subsequent risk of cancer diagnosis in UK Biobank. Cox models were used to estimate the relative risks of each cancer of interest in multi-morbid participants, using the Cambridge Multimorbidity Score. The extent to which reverse causation, residual confounding and ascertainment bias may have impacted on the findings was robustly investigated.

**Results:** Of the 436,990 participants included in the study who were cancer-free at baseline, 21.6% (99,965) were multi-morbid ( $\geq 2$  diseases). Over a median follow-up time of 10.9 [IQR 10.0-11.7] years, 9,019 prostate, 7,994 breast, 5,241 colorectal, and 3,591 lung cancers were diagnosed. After exclusion of the first year of follow-up, there was no clear association between multi-morbidity and risk of colorectal, prostate or breast cancer diagnosis. Those with  $\geq 4$  diseases at recruitment had double the risk of a subsequent lung cancer diagnosis compared to those with no diseases (HR 2.00 [95% CI 1.70-2.35] p for trend  $< 0.001$ ). These findings were robust to sensitivity analyses aimed at reducing the

impact of reverse causation, residual confounding from known cancer risk factors and ascertainment bias.

**Conclusions:** Individuals with multi-morbidity are at an increased risk of lung cancer diagnosis. While this association did not appear to be due to common sources of bias in observational studies, further research is needed to understand what underlies this association.

**Keywords:** Cancer risk; Multi-morbidity; UK Biobank.

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. 2023 Jul 5.

doi: 10.1007/s11357-023-00852-z. Online ahead of print.

## [Deprescribing in cardiometabolic conditions in older patients: a systematic review](#)

[Elizabeth Hickman](#)<sup>1</sup>, [Mansha Seawoodharry](#)<sup>2</sup>, [Clare Gillies](#)<sup>2</sup>, [Kamlesh Khunti](#)<sup>2</sup>, [Samuel Seidu](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 37402905

- DOI: [10.1007/s11357-023-00852-z](https://doi.org/10.1007/s11357-023-00852-z)

## Abstract

We conduct a systematic review to investigate current deprescribing practices and evaluate outcomes and adverse events with deprescribing of preventive medications in older patients with either an end-of-life designation or residing in long-term care facilities with cardiometabolic conditions. Studies were identified using a literature search of MEDLINE, EMBASE, Web of Science, clinicaltrials.gov.uk, CINAHL, and the Cochrane Register from inception to March 2022. Studies reviewed included observational studies and randomised control trials (RCTs). Data was extracted on baseline characteristics, deprescribing rates, adverse events and outcomes, and quality of life indicators, and was discussed using a narrative approach. Thirteen studies were identified for inclusion. Deprescribing approaches included complete withdrawal, dose reduction or tapering, or switching to an alternative medication, for at least one preventive medication. Deprescribing success rates ranged from 27 to 94.7%. The studies reported no significant changes in laboratory values or adverse outcomes but did find mixed outcomes for hospitalisations and a slight increase in mortality rates when comparing the intervention and control groups. Lack of good-quality randomised control trials suggests that deprescribing in the older population residing in long-term care facilities with cardiometabolic conditions and multimorbidity is feasible when controlled and regularly monitored by an appropriate healthcare clinician, and that the benefits outweigh the potential harm in this cohort of patients. Due to the limited evidence and the heterogeneity of studies, a meta-analysis was not performed and as such further research is required to assess the benefits of deprescribing in this patient population. Systematic review registration: PROSPERO CRD42021291061.

**Keywords:** Cardiometabolic; Deprescribing; End-of-life; Multimorbidity; Polypharmacy.

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. 2023 Jul 2.

doi: 10.1002/acr.25184. Online ahead of print.

# Multimorbidity Patterns and Rheumatoid Arthritis Disease Outcomes: Findings from a Multicenter, Prospective Cohort

[Sarah Dutt](#)<sup>1,2</sup>, [Punyasha Roul](#)<sup>1,2</sup>, [Yangyuna Yang](#)<sup>1,2</sup>, [Tate M Johnson](#)<sup>1,2</sup>, [Kaleb Michaud](#)<sup>2,3</sup>, [Brian Sauer](#)<sup>4</sup>, [Grant W Cannon](#)<sup>4</sup>, [Joshua F Baker](#)<sup>5</sup>, [Jeffrey R Curtis](#)<sup>6</sup>, [Ted R Mikuls](#)<sup>1,2</sup>, [Bryant R England](#)<sup>1,2</sup>

Affiliations expand

- PMID: 37394710

- DOI: [10.1002/acr.25184](https://doi.org/10.1002/acr.25184)

## Abstract

**Objective:** To determine whether unique multimorbidity patterns are associated with long-term rheumatoid arthritis (RA) disease severity.

**Methods:** We conducted a cohort study within the Veterans Affairs Rheumatoid Arthritis (VARA) registry. We applied previously derived multimorbidity patterns based on the presence of diagnostic codes for relevant conditions prior to enrollment using linked administrative data. Disease activity and functional status were assessed longitudinally up to 5-years after enrollment. The association of multimorbidity patterns with disease activity and functional status were assessed using generalized estimating equations models adjusting for relevant confounders.

**Results:** We studied 2,956 participants of which 88.2% were male, 76.9% reported white race, and 79.3% had a smoking history. Mental health and substance abuse ( $\beta$  0.12 [0.00, 0.23]), cardiovascular ( $\beta$  0.25 [0.12, 0.38]), and chronic pain ( $\beta$  0.21 [0.11, 0.31]) multimorbidity were associated with higher DAS28 scores. Mental health and substance abuse ( $\beta$  0.09 [0.03, 0.15]), cardiovascular ( $\beta$  0.11 [0.04, 0.17]), and chronic pain

multimorbidity ( $\beta$  0.15 [0.10, 0.20]) were also associated with higher MDHAQ scores. The metabolic pattern of multimorbidity was not associated with DAS28 or MDHAQ. The number of multimorbidity patterns present was highly associated with DAS28 and MDHAQ ( $p$  trend < 0.001), and patients with all four multimorbidity patterns had the highest DAS28 ( $\beta$  0.59 [0.36, 0.83]) and MDHAQ ( $\beta$  0.27 [0.16, 0.39]) scores.

**Conclusion:** Mental health and substance abuse, chronic pain, and cardiovascular multimorbidity patterns are associated with increased RA disease activity and poorer functional status. Identifying and addressing these multimorbidity patterns may facilitate achieving RA treatment targets. This article is protected by copyright. All rights reserved.

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

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. 2023 Jul 4;105447.

doi: 10.1016/j.yrtph.2023.105447. Online ahead of print.

## [Safety data sheets as an information pathway on hazards of occupationally used cleaning agents](#)

[Behnaz Erfani](#)<sup>1</sup>, [Libe A Vilela](#)<sup>1</sup>, [Anneli Julander](#)<sup>2</sup>, [Linda Schenk](#)<sup>3</sup>

Affiliations expand

- PMID: 37414128
- DOI: [10.1016/j.yrtph.2023.105447](https://doi.org/10.1016/j.yrtph.2023.105447)

## Abstract



To investigate consistency and accessibility of asthma and skin allergy hazard information in safety data sheets (SDSs) for cleaning agents on the Swedish market, we compiled a database of 504 SDSs and 351 therein declared ingredients. Labelling of products was compared to that of ingredients according to harmonised classification. For each ingredient, also notified classification and three additional sources on sensitising properties were compared. Product labelling most frequently indicated corrosion and irritation hazards. Only 3% of products were labelled as skin sensitisers and none as astmagens. According to harmonised classification, 9% of products contained skin sensitisers, using other information sources increased the number to 46%. While 2% of products contained respiratory sensitisers according to harmonised classification, the number increased to 17% when using other information sources. Furthermore, sensitisers were declared across several sections of the SDSs, hampering easy access of such information. In conclusion, there are inconsistencies in hazard identification of cleaning agents and their ingredients. Hence, SDSs may not altogether fulfil its hazard information role. Improved criteria for identifying sensitisers and respiratory irritants are warranted. Additionally, we argue that all ingredients should be listed in section 3 regardless of concentration, to facilitate access of information about sensitising properties.

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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: Linda Schenk reports financial support was provided by AFA Insurance.

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Mol Immunol

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. 2023 Jul 4;160:95-102.

doi: 10.1016/j.molimm.2023.06.011. Online ahead of print.

## Pro-inflammatory action of formoterol in human bronchial epithelia

[Xing-Jian Liu<sup>1</sup>](#), [Hao Pang<sup>2</sup>](#), [Yu-Qian Long<sup>2</sup>](#), [Ji-Qing Wang<sup>2</sup>](#), [Ya Niu<sup>3</sup>](#), [Rui-Gang Zhang<sup>4</sup>](#)

Affiliations expand

- PMID: 37413911

- DOI: [10.1016/j.molimm.2023.06.011](https://doi.org/10.1016/j.molimm.2023.06.011)

## Abstract

Despite the wide usage of  $\beta_2$ -adrenoceptor agonists in asthma treatment, they do have side effects such as aggravating inflammation. We previously reported that isoprenaline induced  $\text{Cl}^-$  secretion and IL-6 release via cAMP-dependent pathways in human bronchial epithelia, but the mechanisms underlying the inflammation-aggravation effects of  $\beta_2$ -adrenoceptor agonists remain poorly understood. In this study, we investigated formoterol, a more specific  $\beta_2$ -adrenoceptor agonist, -mediated signaling pathways involved in the production of IL-6 and IL-8 in 16HBE14o- human bronchial epithelia. The effects of formoterol were detected in the presence of PKA, exchange protein directly activated by cAMP (EPAC), cystic fibrosis transmembrane conductance regulator (CFTR), extracellular signal-regulated protein kinase (ERK)1/2 and Src inhibitors. The involvement of  $\beta$ -arrestin2 was determined using siRNA knockdown. Our results indicate that formoterol can induce IL-6 and IL-8 secretion in concentration-dependent manner. The PKA-specific inhibitor, H89, partially inhibited IL-6 release, but not IL-8. Another intracellular cAMP receptor, EPAC, was not involved in either IL-6 or IL-8 release. PD98059 and U0126, two ERK1/2 inhibitors, blocked IL-8 while attenuated IL-6 secretion induced by formoterol. Furthermore, formoterol-induced IL-6 and IL-8 release was attenuated by Src inhibitors, namely dasatinib and PP1, and CFTRinh172, a CFTR inhibitor. In addition, knockdown of  $\beta$ -arrestin2 by siRNA only suppressed IL-8 release when a high concentration of formoterol (1  $\mu\text{M}$ ) was used. Taken together, our results suggest that formoterol stimulates IL-6 and IL-8 release which involves PKA/Src/ERK1/2 and/or  $\beta$ -arrestin2 signaling pathways.

**Keywords:** Bronchial epithelia; ERK1/2; PKA;  $\beta(2)$ -adrenoceptor;  $\beta$ -arrestin2.

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## Conflict of interest statement

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

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JMIR Res Protoc

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. 2023 Jul 6;12:e44710.  
doi: 10.2196/44710.

# Capability, Opportunity, and Motivation Model for Behavior Change in People With Asthma: Protocol for a Cross-Sectional Study

[Alice Munns](#)<sup>#1</sup>, [Laura Wiffen](#)<sup>#1</sup>, [Thomas Brown](#)<sup>#1,2</sup>, [Alessandra Fasulo](#)<sup>2</sup>, [Milan Chauhan](#)<sup>1</sup>, [Leon D'Cruz](#)<sup>1</sup>, [Daphne Kaklamanou](#)<sup>#2</sup>, [Anoop J Chauhan](#)<sup>#1,2</sup>

Affiliations expand

- PMID: 37410518
- DOI: [10.2196/44710](https://doi.org/10.2196/44710)

## Abstract

**Background:** Asthma is a common lung condition that cannot be cured, but it can usually be effectively managed using available treatments. Despite this, it is widely acknowledged that 70% of patients do not adhere to their asthma treatment. Personalizing treatment by providing the most appropriate interventions based on the patient's psychological or behavioral needs produces successful behavior change. However, health care providers have limited available resources to deliver a patient-centered approach for their psychological or behavioral needs, resulting in a current one-size-fits-all strategy due to the nonfeasible nature of existing surveys. The solution would be to provide health care professionals with a clinically feasible questionnaire that identifies the patient's personal psychological and behavioral factors related to adherence.

**Objective:** We aim to apply the capability, opportunity, and motivation model of behavior change (COM-B) questionnaire to detect a patient's perceived psychological and behavioral barriers to adherence. Additionally, we aim to explore the key psychological and behavioral barriers indicated by the COM-B questionnaire and adherence to treatment in patients with confirmed asthma with heterogeneous severity. Exploratory objectives will include a focus on the associations between the COM-B questionnaire responses and asthma phenotype, including clinical, biological, psychosocial, and behavioral components.

**Methods:** In a single visit, participants visiting Portsmouth Hospital's asthma clinic with a diagnosis of asthma will be asked to complete a 20-minute questionnaire on an iPad about their psychological and behavioral barriers following the theoretical domains framework and capability, opportunity, and motivation model. Participants' data are routinely collected, including demographics, asthma characteristics, asthma control, asthma quality of life, and medication regime, which will be recorded on an electronic data capture form.

**Results:** The study is already underway, and it is anticipated that the results will be available by early 2023.

**Conclusions:** The COM-B asthma study will investigate an easily accessible theory-based tool (a questionnaire) for identifying psychological and behavioral barriers in patients with asthma who are not adhering to their treatment. This will provide useful information on the behavioral barriers to asthma adherence and whether or not a questionnaire can be used to identify these needs. The highlighted barriers will improve health care professionals' knowledge of this important subject, and participants will benefit from the study by removing their barriers. Overall, this will enable health care professionals to use effective individualized interventions to support improved medication adherence while also recognizing and meeting the psychological needs of patients with asthma.

**Trial registration:** ClinicalTrials.gov [NCT05643924](https://clinicaltrials.gov/ct2/show/NCT05643924);  
<https://clinicaltrials.gov/ct2/show/NCT05643924>.

**International registered report identifier (irrid):** DERR1-10.2196/44710.

**Keywords:** COM-B; adherence; asthma; behavioral barriers; capability, opportunity, and motivation model of behavior change; medication; psychological barriers; theoretical domains framework.

©Alice Munns, Laura Wiffen, Thomas Brown, Alessandra Fasulo, Milan Chauhan, Leon D'Cruz, Daphne Kaklamanou, Anoop J Chauhan. Originally published in JMIR Research Protocols (<https://www.researchprotocols.org>), 06.07.2023.

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J Allergy Clin Immunol Pract

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. 2023 Jul 3;S2213-2198(23)00716-X.

doi: 10.1016/j.jaip.2023.06.051. Online ahead of print.

## [Long-term cost-effectiveness of digital inhaler adherence technologies in difficult-to-treat asthma](#)

[Susanne J van de Hei<sup>1</sup>](#), [Chong H Kim<sup>2</sup>](#), [Persijn J Honkoop<sup>3</sup>](#), [Jacob K Sont<sup>3</sup>](#), [Tjard R J Schemer<sup>4</sup>](#), [Elaine MacHale<sup>5</sup>](#), [Richard W Costello<sup>5</sup>](#), [Janwillem W H Kocks<sup>6</sup>](#), [Maarten J Postma<sup>7</sup>](#), [Job F M van Boven<sup>8</sup>](#)

Affiliations expand

- PMID: 37406806
- DOI: [10.1016/j.jaip.2023.06.051](https://doi.org/10.1016/j.jaip.2023.06.051)

## Abstract

**Background:** Digital inhalers can monitor inhaler usage, support difficult-to-treat asthma management and inform step-up treatment decisions yet their economic value is unknown, hampering wide-scale implementation.

**Objective:** We aimed to assess the long-term cost-effectiveness of digital inhaler-based medication adherence management in difficult-to-treat asthma.

**Methods:** A model-based cost-utility analysis was performed. The Markov model structure was determined by biological and clinical understanding of asthma and was further informed by guideline-based assessment of model development. Internal and external validation was performed using the AdViSHE tool. The INCA Sun randomized clinical trial data were incorporated into the model to evaluate the cost-effectiveness of digital inhalers. Several long-term clinical case scenarios were assessed (reduced number of exacerbations, increased asthma control, introduction of biosimilars [25% price-cut on biologics]).

**Results:** The long-term modelled cost-effectiveness based on a societal perspective indicated 1-year per-patient costs for digital inhalers and usual care (i.e., regular inhalers) of €7,546 and €10,752, respectively, reflecting cost savings of €3,207 for digital inhalers. Using a 10-year intervention duration and time horizon resulted in cost savings of €26,309 for digital inhalers. In the first year, add-on biologic therapies accounted for 69% of the total costs in the usual care group, and for 49% in the digital inhaler group. Scenario analyses indicated consistent cost savings ranging from €2,287 (introduction biosimilars) to €4,581 (increased control, decreased exacerbations).

**Conclusion:** In patients with difficult-to-treat asthma, digital inhaler based interventions can be cost-saving in the long-term by optimizing medication adherence and inhaler technique and reducing add-on biologic prescriptions.

**Keywords:** adherence; asthma; cost-effectiveness; digital; eHealth; electronic monitoring; smart inhaler.

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Pneumologie

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. 2023 Jul 5.

doi: 10.1055/a-2070-2135. Online ahead of print.

# [Diagnosis and treatment of asthma: a guideline for respiratory specialists 2023 – published by the German Respiratory Society (DGP) e. V]

[Article in German]

[Marek Lommatzsch](#)<sup>1</sup>, [Carl-Peter Criée](#)<sup>2</sup>, [Carmen C M de Jong](#)<sup>3</sup>, [Monika Gappa](#)<sup>4</sup>, [Christian Geßner](#)<sup>5</sup>, [Michael Gerstlauer](#)<sup>6</sup>, [Nina Hämäläinen](#)<sup>7</sup>, [Peter Haidl](#)<sup>8</sup>, [Eckard Hamelmann](#)<sup>9</sup>, [Fritz Horak](#)<sup>10</sup>, [Marco Idzko](#)<sup>11</sup>, [Atanas Ignatov](#)<sup>12</sup>, [Andreas Rembert Koczulla](#)<sup>13 14</sup>, [Stephanie Korn](#)<sup>15</sup>, [Michael Köhler](#)<sup>16</sup>, [Christiane Lex](#)<sup>17</sup>, [Jochen Meister](#)<sup>18</sup>, [Katrin Milger-Kneidinger](#)<sup>19</sup>, [Dennis Nowak](#)<sup>20</sup>, [Monika Nothacker](#)<sup>21</sup>, [Oliver Pfaar](#)<sup>22</sup>, [Wolfgang Pohl](#)<sup>23</sup>, [Alexandra M Preisser](#)<sup>24</sup>, [Klaus F Rabe](#)<sup>25</sup>, [Josef Riedler](#)<sup>26</sup>, [Olaf Schmidt](#)<sup>27</sup>, [Jens Schreiber](#)<sup>28</sup>, [Antje Schuster](#)<sup>29</sup>, [Maren Schuhmann](#)<sup>30</sup>, [Thomas Spindler](#)<sup>31</sup>, [Christian Taube](#)<sup>32</sup>, [Johann Christian Virchow](#)<sup>1</sup>, [Christian Vogelberg](#)<sup>33</sup>, [Claus Franz Vogelmeier](#)<sup>14</sup>, [Felix Wantke](#)<sup>34</sup>, [Wolfram Windisch](#)<sup>35</sup>, [Heinrich Worth](#)<sup>36</sup>, [Angela Zacharasiewicz](#)<sup>37</sup>, [Roland Buhl](#)<sup>38</sup>; Weitere beteiligte Wissenschaftliche Fachgesellschaften und Organisationen: [Deutsche Atemwegsliga e. V.](#); [Deutsche Gesellschaft für Arbeitsmedizin und Umweltmedizin e. V.](#); [Deutsche Gesellschaft für Allergologie und klinische Immunologie e. V.](#); [Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e. V.](#); [Deutsche Gesellschaft für Rehabilitationswissenschaften e. V.](#); [Gesellschaft für Pädiatrische Allergologie und Umweltmedizin e. V.](#); [Gesellschaft für Pädiatrische Pneumologie e. V.](#); [Bundesverband der Pneumologen, Schlaf- und Beatmungsmediziner](#); [Österreichische Gesellschaft für Kinder- und Jugendheilkunde](#); [Österreichische Gesellschaft für Pneumologie](#); [Deutsche Patientenliga Atemwegserkrankungen e. V.](#)

Affiliations expand

- PMID: 37406667
- DOI: [10.1055/a-2070-2135](https://doi.org/10.1055/a-2070-2135)

## Abstract

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

The management of asthma has fundamentally changed during the past decades. The present guideline for the diagnosis and treatment of asthma was developed for respiratory specialists who need detailed and evidence-based information on the new diagnostic and therapeutic options in asthma. The guideline shows the new role of biomarkers, especially blood eosinophils and fractional exhaled NO (FeNO), in diagnostic algorithms of asthma. Of note, this guideline is the first worldwide to announce symptom prevention and asthma remission as the ultimate goals of asthma treatment, which can be achieved by using individually tailored, disease-modifying anti-asthmatic drugs such as inhaled steroids, allergen immunotherapy or biologics. In addition, the central role of the treatment of comorbidities is emphasized. Finally, the document addresses several challenges in asthma management, including asthma treatment during pregnancy, treatment of severe asthma or the diagnosis and treatment of work-related asthma.

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## Conflict of interest statement

Eine Übersicht der Interessenkonflikte findet sich im Internet unter <http://awmf.org>; AWMF-Registriernummer 020-009.

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J Asthma

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. 2023 Jul 5;1-14.

doi: 10.1080/02770903.2023.2231078. Online ahead of print.

## Age-related differences in associations between uncontrolled asthma, comorbidities and biomarkers in adult-onset asthma

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

Affiliations expand

- PMID: 37405375
- DOI: [10.1080/02770903.2023.2231078](https://doi.org/10.1080/02770903.2023.2231078)

## Abstract

**Objective:** Adult-onset asthma is a recognized but heterogeneous phenotype and has been described to associate with poor asthma control. Knowledge about associations between clinical characteristics including comorbidities and control of adult-onset asthma is limited, especially in older populations. We aimed to study how clinical biomarkers and comorbidities associate with uncontrolled asthma among middle-aged and older individuals with adult-onset asthma.

**Methods:** Clinical examinations including structured interview, asthma control test (ACT), spirometry, skin prick test (SPT), blood sampling and measurement of exhaled fractional nitric oxide (FeNO) was performed in a population-based adult-onset asthma cohort in 2019-2020 (n = 227, 66.5% female). Analyses were performed among all included, and separately in middle-aged (37-64y, n = 120) and older ( $\geq 65$ y, n = 107) participants.

**Results:** In bivariate analysis, uncontrolled asthma ( $ACT \leq 19$ ) was significantly associated with a blood neutrophil count  $\geq 5/\mu l$ ,  $BMI \geq 30$  and several comorbidities. In multivariable regression analysis, uncontrolled asthma was associated with neutrophils  $\geq 5/\mu l$  (OR 2.35; 95% CI 1.11-4.99). In age-stratified analysis,  $BMI \geq 30$  (OR 3.04; 1.24-7.50), eosinophils  $\geq 0.3/\mu l$  (OR 3.17; 1.20-8.37), neutrophils  $\geq 5/\mu l$  (OR 4.39; 1.53-12.62) and allergic rhinitis (OR 5.10; 1.59-16.30) were associated with uncontrolled asthma among the middle-aged. Among the older adults, uncontrolled asthma was only associated with comorbidities: chronic rhinitis (OR 4.08; 1.62-10.31), ischemic heart disease (OR 3.59; 1.17-10.98), malignancy (OR 3.10; 1.10-8.73) and depression/anxiety (OR 16.31; 1.82-146.05).

**Conclusions:** In adult-onset asthma, comorbidities were strongly associated with uncontrolled asthma among older adults, while clinical biomarkers including eosinophils and neutrophils in blood were associated with uncontrolled asthma among middle-aged.

**Keywords:** eosinophils; epidemiology; inflammation; neutrophils; phenotype; risk factors.

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. 2023 Jul 4;ftad015.

doi: 10.1093/femspd/ftad015. Online ahead of print.

# Chlamydia pneumoniae– Immunoglobulin E antibody responses in serum from children with asthma

[Tamar A Smith-Norowitz<sup>1</sup>](#), [Anastasiya Shulman<sup>1</sup>](#), [Haram Abdelmajid<sup>1</sup>](#), [Margaret R Hammerschlag<sup>1</sup>](#), [Rauno Joks<sup>2</sup>](#), [Diana Weaver<sup>1</sup>](#), [Stephan Kohlhoff<sup>1</sup>](#)

Affiliations expand

- PMID: 37403376
- DOI: [10.1093/femspd/ftad015](https://doi.org/10.1093/femspd/ftad015)

## Abstract

*Chlamydia pneumoniae* is an obligate intracellular bacterium that causes respiratory infection in humans. An association between persistent *C. pneumoniae* infection and asthma pathogenesis has been described. It is unknown whether specific IgE is a marker of persistent immune activation responses. Therefore, the association between *C. pneumoniae* specific IgE antibodies (Abs) and interferon (IFN)-gamma produced by *C. pneumoniae*-stimulated PBMC was examined. Blood was collected and serum separated. Peripheral blood mononuclear cells (PBMC) from 63 children with or without stable asthma (N = 45 and 18, respectively) were infected or not infected with *C. pneumoniae* AR-39 and cultured up to 7 days. Supernatants were collected, and IFN-gamma levels measured (ELISA). Serum *C. pneumoniae*- IgE Abs were detected by immunoblotting. *C. pneumoniae* IgE Abs were detected in asthmatics (27%), compared with non-asthmatics (11%) (P = NS). IFN-gamma responses were more prevalent among asthmatics who had positive *C. pneumoniae*-IgE Abs (91%) compared with asthmatics without *C. pneumoniae*-IgE Abs (20%) (P = 0.0046). IFN-gamma responses in *C. pneumoniae* stimulated PBMC from children with asthma were significantly more frequent in children who had specific anti-*C. pneumoniae* IgE Abs compared to those who did not. This immune response may reflect persistent infection which may contribute to ongoing asthma symptoms.

**Keywords:** *Chlamydia pneumoniae*; Immunoglobulin E; Interferon-gamma; asthma.

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BMC Pulm Med

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. 2023 Jul 4;23(1):243.

doi: 10.1186/s12890-023-02502-8.

# [Assessing the genetic relationship between gastroesophageal reflux disease and chronic respiratory diseases: a mendelian randomization study](#)

[Xiaoxue Cheng](#) <sup>#1</sup>, [Jiang Shi](#) <sup>#2 3 4</sup>, [Ding Zhang](#) <sup>#5</sup>, [Caichen Li](#) <sup>#2 3 4</sup>, [Haoxiang Xu](#) <sup>#6</sup>, [Jianxing He](#) <sup>2 3 4</sup>, [Wenhua Liang](#) <sup>7 8 9</sup>

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- PMID: 37403021
- PMCID: [PMC10318641](#)
- DOI: [10.1186/s12890-023-02502-8](#)

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## Abstract

**Background:** Previous observational studies have found an association between gastroesophageal reflux disease (GERD) and chronic respiratory diseases, but it remains uncertain whether GERD causally influences these diseases. In this study, we aimed to estimate the causal associations between GERD and 5 chronic respiratory diseases.

**Methods:** 88 GERD-associated single nucleotide polymorphisms (SNPs) identified by the latest genome-wide association study were included as instrumental variables. Individual-level genetic summary data of participants were obtained from corresponding studies and the FinnGen

consortium. We applied the inverse-variance weighted method to estimate the causality between genetically predicted GERD and 5 chronic respiratory diseases. Furthermore, the associations between GERD and common risk factors were investigated, and mediation analyses were conducted using multivariable MR. Various sensitivity analyses were also performed to verify the robustness of the findings.

**Results:** Our study demonstrated that genetically predicted GERD was causally associated with an increased risk of asthma (OR 1.39, 95%CI 1.25-1.56,  $P < 0.001$ ), idiopathic pulmonary fibrosis (IPF) (OR 1.43, 95%CI 1.05-1.95,  $P = 0.022$ ), chronic obstructive disease (COPD) (OR 1.64, 95%CI 1.41-1.93,  $P < 0.001$ ), chronic bronchitis (OR 1.77, 95%CI 1.15-2.74,  $P = 0.009$ ), while no correlation was observed for bronchiectasis (OR 0.93, 95%CI 0.68-1.27,  $P = 0.645$ ). Additionally, GERD was associated with 12 common risk factors for chronic respiratory diseases. Nevertheless, no significant mediators were discovered.

**Conclusions:** Our study suggested that GERD was a causal factor in the development of asthma, IPF, COPD and chronic bronchitis, indicating that GERD-associated micro-aspiration of gastric contents process might play a role in the development of pulmonary fibrosis in these diseases.

**Keywords:** Causality; Chronic respiratory diseases; Gastroesophageal reflux disease; Genetic; Mendelian randomization.

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# Conflict of interest statement

The authors declare no competing interests.

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

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[Editorial](#)

Drug Ther Bull

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. 2023 Jul 4;dtb.2023.000013.

doi: 10.1136/dtb.2023.000013. Online ahead of print.

# Improving asthma prescribing: is FeNO the answer?

[Jo Congleton](#)<sup>1</sup>

Affiliations expand

- PMID: 37402644
- DOI: [10.1136/dtb.2023.000013](https://doi.org/10.1136/dtb.2023.000013)

*No abstract available*

**Keywords:** Asthma; Inappropriate Prescribing.

## Conflict of interest statement

Competing interests: None declared. Refer to the online supplementary files to view the ICMJE form(s).

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[Editorial](#)

Respirology

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. 2023 Jul 4.

doi: 10.1111/resp.14551. Online ahead of print.

# Minimize systemic oral corticosteroids use and reduce harm for patients with asthma

[Fanny Wai San Ko](#)<sup>1</sup>, [Sundeep Salvi](#)<sup>2,3</sup>

Affiliations [expand](#)

- PMID: 37402501
- DOI: [10.1111/resp.14551](https://doi.org/10.1111/resp.14551)

*No abstract available*

**Keywords:** asthma; inhaled corticosteroids; systemic oral corticosteroids.

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Pediatr Pulmonol

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. 2023 Jul 4.

doi: [10.1002/ppul.26575](https://doi.org/10.1002/ppul.26575). Online ahead of print.

## Asthma medication use and health care utilization evolution during pandemic times

[Lisa Ulrich](#)<sup>1,2,3</sup>, [Joshua Yell](#)<sup>4</sup>, [Melissa Holtzlander](#)<sup>1,2</sup>

Affiliations expand

- PMID: 37401870
- DOI: [10.1002/ppul.26575](https://doi.org/10.1002/ppul.26575)

## Abstract

Pediatric asthma care was significantly impacted by the Coronavirus Disease (COVID-19) pandemic, with significant decline in asthma health care utilization noted early in the pandemic. We compared Emergency Department (ED) utilization rates and prescription fill rates of controller and quick relief asthma medications between March and December 2020 versus 2021 in a county-specific pediatric Medicaid population to evaluate for changes later in the pandemic. Our data showed an increase in ED utilization by 46.7% (p=.0371) in the second year of the pandemic. There was no significant change in prescription fills for reliever medications (p=.1309) during this time with increased ED utilization for asthma but there was a significant decline in controller medication fills (p=.0039). This data suggests a potential explanation for resurgence of asthma health care utilization because of decreased controller medication fill and use during a time frame that also saw increased viral positivity rates. The poor medication adherence rates despite this increase in ED visits suggests that new interventions may be needed to assist patients with asthma medication adherence.

**Keywords:** asthma; coronavirus; health care utilization; pandemic.

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[Review](#)

Clin Exp Allergy

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. 2023 Jul 3.

doi: 10.1111/cea.14366. Online ahead of print.

# Childhood body mass index trajectories and asthma and allergies: A systematic review

[Chia-Lun Chang](#)<sup>1</sup>, [Gulshan Bano Ali](#)<sup>1</sup>, [Jonathan Pham](#)<sup>1,2</sup>, [Shyamali C Dharmage](#)<sup>1,3</sup>, [Caroline J Lodge](#)<sup>1,3</sup>, [Mimi L K Tang](#)<sup>4,5,6</sup>, [Adrian J Lowe](#)<sup>1,3</sup>

Affiliations expand

- PMID: 37401045
- DOI: [10.1111/cea.14366](https://doi.org/10.1111/cea.14366)

## Abstract

**Background:** Previous systematic reviews have focused on associations between single time point measures of Body Mass Index (BMI) and asthma and allergic diseases. As BMI changes dynamically during childhood, examination of associations between longitudinal trajectories in BMI and allergic diseases is needed to fully understand the nature of these relationships.

**Objective:** To systematically synthesise the association between BMI trajectories in childhood (0-18 years) and allergic diseases (asthma, eczema, allergic rhinitis, or food allergies outcomes).

**Design:** We conducted a systematic review following the PRISMA guidelines, and two independent reviewers assessed the study quality using the ROBINS-E and GRADE tools. A narrative synthesis was performed as the statistical heterogeneity did not allow a meta-analysis.

**Data sources:** A search was performed on PubMed and EMBASE databases on 4th January 2023.

**Eligibility criteria:** Longitudinal cohort studies assessing the associations between childhood BMI trajectories and allergic diseases were included.

**Results:** Eleven studies met the inclusion criteria with a total of 37,690 participants between 0 and 53 years of age. Ten studies examined asthma outcomes, three assessed association with allergic rhinitis, two assessed eczema, and one assessed food allergy. High heterogeneity and high risk of bias were observed. Overall, the quality of evidence was very low. Nevertheless, two consistent findings were identified: (1) a persistently high BMI between 6 and 10 years of age may be associated with an increased risk of asthma at 18 years and (2) a rapid increase in BMI in the first 2 years of life may be associated with subsequent asthma.

**Conclusions:** Maintaining a normal BMI trajectory during childhood may reduce the risk of asthma. Future research that adequately addresses confounding and includes longer-term follow-up is needed. Moreover, additional studies examining potential associations with eczema, food allergies, and allergic rhinitis outcomes are needed.

**Keywords:** Paediatric; allergy; asthma; body mass index trajectories; obesity.

- [45 references](#)

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. 2023 Jul 3.

doi: 10.1111/cea.14369. Online ahead of print.

# Treatment of gastro-oesophageal disease in patients with asthma

[Megan Dale](#)<sup>1</sup>, [Ayoade Adesina](#)<sup>2</sup>

[Affiliations expand](#)

- PMID: 37401040
- DOI: [10.1111/cea.14369](https://doi.org/10.1111/cea.14369)

*No abstract available*

- [9 references](#)

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Int Arch Occup Environ Health

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. 2023 Jul 4.

doi: 10.1007/s00420-023-01994-5. Online ahead of print.

# Urine 2-hydroxyphenanthrene is associated with current asthma: evidence from NHANES 2007–2012

[Lingyi Lu<sup>1</sup>](#), [Tingfeng Mao<sup>1</sup>](#), [Rui Xu<sup>1</sup>](#), [Lanxia Liu<sup>1</sup>](#), [Jiefeng Qian<sup>1</sup>](#), [Kai Yang<sup>1</sup>](#), [Anjie Yuan<sup>1</sup>](#), [Xinyue Wang<sup>1</sup>](#), [Rong Ni<sup>2</sup>](#)

Affiliations expand

- PMID: 37400582
- DOI: [10.1007/s00420-023-01994-5](https://doi.org/10.1007/s00420-023-01994-5)

## Abstract

**Objective:** The current study aims to explore the effects of nine urine monohydroxy PAH metabolites (OHPAH) including 1-hydroxynaphthalene (1-OHNAP), 2-hydroxynaphthalene (2-OHNAP), 3-hydroxyfluorene (3-OHFLU), 9-hydroxyfluorene (9-OHFLU), 1-hydroxyphenanthrene (1-OHPHE), 2-hydroxyphenanthrene (2-OHPHE), 3-hydroxyphenanthrene (3-OHPHE), and 1-hydroxypyrene (1-OHPYR) on current asthma in people in the United States using a variety of statistical techniques.

**Methods:** A cross-sectional examination of a subsample of 3804 adults aged  $\geq 20$  from the National Health and Nutrition Examination Survey (NHANES) was conducted between 2007 and 2012. To investigate the relationship between urine OHPAHs levels and current asthma, multivariate logistic regression, Bayesian kernel machine regression (BKMR), and quantile g-computation (qgcomp) were utilized.

**Results:** In the multivariate logistic regression model, after controlling for confounders, urine 2-OHPHE was associated with current asthma in both male (AOR = 7.17, 95% CI: 1.28–40.08) and female (AOR = 2.91, 95% CI: 1.06–8.01) smokers. In the qgcomp analysis, 2-OHPHE (39.5%), 1-OHNAP (33.1%), and 2-OHNAP (22.5%) were the major positive contributors to the risk of current asthma (OR = 2.29, 95% CI: 0.99, 5.25), and in female smokers, 9-OHFLU (25.8%), 2-OHFLU (21.5%), and 2-OHPHE (15.1%) were the major positive contributors (OR = 2.19, 95% CI: 1.06, 4.47). The results of the BKMR model basically agreed with qgcomp analysis.

**Conclusion:** Our results demonstrate a strong association of urine 2-OHPHE with current asthma, and further longitudinal studies are needed to understand the precise relationship between PAH exposure and current asthma risk.

**Keywords:** Asthma; BKMR; NHANES; Polycyclic aromatic hydrocarbon; qgcomp.

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Respirology

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. 2023 Jul 3.

doi: 10.1111/resp.14534. Online ahead of print.

## Elevated blood lactate in COPD exacerbations associates with adverse clinical outcomes and signals excessive treatment with $\beta_2$ -agonists

[Martin I MacDonald](#)<sup>1,2,3</sup>, [Kevan R Polkinghorne](#)<sup>2</sup>, [Chris J MacDonald](#)<sup>4</sup>, [Paul Leong](#)<sup>1,2,3</sup>, [Kais Hamza](#)<sup>5</sup>, [Gayan Kathriachchige](#)<sup>1</sup>, [Christian Robert Osadnik](#)<sup>1,6</sup>, [Paul T King](#)<sup>1,2,3</sup>, [Philip G Bardin](#)<sup>1,2,3</sup>

Affiliations expand

- PMID: 37400102
- DOI: [10.1111/resp.14534](https://doi.org/10.1111/resp.14534)

## Abstract

**Background and objective:** Raised blood lactate secondary to high dose  $\beta_2$ -agonist treatment has been reported in asthma exacerbations but has not been investigated during acute exacerbations of COPD (AECOPD). We explored associations of blood lactate measurements with disease outcomes and  $\beta_2$ -agonist treatments during AECOPD.

**Methods:** Retrospective (n = 199) and prospective studies (n = 142) of patients hospitalized with AECOPD were conducted. The retrospective cohort was identified via medical records and the prospective cohort was recruited during hospitalization for AECOPD. Baseline demographics, comorbidities,  $\beta_2$ -agonist treatment, biochemical measurements and clinical outcomes were compared between patients with normal ( $\leq 2.0$  mmol/L) versus elevated lactate ( $> 2.0$  mmol/L). Regression analyses examined associations of lactate measurements with  $\beta_2$ -agonist dosages.

**Results:** Demographic data and comorbidities were similar between high versus normal lactate groups in both cohorts. The populations were elderly (mean  $> 70$  years), predominantly male ( $> 60\%$ ) with reduced FEV<sub>1</sub> (%)  $48.2 \pm 19$  (prospective cohort). Lactate was elevated in approximately 50% of patients during AECOPD and not related to evidence of sepsis. In the prospective cohort, patients with high lactate had more tachypnoea, tachycardia, acidosis and hyperglycaemia ( $p < 0.05$ ) and received more non-invasive ventilation (37% vs. 9.7%,  $p < 0.001$ , prospective cohort). There was a trend to longer hospitalization (6 vs. 5 days,  $p = 0.06$ , prospective cohort). Higher cumulative  $\beta_2$ -agonist dosages were linked to elevated lactate levels (OR 1.04,  $p = 0.01$ ).

**Conclusion:** Elevated lactate during AECOPD was common, unrelated to sepsis and correlated with high cumulative doses of  $\beta_2$ -agonists. Raised lactate may indicate excessive  $\beta_2$ -agonist treatment and should now be investigated as a possible biomarker.

**Keywords:** COPD; biomarker; blood lactate; chronic obstructive pulmonary disease; exacerbations; non-invasive ventilation; salbutamol;  $\beta_2$ -agonist.

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JMIR Res Protoc

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. 2023 Jul 3;12:e45585.  
doi: 10.2196/45585.

# Remote Patient Monitoring and Teleconsultation to Improve Health Outcomes and Reduce Health Care Utilization of Pediatric Asthma (ALPACA Study): Protocol for a Randomized Controlled Effectiveness Trial

[Mattienne van der Kamp](#)<sup>1,2</sup>, [Vera Hengeveld](#)<sup>1</sup>, [Nico Willard](#)<sup>3</sup>, [Boony Thio](#)<sup>1</sup>, [Pascal de Graaf](#)<sup>3</sup>, [Inge Geven](#)<sup>3</sup>, [Monique Tabak](#)<sup>2</sup>

Affiliations expand

- PMID: 37399066
- DOI: [10.2196/45585](#)

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## Abstract

**Background:** Childhood asthma is imposing a great financial burden on the pediatric health care system. Asthma costs are directly related to the level of asthma control. A substantial part of these costs may be preventable by the timely and adequate assessment of asthma deterioration in daily life and proper asthma management. The use of eHealth technology may assist such timely and targeted medical anticipation.

**Objective:** This paper describes the Ambulatory Pediatric Asthma Care (ALPACA) study protocol to investigate the effectiveness of an eHealth intervention consisting of remote patient monitoring and teleconsultation integrated into the daily clinical care of pediatric patients with asthma. This intervention aims to reduce health care utilization and costs and improve health outcomes compared to a control group that receives standard care. In addition, this study aims to improve future eHealth pediatric asthma care by gaining insights from home-monitoring data.

**Methods:** This study is a prospective randomized controlled effectiveness trial. A total of 40 participants will be randomized to either 3 months of eHealth care (intervention group) or standard care (control group). The eHealth intervention consists of remote patient monitoring (spirometry, pulse oximetry, electronic medication adherence tracking, and asthma control questionnaire) and web-based teleconsultation (video sharing, messages). All participants will have a 3-month follow-up with standard care to evaluate whether the possible effects of eHealth care are longer lasting.

During the entire study and follow-up period, all participants will use blinded observational home monitoring (sleep, cough/wheeze sounds, air quality in bedroom) as well.

**Results:** This study was approved by the Medical Research Ethics Committees United. Enrollment began in February 2023, and the results of this study are expected to be submitted for publication in July 2024.

**Conclusions:** This study will contribute to the existing knowledge on the effectiveness of eHealth interventions that combine remote patient monitoring and teleconsultation for health care utilization, costs, and health outcomes. Furthermore, the observational home-monitoring data can contribute to improved identification of early signs of asthma deterioration in pediatric patients. Researchers and technology developers could use this study to guide and improve eHealth development, while health care professionals, health care institutions, and policy makers may employ our results to make informed decisions to steer toward high-quality, efficient pediatric asthma care.

**Trial registration:** ClinicalTrials.gov [NCT05517096](https://clinicaltrials.gov/ct2/show/NCT05517096);  
<https://clinicaltrials.gov/ct2/show/NCT05517096>.

**International registered report identifier (irrid):** PRR1-10.2196/45585.

**Keywords:** adherence; asthma; asthma care; children; health care costs; health care utilization; home monitoring; nebulizer; pediatric care; protocol; randomized controlled trial; remote monitoring; spirometry; telemedicine; utilization.

©Mattienne van der Kamp, Vera Hengeveld, Nico Willard, Boony Thio, Pascal de Graaf, Inge Geven, Monique Tabak. Originally published in JMIR Research Protocols  
(<https://www.researchprotocols.org>), 03.07.2023.

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Clin Rev Allergy Immunol

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. 2023 Jul 3.

doi: 10.1007/s12016-023-08966-0. Online ahead of print.

# [γδ T Cells and Allergic Diseases](#)

[Uei-Hsiang Hsu](#)<sup>1</sup>, [Bor-Luen Chiang](#)<sup>2,3</sup>

[Affiliations expand](#)

- PMID: 37395986
- DOI: [10.1007/s12016-023-08966-0](#)

## Abstract

Gamma-delta (γδ) T cells play an essential role in allergic diseases and have emerged as a potential treatment target in recent decades. To clarify the effects of γδ T cells on atopic illnesses, we reviewed the literature on the physical roles and functions of various subsets of γδ T cells, including type 1 T helper (Th1)-like, type 2 T helper- (Th2)-like, and type 17 T helper (Th17)-like γδ T cells. Mouse Vγ1 T cells increase interleukin (IL)-4 levels and trigger B cell class switching and immunoglobulin E production. Meanwhile, mouse Vγ4 T cells and human CD8<sup>low</sup>Vδ1 T cells secrete interferon-γ and exert an anti-allergy effect similar to that of Th1 cells. Moreover, mouse Vγ6 T cells produce IL-17A, while Th17-like γδ T cells enhance neutrophil and eosinophil infiltration in the acute phase of inflammation, but exert anti-inflammatory effects in the chronic phase. Human Vγ9δ2 T cells may exhibit Th1- or Th2-like characteristics in response to certain types of stimulation. In addition, the microbiota can modulate epithelial γδ T cell survival through aryl hydrocarbon receptors; these γδ T cells play crucial roles in the repair of epithelial damage, antibacterial protection, antigen tolerance, and effects of dysbiosis on allergic diseases.

**Keywords:** Allergic rhinitis; Allergy disease; Asthma; Atopic dermatitis; Microbiota; γδ T cel.

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Allergy

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. 2023 Jul 2.

doi: 10.1111/all.15796. Online ahead of print.

# Two-year results of tapered dupilumab for CRSwNP demonstrates enduring efficacy established in the first 6 months

[Rik Johannes Leonardus van der Lans<sup>1</sup>](#), [Josje Janna Otten<sup>1</sup>](#), [Gwijde Flavius Jacobus Petrus Maria Adriaansen<sup>1</sup>](#), [Dinand Rienk Hoven<sup>1</sup>](#), [Linda Berendina Benoist<sup>1</sup>](#), [Wytske Johanna Fokkens<sup>1</sup>](#), [Sietze Reitsma<sup>1</sup>](#)

Affiliations expand

- PMID: 37394895
- DOI: [10.1111/all.15796](https://doi.org/10.1111/all.15796)

## Abstract

**Background:** Dupilumab is an anti-T2-inflammatory biological registered for chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP), indicated by integrated CRS-care pathways when optimal medico-surgical treatment yields insufficient CRS control. This study aims to evaluate long-term results with focus on established therapeutic efficacy while tapering dupilumab.

**Methods:** Real-life, prospective observational cohort study in single tertiary referral center with add-on dupilumab as primary biological treatment in adult ( $\geq 18$  years) biological-naïve CRSwNP patients per the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS)2020-indication with a 2-year follow-up. Tapering (increasing interdose interval) applied every 24 weeks, conditional to sufficient treatment response and CRS control.

**Results:** Mean scores (s.d.) of all co-primary outcomes improved significantly from baseline ( 228) to the 48 ( 214) and 96-weeks ( 99) timepoints: Nasal Polyp Score (0-8) improved from 5,3 (1,9) to 1,4 (1,8) and 1,3 (1,7); SinoNasal Outcome Test (SNOT)-22 (0-110) improved from 53,6 (19,6) to 20,2 (15,4) and 21,2 (15,6); Sniffin'Sticks-12 identification test (0-12; 0-6 anosmia, 7-10 hyposmia, 11-12 normosmia) improved from 3,7 (2,4) to 7,7 (2,9) and 7,3 (3,04); Asthma Control Test (5-25;  $>19$  indicating well-controlled asthma) improved from 18,5 (4,8) to 21,8 (3,8) and 21,4 (3,9). Tapering was feasible in 79,5% of the patients at the 24-weeks timepoint, and in 93,7% and 95,8% at the 48- and 96-weeks timepoints, respectively. One-way repeated-measures ANOVA demonstrated no significant alterations of individual co-primary outcome mean-scores from 24 weeks onward.

**Conclusion:** This first long-term real-life prospective observational cohort study shows high therapeutic efficacy of dupilumab for severe CRSwNP in the first 2 years. Therapeutic efficacy is principally established within 24 weeks and endures while tapering dupilumab conditional to treatment response and CRS control.

**Keywords:** CRSwNP; biological therapy; dupilumab; long term; nasal polyps; observational study; sinusitis; treatment outcome.

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. 2023 Jul 3;220(7):e20221212.

doi: 10.1084/jem.20221212. Epub 2023 Jun 2.

## Type 2 inflammation and biological therapies in asthma: Targeted medicine taking flight

[Imran Howell](#)<sup>1</sup>, [Aleksandra Howell](#)<sup>1</sup>, [Ian D Pavord](#)<sup>1</sup>

Affiliations expand

- PMID: 37265457

- PMCID: [PMC10239209](#)



- DOI: [10.1084/jem.20221212](https://doi.org/10.1084/jem.20221212)

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## Abstract

The field of asthma has undergone a dramatic change in recent years. Advances in our understanding of type 2 airway inflammation have driven the discovery of monoclonal antibodies targeting specific aspects of the immune pathway. In landmark trials, these drugs have shown efficacy in reducing asthma attacks and exposure to oral corticosteroids, important causes of morbidity in people with asthma. Our review explores the key features of type 2 inflammation in asthma and summarizes the clinical trial evidence of the novel monoclonal antibody treatments and future avenues for treatment.

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## Conflict of interest statement

Disclosures: I.D. Pavord reported having, over the last 5 years, received speaker's honoraria for speaking at sponsored meetings from Astra Zeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini, and GSK, as well as payments for organizing educational events from Astra Zeneca, GSK, Sanofi/Regeneron, and Teva. He has also received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, Astra Zeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi, and Knopp, as well as payments to support FDA approval meetings from GSK; receiving sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, Astra Zeneca, Teva, and Chiesi; and has received a grant from Chiesi to support a phase 2 clinical trial in Oxford. No other disclosures were reported.

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

### SUPPLEMENTARY INFO

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J Pediatr Psychol

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. 2023 Jul 5;48(6):572-582.  
doi: 10.1093/jpepsy/jsad022.

# Depressive Symptom Trajectories Across Adolescence and Adulthood Among Individuals With Asthma

[Nicole M Ruppe](#)<sup>1,2</sup>, [Ashley H Clawson](#)<sup>3</sup>, [Rachel L Ankney](#)<sup>1</sup>, [Ginger Welch](#)<sup>4</sup>, [Larry L Mullins](#)<sup>1,2</sup>, [John M Chaney](#)<sup>1,2</sup>

Affiliations expand

- PMID: 37130344
- PMCID: [PMC10321385](#)
- DOI: [10.1093/jpepsy/jsad022](#)

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## Abstract

**Objective:** Individuals with asthma experience increased depressive symptoms, which is associated with deleterious health outcomes. No studies have examined depressive symptom trajectories among individuals with asthma despite increased risk. This study expanded prior literature by identifying the following: (1) depressive symptoms trajectories for individuals with and without asthma and (2) predictors of baseline levels and changes in symptoms across time for individuals with asthma.

**Methods:** Adolescents with (N = 965) and without (N = 7,392) asthma self-reported on depressive symptoms (CESD-9) across development. Covariates included: demographics and persistence of asthma. Latent growth curve modeling (LGCM) was used to identify depressive symptom trajectories and their predictors.

**Results:** A multigroup LCGM identified no significant differences between depressive symptom trajectories of individuals with and without asthma. Depressive symptoms followed a quadratic shape across time for individuals with asthma (Mintercept = 5.73,  $p < .00$ ; Mlinear = -0.38,  $p < .001$ ; Mquad = 0.03,  $p < .001$ ), with a linear deceleration in depressive symptoms during adolescence and an acceleration of symptoms into adulthood. Next predictors of depressive trajectories among individuals with asthma were examined. Female sex ( $B = 0.58$ ,  $p < .001$ ), lower parent education ( $B = -0.57$ ,  $p < .001$ ), older age ( $B = 0.19$ ,  $p < .001$ ), and identifying as Black ( $B = 0.31$ ,  $p = .04$ ) were associated with greater baseline depressive symptoms. Older individuals exhibited faster linear

symptom decelerations ( $B = -0.56$ ,  $p < .001$ ) and faster symptom accelerations ( $B = 0.73$ ,  $p < .001$ ). American Indian (AIAN) individuals exhibited faster linear symptom decelerations ( $B = -1.98$ ,  $p = .005$ ) and faster quadratic accelerations ( $B = 3.33$ ,  $p = .007$ ).

**Discussion:** Our results suggest that the depressive symptom trajectories of individuals with asthma are curvilinear and similar to individuals without asthma. When examining predictors of depressive symptom trajectories for those with asthma, socioeconomic disadvantage and racial marginalization were associated with greater baseline depressive symptoms. Although AIAN youth demonstrated more favorable trajectories in adolescence, they also exhibited worse trajectories across young adulthood and adulthood. Findings suggest the need to better understand the impact of multilevel risk and protective factors on depressive symptoms trajectories for individuals with asthma, especially marginalized populations.

**Keywords:** adolescents; asthma; depression; emerging/young adults; longitudinal research.

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## Conflict of interest statement

The authors have no conflicts of interest to disclose.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

FULL TEXT LINKS



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

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BMC Pediatr

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. 2023 Jul 6;23(1):343.

doi: 10.1186/s12887-023-04156-1.

**Blood eosinophil related to maternal allergic rhinitis is associated with the**

# incidence of allergic rhinitis in offspring: COCOA study

[Eun-A Choi](#)<sup>1</sup>, [Geumkyung Nah](#)<sup>1</sup>, [Woo-Sung Chang](#)<sup>1</sup>, [So-Yeon Lee](#)<sup>2</sup>, [Dong In Suh](#)<sup>3</sup>, [Kyung Won Kim](#)<sup>4</sup>, [Youn Ho Shin](#)<sup>5</sup>, [Kangmo Ahn](#)<sup>6</sup>, [Soo-Jong Hong](#)<sup>2</sup>, [Young Youl Kim](#)<sup>1</sup>, [Hye-Ja Lee](#)<sup>7</sup>

Affiliations expand

- PMID: 37415120
- DOI: [10.1186/s12887-023-04156-1](https://doi.org/10.1186/s12887-023-04156-1)

## Abstract

**Objective:** The identification of allergic rhinitis (AR) in early life is important for the target of intervention. AR is caused by various environmental factors, including house dust mites. We investigated the relationship between the Dermatophagoides farinae (Der f)-IgE and eosinophil in mothers with AR at delivery and the eosinophil levels and AR incidence in children.

**Methods:** The study participants were 983 mother-child pairs from the COhort for Childhood Origin of Asthma and Allergic Diseases. AR was diagnosed by a doctor at delivery in mother and at 3 years of age in offspring. The association between eosinophil level and AR was assessed using logistic regression analysis.

**Results:** The Der f-IgE level in mother having AR at delivery was associated with the mother's eosinophil level, and the mother's eosinophil level was associated with the child's eosinophil level both at age 1 and 3. The risk of AR at age 3 in children was increased according to increased eosinophil levels in mothers at delivery and in children both aged 1 and 3 years (adjusted odds ratio [aOR] and 95% confidence interval [CI]: 2.57 [1.14-5.78], 2.28 [1.02-5.13], respectively). The risk of childhood AR at the age of 3 is increased when both mothers and children have high eosinophils (aOR and 95% CI: 2.62 [1.01-6.79], 1.37 [0.98-1.91]).

**Conclusions:** Der f-IgE in mothers at delivery was related to eosinophil levels in mothers with AR and higher level of eosinophils in both mother and children was associated with the increased risk of AR incidence at the first 3 years of life of children.

**Keywords:** Allergic Rhinitis; Der f-IgE; Eosinophil; Mothers and children.

- [37 references](#)

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Eur J Health Econ



. 2023 Jul 7.

doi: 10.1007/s10198-023-01598-3. Online ahead of print.

# Quality of life and healthcare costs of patients with allergic respiratory diseases: a cross-sectional study

[Vivienne Hillerich](#)<sup>#1</sup>, [Frederik Valbert](#)<sup>#2</sup>, [Silke Neusser](#)<sup>2</sup>, [Oliver Pfaar](#)<sup>2</sup>, [Ludger Klimek](#)<sup>4</sup>, [Annette Sperl](#)<sup>4</sup>, [Thomas Werfel](#)<sup>5</sup>, [Eckard Hamelmann](#)<sup>6</sup>, [Cordula Riederer](#)<sup>7</sup>, [Stefanie Wobbe-Ribinski](#)<sup>7</sup>, [Anja Neumann](#)<sup>2</sup>, [Jürgen Wasem](#)<sup>2</sup>, [Janine Biermann-Stallwitz](#)<sup>2</sup>

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- PMID: 37414970
- DOI: [10.1007/s10198-023-01598-3](https://doi.org/10.1007/s10198-023-01598-3)

## Abstract

**Background:** Allergic rhinitis (AR) and allergic asthma (AA) are chronic respiratory diseases that represent a global health problem. One aim of this study was to analyze the Health-related Quality of Life (HRQoL) of the patients in order to identify statistically significant influencing factors that determine HRQoL. Another aim was to assess and analyze data on cost-of-illness from a statutory health insurance perspective.

**Methods:** The EQ-5D-5L was used to evaluate the patients' HRQoL. To identify the factors influencing the HRQoL, a multinomial logistic regression analysis was conducted using

groups based on the EQ-5D-5L index value as dependent variable. Routine data were analyzed to determine total healthcare costs.

**Results:** The average EQ-5D-5L index was 0.85 (SD 0.20). A high age, the amount of disease costs, low internal health-related control beliefs and high ozone exposure in the residential area were found to be statistically significant influencing factors for a low HRQoL, whereas low age, male sex and a good possibility to avoid the allergens were found to be statistically significant factors influencing a high HRQoL. On average, the study participants incurred annual costs of €3072 (SD: 3485), of which €699 (SD: 743) could be assigned to allergic respiratory diseases.

**Conclusions:** Overall, the patients in the VerSITA study showed a high level of HRQoL. The identified influencing factors can be used as starting points for improving the HRQoL of patients with allergic respiratory diseases. From the perspective of a statutory health insurance, per person expenditures for allergic respiratory diseases are rather low.

**Keywords:** Asthma; Health Economics; Health-Related Quality of Life; Healthcare Costs; Rhinitis.

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- [71 references](#)

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Eur Arch Otorhinolaryngol

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. 2023 Jul 6.

doi: 10.1007/s00405-023-08083-w. Online ahead of print.

# Evaluation of the quality of guidelines for sublingual immunotherapy of allergic rhinitis

[Qian Wang](#)<sup>1</sup>, [Ruifang Zhu](#)<sup>1,2</sup>, [Yan Ning](#)<sup>1</sup>, [Yaoqing Feng](#)<sup>1</sup>, [Yan Feng](#)<sup>1,2</sup>, [Shifan Han](#)<sup>3,4</sup>

Affiliations expand

- PMID: 37410146
- DOI: [10.1007/s00405-023-08083-w](https://doi.org/10.1007/s00405-023-08083-w)

## Abstract

**Background:** Guidelines are intended to facilitate evidence-based clinical decision-making and knowledge translation; however, the quality and rigor of the guidelines are different. This study was conducted to assess the quality of sublingual immunotherapy guidelines for allergic rhinitis, in order to provide a reference for evidence-based clinical treatment and management of sublingual immunotherapy.

**Methods:** Using both Chinese and English search methods, articles were obtained from PubMed, Cochrane, Web of Science, CNKI, CBM, WanFang Data, VIP, and other databases from the construction of the database to September 2020. The AGREE II instrument was used by two researchers to independently evaluate the quality of the extracted articles, and the consistency of the researchers was evaluated using the inter-group correlation coefficient.

**Results:** Ten articles were included in this study, of which two articles ranked A level, six articles ranked B level, and two articles ranked C level. The six sections of AGREE II included scope and aim, clarity, participant, applicability, rigor, and editorial independence, with standardized scores of 78.06%, 45.83%, 42.81%, 77.50%, 50.42%, and 46.25%, respectively.

**Conclusion:** The quality of the current guidelines for sublingual immunotherapy is average. The formulation methodology and reporting standards of these guidelines must be developed. By standardizing the treatment of sublingual immunotherapy properly, it is recommended that guideline makers refer to the AGREE II to formulate high-quality guidelines and promote their wide application.

**Keywords:** AGREE II; Allergic rhinitis; Guideline; Sublingual immunotherapy.

- [20 references](#)

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Cureus

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. 2023 Jul 4;15(7):e41374.

doi: 10.7759/cureus.41374. eCollection 2023 Jul.

# [The Combined Effects of Sublingual Immunotherapy and Lactobacillus acidophilus–Producing Extract on Cedar Pollinosis Symptoms](#)

[Ito Hirobumi](#)<sup>1</sup>, [Yasuhiro Sasuga](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 37408939
- PMCID: [PMC10319452](#)
- DOI: [10.7759/cureus.41374](#)

## Abstract



**Introduction:** Sublingual immunotherapy (SLIT), in which standardized cedar pollen extract solution is administered, has been used to treat cedar pollinosis, but SLIT is problematic because it takes a long time to become effective, and some cases are ineffective even after long-term treatment. It has also been reported that lactobacillus acidophilus extract (LEX), a food-derived ingredient, alleviates various allergic symptoms. This study examined the usefulness of LEX as a treatment for cedar pollinosis in comparison with SLIT. We also examined whether the combined use of SLIT and LEX could have an early-onset of therapeutic effect on cedar pollinosis. We also examined the usefulness of LEX as a salvage therapy for patients who failed to respond to SLIT.

**Subjects and methods:** Fifteen patients with cedar pollinosis were divided into three groups. The three groups were: three patients in the standardized cedar pollen extract group (S group), seven patients in the lactobacillus-producing extract group (L group), and five patients in the combination group of standardized cedar pollen extract and lactobacillus-producing extract (SL group). The subjects were treated for three years, corresponding to the three scattering seasons of cedar pollen, and observed according to the evaluation items. The evaluation items were severity score based on examination findings, subjective symptom score (QOL score) based on the Japanese Standard QOL Questionnaire for Allergic Rhinitis (JRQLQ No. 1) questionnaire, nonspecific IgE level measurement by blood test, and cedar pollen-specific IgE level measurement.

**Results:** After three years of observation, there were no significant differences in severity score and nonspecific IgE levels among the three groups, while QOL score decreased significantly between the first and third years of treatment in the L group. Cedar pollen-specific IgE levels in the S and SL groups showed an increase in the first year and a gradual decrease in the second and third years of treatment compared to the pre-treatment period. In group L, no increase was observed in the first year, and a significant decrease was observed in the second and third years during the cedar pollen dispersal period.

**Conclusions:** The results of severity and quality of life scores indicated that it took three years of treatment for the S and SL groups to show efficacy, while the L group showed improvement in quality of life scores and cedar pollen-specific IgE levels from the first year, suggesting that LEX is useful as a treatment for cedar pollinosis. The efficacy of combination therapy with SLIT and LEX was not clear, but since the effect of LEX was observed from the early stage of treatment, it was thought that the combination therapy with LEX intake from the early stage of treatment may be effective in reducing the incidence of ineffective cases. The combination therapy of SLIT and LEX may also be useful as a salvage therapy.

**Keywords:** combination effect; fast onset of effects; food ingredients; ineffective cases; japanese cedar pollen; lactobacillus acidophilus produced extract (lex); pollinosis; salvage therapy; seasonal allergic rhinitis; sublingual immunotherapy (slit).

## Conflict of interest statement

The authors have declared that no competing interests exist.

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

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J Asthma

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. 2023 Jul 5;1-14.

doi: [10.1080/02770903.2023.2231078](https://doi.org/10.1080/02770903.2023.2231078). Online ahead of print.

# Age-related differences in associations between uncontrolled asthma, comorbidities and biomarkers in adult-onset asthma

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

Affiliations [expand](#)

- PMID: 37405375
- DOI: [10.1080/02770903.2023.2231078](https://doi.org/10.1080/02770903.2023.2231078)

## Abstract

**Objective:** Adult-onset asthma is a recognized but heterogeneous phenotype and has been described to associate with poor asthma control. Knowledge about associations between clinical characteristics including comorbidities and control of adult-onset asthma is limited, especially in older populations. We aimed to study how clinical biomarkers and comorbidities associate with uncontrolled asthma among middle-aged and older individuals with adult-onset asthma.

**Methods:** Clinical examinations including structured interview, asthma control test (ACT), spirometry, skin prick test (SPT), blood sampling and measurement of exhaled fractional nitric oxide (FeNO) was performed in a population-based adult-onset asthma cohort in 2019-2020 (n = 227, 66.5% female). Analyses were performed among all included, and separately in middle-aged (37-64y, n = 120) and older ( $\geq 65$ y, n = 107) participants.

**Results:** In bivariate analysis, uncontrolled asthma ( $ACT \leq 19$ ) was significantly associated with a blood neutrophil count  $\geq 5/\mu l$ , BMI  $\geq 30$  and several comorbidities. In multivariable regression analysis, uncontrolled asthma was associated with neutrophils  $\geq 5/\mu l$  (OR 2.35; 95% CI 1.11-4.99). In age-stratified analysis, BMI  $\geq 30$  (OR 3.04; 1.24-7.50), eosinophils  $\geq 0.3/\mu l$  (OR 3.17; 1.20-8.37), neutrophils  $\geq 5/\mu l$  (OR 4.39; 1.53-12.62) and allergic rhinitis (OR 5.10; 1.59-16.30) were associated with uncontrolled asthma among the middle-aged. Among the older adults, uncontrolled asthma was only associated with comorbidities: chronic rhinitis (OR 4.08; 1.62-10.31), ischemic heart disease (OR 3.59; 1.17-10.98), malignancy (OR 3.10; 1.10-8.73) and depression/anxiety (OR 16.31; 1.82-146.05).

**Conclusions:** In adult-onset asthma, comorbidities were strongly associated with uncontrolled asthma among older adults, while clinical biomarkers including eosinophils and neutrophils in blood were associated with uncontrolled asthma among middle-aged.

**Keywords:** eosinophils; epidemiology; inflammation; neutrophils; phenotype; risk factors.

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Clin Exp Allergy

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. 2023 Jul 3.

# Childhood body mass index trajectories and asthma and allergies: A systematic review

[Chia-Lun Chang](#)<sup>1</sup>, [Gulshan Bano Ali](#)<sup>1</sup>, [Jonathan Pham](#)<sup>1,2</sup>, [Shyamali C Dharmage](#)<sup>1,3</sup>, [Caroline J Lodge](#)<sup>1,3</sup>, [Mimi L K Tang](#)<sup>4,5,6</sup>, [Adrian J Lowe](#)<sup>1,3</sup>

Affiliations expand

- PMID: 37401045
- DOI: [10.1111/cea.14366](https://doi.org/10.1111/cea.14366)

## Abstract

**Background:** Previous systematic reviews have focused on associations between single time point measures of Body Mass Index (BMI) and asthma and allergic diseases. As BMI changes dynamically during childhood, examination of associations between longitudinal trajectories in BMI and allergic diseases is needed to fully understand the nature of these relationships.

**Objective:** To systematically synthesise the association between BMI trajectories in childhood (0-18 years) and allergic diseases (asthma, eczema, allergic rhinitis, or food allergies outcomes).

**Design:** We conducted a systematic review following the PRISMA guidelines, and two independent reviewers assessed the study quality using the ROBINS-E and GRADE tools. A narrative synthesis was performed as the statistical heterogeneity did not allow a meta-analysis.

**Data sources:** A search was performed on PubMed and EMBASE databases on 4th January 2023.

**Eligibility criteria:** Longitudinal cohort studies assessing the associations between childhood BMI trajectories and allergic diseases were included.

**Results:** Eleven studies met the inclusion criteria with a total of 37,690 participants between 0 and 53 years of age. Ten studies examined asthma outcomes, three assessed association with allergic rhinitis, two assessed eczema, and one assessed food allergy. High heterogeneity and high risk of bias were observed. Overall, the quality of evidence was

very low. Nevertheless, two consistent findings were identified: (1) a persistently high BMI between 6 and 10 years of age may be associated with an increased risk of asthma at 18 years and (2) a rapid increase in BMI in the first 2 years of life may be associated with subsequent asthma.

**Conclusions:** Maintaining a normal BMI trajectory during childhood may reduce the risk of asthma. Future research that adequately addresses confounding and includes longer-term follow-up is needed. Moreover, additional studies examining potential associations with eczema, food allergies, and allergic rhinitis outcomes are needed.

**Keywords:** Paediatric; allergy; asthma; body mass index trajectories; obesity.

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Clin Rev Allergy Immunol

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. 2023 Jul 3.

doi: 10.1007/s12016-023-08966-0. Online ahead of print.

## [γδ T Cells and Allergic Diseases](#)

[Uei-Hsiang Hsu](#)<sup>1</sup>, [Bor-Luen Chiang](#)<sup>2,3</sup>

[Affiliations expand](#)

- PMID: 37395986

- DOI: [10.1007/s12016-023-08966-0](https://doi.org/10.1007/s12016-023-08966-0)

## Abstract

Gamma-delta ( $\gamma\delta$ ) T cells play an essential role in allergic diseases and have emerged as a potential treatment target in recent decades. To clarify the effects of  $\gamma\delta$  T cells on atopic illnesses, we reviewed the literature on the physical roles and functions of various subsets of  $\gamma\delta$  T cells, including type 1 T helper (Th1)-like, type 2 T helper- (Th2)-like, and type 17 T helper (Th17)-like  $\gamma\delta$  T cells. Mouse V $\gamma$ 1 T cells increase interleukin (IL)-4 levels and trigger B cell class switching and immunoglobulin E production. Meanwhile, mouse V $\gamma$ 4 T cells and human CD8<sup>low</sup>V $\delta$ 1 T cells secrete interferon- $\gamma$  and exert an anti-allergy effect similar to that of Th1 cells. Moreover, mouse V $\gamma$ 6 T cells produce IL-17A, while Th17-like  $\gamma\delta$  T cells enhance neutrophil and eosinophil infiltration in the acute phase of inflammation, but exert anti-inflammatory effects in the chronic phase. Human V $\gamma$ 9 $\delta$ 2 T cells may exhibit Th1- or Th2-like characteristics in response to certain types of stimulation. In addition, the microbiota can modulate epithelial  $\gamma\delta$  T cell survival through aryl hydrocarbon receptors; these  $\gamma\delta$  T cells play crucial roles in the repair of epithelial damage, antibacterial protection, antigen tolerance, and effects of dysbiosis on allergic diseases.

**Keywords:** Allergic rhinitis; Allergy disease; Asthma; Atopic dermatitis; Microbiota;  $\gamma\delta$  T cel.

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Inflamm Bowel Dis

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# Aeroallergen-related Diseases Predate the Diagnosis of Inflammatory Bowel Disease

[Namarik Alenezy](#)<sup>1,2</sup>, [Zoann Nugent](#)<sup>2,3</sup>, [Sari Herman](#)<sup>2,4</sup>, [Karver Zaborniak](#)<sup>1</sup>, [Clare D Ramsey](#)<sup>1</sup>, [Charles N Bernstein](#)<sup>1,2</sup>

Affiliations expand

- PMID: 36018043
- DOI: [10.1093/ibd/izac184](https://doi.org/10.1093/ibd/izac184)

## Abstract

**Objective:** This study aimed to determine whether having a diagnosis of asthma or allergic rhinitis (AR) increased the risk of being diagnosed with inflammatory bowel disease (IBD) and whether there was increased incidence of these diseases after a diagnosis of IBD.

**Design:** This is a retrospective, historical cohort-based study. We used the administrative data of Manitoba Health and the population-based University of Manitoba IBD Epidemiology Database. We used numbers of prescriptions for drugs used to treat asthma and to treat AR to identify diagnoses of asthma and AR, respectively. We calculated relative risks (RRs) to assess incidence of IBD compared with matched controls after diagnoses of asthma and AR and hazard ratios to determine the incidence of asthma and AR after IBD diagnosis.

**Results:** Compared with controls, a diagnosis of asthma or AR preceding a diagnosis of IBD was increased in cases (RR, 1.62; 95% confidence interval [CI], 1.50-1.75; and RR, 2.10; 95% CI, 1.97-2.24) with a similar outcome by subtype of IBD (Crohn's disease vs ulcerative colitis) and by sex. On sensitivity analysis, diagnoses of asthma or AR were comparable when considering at least 5, 10, 15 or 20 drug prescriptions. Persons with IBD were more likely to develop asthma or AR than controls after being diagnosed with IBD (hazard ratio for asthma, 1.31, 95% CI, 1.18-1.45; and hazard ratio for AR, 2.62, 95% CI, 2.45-2.80).

**Conclusions:** The association between asthma, AR, and IBD suggest the possibility that whatever triggers the onset of these atopic diseases may trigger the onset of IBD as well, and aeroallergens are plausible culprits.

## Plain language summary

This study demonstrates that a preexisting diagnosis of asthma or allergic rhinitis is associated with an increased risk of subsequently developing IBD. These data reinforce the importance of considering that gastrointestinal complaints in patients with asthma and allergic rhinitis may reflect a possible diagnosis of IBD. It also raises the possibility that aeroallergens may be environmental cause(s) of IBD.

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MeSH termsexpand

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

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Am J Respir Crit Care Med

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. 2023 Jul 6.

doi: 10.1164/rccm.202303-0458OC. Online ahead of print.

## [Icenticaftor, a CFTR Potentiator, in COPD: A Multicenter, Parallel-Group, Double-Blind Clinical Trial](#)

[Fernando J Martinez](#)<sup>1</sup>, [Gerard J Criner](#)<sup>2</sup>, [Christian Gessner](#)<sup>3</sup>, [Margret Jandl](#)<sup>4</sup>, [Fernando Scherbovsky](#)<sup>5</sup>, [Masaharu Shinkai](#)<sup>6</sup>, [Thomas M Siler](#)<sup>7</sup>, [Claus F Vogelmeier](#)<sup>8</sup>, [Robert Voves](#)<sup>9</sup>, [Jadwiga A Wedzicha](#)<sup>10</sup>, [Christian Bartels](#)<sup>11</sup>, [Ivan Bottoli](#)<sup>12</sup>, [Stuart Byiers](#)<sup>11</sup>, [Pamela](#)



[Cardenas](#)<sup>13</sup>, [Joerg H Eckert](#)<sup>11</sup>, [Florian S Gutzwiller](#)<sup>11</sup>, [Barbara Knorr](#)<sup>13</sup>, [Mahavir Kothari](#)<sup>14</sup>, [Rutvick Parlikar](#)<sup>14</sup>, [Ana-Maria Tanase](#)<sup>11</sup>, [Frits M E Franssen](#)<sup>15</sup>

Affiliations expand

- PMID: 37411039
- DOI: [10.1164/rccm.202303-0458OC](https://doi.org/10.1164/rccm.202303-0458OC)

## Abstract

**Rationale:** CF transmembrane conductance regulator (CFTR) dysfunction is associated with mucus accumulation and worsening COPD symptoms. This Phase 2b dose-finding study compared a CFTR potentiator, icenticaftor (QBW251), with placebo in patients with COPD and chronic bronchitis.

**Methods:** COPD patients on triple therapy for at least three months were randomized to six treatment arms (icenticaftor 450, 300, 150, 75, or 25mg or placebo b.i.d.) in a 24-week, multicenter, parallel-group, double-blind study. The primary endpoint was change from baseline in trough FEV<sub>1</sub> after 12 weeks. Secondary endpoints included change from baseline in trough FEV<sub>1</sub>, Evaluating Respiratory Symptoms in COPD (E-RS) total and cough and sputum scores after 24 weeks. Multiple Comparison Procedure-Modelling characterized dose-response. Rescue medication use, exacerbations, and change in serum fibrinogen levels after 24 weeks were exploratory and post-hoc analyses, respectively. **Measurements and Main Results:** 974 patients were randomized. After 12 weeks of icenticaftor treatment, no dose-response for change from baseline in trough FEV<sub>1</sub> was observed; however, it was observed for E-RS cough and sputum score. A dose-response was observed after 24 weeks for trough FEV<sub>1</sub>, E-RS cough and sputum and total scores, rescue medication use and fibrinogen. 300mg b.i.d. was consistently the most effective dose. Improvements for 300mg b.i.d. versus placebo were also seen in pairwise comparisons of these endpoints. All treatments were well tolerated.

**Conclusions:** The primary endpoint was negative as icenticaftor did not improve trough FEV<sub>1</sub> over 12 weeks. Although the findings must be interpreted with caution, icenticaftor improved trough FEV<sub>1</sub>, cough, sputum, rescue medication use and lowered fibrinogen levels at 24 weeks. Clinical trial registration available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**Clinical trials:** gov, ID: [NCT04072887](https://clinicaltrials.gov/ct2/show/study/NCT04072887).

**Keywords:** CFTR dysfunction; CFTR potentiator; COPD; Chronic Bronchitis; icenticaftor.

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. 2023 Jul 3;12:e45585.

doi: 10.2196/45585.

# [Remote Patient Monitoring and Teleconsultation to Improve Health Outcomes and Reduce Health Care Utilization of Pediatric Asthma \(ALPACA Study\): Protocol for a Randomized Controlled Effectiveness Trial](#)

[Mattienne van der Kamp](#)<sup>1,2</sup>, [Vera Hengeveld](#)<sup>1</sup>, [Nico Willard](#)<sup>3</sup>, [Boony Thio](#)<sup>1</sup>, [Pascal de Graaf](#)<sup>3</sup>, [Inge Geven](#)<sup>3</sup>, [Monique Tabak](#)<sup>2</sup>

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- PMID: 37399066
- DOI: [10.2196/45585](https://doi.org/10.2196/45585)

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## Abstract

**Background:** Childhood asthma is imposing a great financial burden on the pediatric health care system. Asthma costs are directly related to the level of asthma control. A substantial part of these costs may be preventable by the timely and adequate assessment of asthma deterioration in daily life and proper asthma management. The use of eHealth technology may assist such timely and targeted medical anticipation.

**Objective:** This paper describes the Ambulatory Pediatric Asthma Care (ALPACA) study protocol to investigate the effectiveness of an eHealth intervention consisting of remote patient monitoring and teleconsultation integrated into the daily clinical care of pediatric patients with asthma. This intervention aims to reduce health care utilization and costs and improve health outcomes compared to a control group that receives standard care. In addition, this study aims to improve future eHealth pediatric asthma care by gaining insights from home-monitoring data.

**Methods:** This study is a prospective randomized controlled effectiveness trial. A total of 40 participants will be randomized to either 3 months of eHealth care (intervention group) or standard care (control group). The eHealth intervention consists of remote patient monitoring (spirometry, pulse oximetry, electronic medication adherence tracking, and asthma control questionnaire) and web-based teleconsultation (video sharing, messages). All participants will have a 3-month follow-up with standard care to evaluate whether the possible effects of eHealth care are longer lasting. During the entire study and follow-up period, all participants will use blinded observational home monitoring (sleep, cough/whheeze sounds, air quality in bedroom) as well.

**Results:** This study was approved by the Medical Research Ethics Committees United. Enrollment began in February 2023, and the results of this study are expected to be submitted for publication in July 2024.

**Conclusions:** This study will contribute to the existing knowledge on the effectiveness of eHealth interventions that combine remote patient monitoring and teleconsultation for health care utilization, costs, and health outcomes. Furthermore, the observational home-monitoring data can contribute to improved identification of early signs of asthma deterioration in pediatric patients. Researchers and technology developers could use this study to guide and improve eHealth development, while health care professionals, health care institutions, and policy makers may employ our results to make informed decisions to steer toward high-quality, efficient pediatric asthma care.

**Trial registration:** ClinicalTrials.gov [NCT05517096](https://clinicaltrials.gov/ct2/show/NCT05517096);  
<https://clinicaltrials.gov/ct2/show/NCT05517096>.

**International registered report identifier (irrid):** PRR1-10.2196/45585.

**Keywords:** adherence; asthma; asthma care; children; health care costs; health care utilization; home monitoring; nebulizer; pediatric care; protocol; randomized controlled trial; remote monitoring; spirometry; telemedicine; utilization.

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SUPPLEMENTARY INFO

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. 2023 Jul 3;31(7):436.

doi: 10.1007/s00520-023-07889-y.

# Defining research priorities and needs in cancer symptoms for adults diagnosed with cancer: an Australian/New Zealand modified Delphi study

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Affiliations expand

- PMID: 37395859

- PMCID: [PMC10317881](#)

- DOI: [10.1007/s00520-023-07889-y](https://doi.org/10.1007/s00520-023-07889-y)

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## Abstract

**Purpose:** This study asked consumers (patients, carers) and healthcare professionals (HCPs) to identify the most important symptoms for adults with cancer and potential treatment interventions.

**Methods:** A modified Delphi study was conducted involving two rounds of electronic surveys based on prevalent cancer symptoms identified from the literature. Round 1 gathered information on participant demographics, opinions and/or experience on cancer symptom frequency and impact, and suggestions for interventions and/or service delivery models for further research to improve management of cancer symptoms. In Round 2, respondents ranked the importance of the top ten interventions identified in Round 1. In Round 3, separate expert panels of consumers and healthcare professionals (HCPs) attempted to reach consensus on the symptoms and interventions previously identified.

**Results:** Consensus was reached for six symptoms across both groups: fatigue, constipation, diarrhoea, incontinence, and difficulty with urination. Notably, fatigue was the only symptom to reach consensus across both groups in Round 1. Similarly, consensus was reached for six interventions across both groups. These were the following: medicinal cannabis, physical activity, psychological therapies, non-opioid interventions for pain, opioids for breathlessness and cough, and other pharmacological interventions.

**Conclusions:** Consumers and HCPs prioritise differently; however, the symptoms and interventions that reached consensus provide a basis for future research. Fatigue should be considered a high priority given its prevalence and its influence on other symptoms. The lack of consumer consensus indicates the uniqueness of their experience and the need for a patient-centred approach. Understanding individual consumer experience is important when planning research into better symptom management.

**Keywords:** Cancer symptoms; Consumers; Delphi; Healthcare professionals; Neoplasms.

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## Conflict of interest statement

CS has received honoraria for advisory board membership from MSD, Merck, Sanofi, Janssen, Ipsen, GSK, and Astra Zeneca. CS has received speaker's fees from BMS and Novartis. LB, MC, KC, PG, JP, MRA, IAD, AL, JV, AW, and VY have no competing interests.

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

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Review

J Toxicol Environ Health B Crit Rev

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. 2023 Jul 4;26(5):275-305.

doi: 10.1080/10937404.2023.2208886. Epub 2023 May 14.

# [Animal models and mechanisms of tobacco smoke-induced chronic obstructive pulmonary disease \(COPD\)](#)

[Priya Upadhyay](#)<sup>1</sup>, [Ching-Wen Wu](#)<sup>1</sup>, [Alexa Pham](#)<sup>1</sup>, [Amir A Zeki](#)<sup>2,3</sup>, [Christopher M Royer](#)<sup>4</sup>, [Urmila P Kodavanti](#)<sup>5</sup>, [Minoru Takeuchi](#)<sup>6</sup>, [Hasan Bayram](#)<sup>7</sup>, [Kent E Pinkerton](#)<sup>1</sup>

Affiliations expand

- PMID: 37183431
- DOI: [10.1080/10937404.2023.2208886](https://doi.org/10.1080/10937404.2023.2208886)

## Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, and its global health burden is increasing. COPD is characterized by emphysema, mucus hypersecretion, and persistent lung inflammation, and clinically by chronic airflow obstruction and symptoms of dyspnea, cough, and fatigue in patients. A cluster of pathologies including chronic bronchitis, emphysema, asthma, and cardiovascular disease in the form of hypertension and atherosclerosis variably coexist in COPD patients. Underlying causes for COPD include primarily tobacco use but may also be driven by exposure to air pollutants, biomass burning, and workplace related fumes and chemicals. While no single animal model might mimic all features of human COPD, a wide variety of published models have collectively helped to improve our understanding of disease processes involved in the genesis and persistence of COPD. In this review, the pathogenesis and associated risk factors of COPD are examined in different mammalian models of the disease. Each animal model included in this review is exclusively created by tobacco smoke (TS) exposure. As animal models continue to aid in defining the pathobiological mechanisms of and possible novel therapeutic interventions for COPD, the advantages and disadvantages of each animal model are discussed.

**Keywords:** animal models; chronic bronchitis; chronic obstructive pulmonary disease (COPD); emphysema; tobacco smoke.

#### SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated data, Grant supportexpand

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

1

J Allergy Clin Immunol Pract

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. 2023 Jul 3;S2213-2198(23)00714-6.

doi: 10.1016/j.jaip.2023.06.049. Online ahead of print.

# Characterization of Obesity in Severe Asthma in the German Asthma Net

[Christina Bal](#), [Wolfgang Pohl](#), [Katrin Milger](#), [Dirk Skowasch](#), [Christian Schulz](#), [Monika Gappa](#), [Cordula Koerner-Rettberg](#), [Margret Jandl](#), [Olaf Schmidt](#), [Sonja Zehetmayer](#), [Christian Taube](#), [Eckard Hamelmann](#), [Roland Buhl](#), [Stephanie Korn](#), [Marco Idzko](#)

- PMID: 37406803
- DOI: [10.1016/j.jaip.2023.06.049](https://doi.org/10.1016/j.jaip.2023.06.049)

## Abstract

**Background:** Asthma is increasingly recognized as heterogeneous, characterized by different endotypes, with obesity not only a distinct phenotype but a risk factor for severe asthma.

**Objective:** We sought to understand the associations of obesity with relevant parameters of severe asthma, including asthma control, disease burden, and lung function.

**Methods:** The German Asthma Net (GAN) Registry is a multi-center international real-life registry capturing long-term follow-up data. This analysis included 2,213 patients (52±16 years, 58% female, 29% with obesity (body mass index  $\geq 30\text{kg/m}^2$ ), 4.2±4.3 exacerbations/year). The primary analysis assessed relationships between BMI and variables through univariate tests, followed by a multiple regression model. Secondary outcomes regarded clinically relevant variables in relation to weight groups.

**Results:** Patients with obesity were more frequently female, more likely to have depression and gastroesophageal reflux, and suffered from worse asthma control, lower quality of life, reduced static lung volumes, more pronounced hypoxemia, and higher blood neutrophil counts, all statistically significant. Blood eosinophils, exhaled nitric oxide, and total immunoglobulin E were independent of obesity. In the multiple regression analysis, obesity was significantly associated with more frequent reflux and depression, reduced static lung function values, older age, poor asthma control, long-acting muscarinic antagonist therapy, and inversely associated with bronchiectasis, and non-smoking status.

**Conclusion:** In this large, well-characterized cohort, we identified the association of obesity with significantly higher disease burden and a similar portfolio of inflammation type-2 markers in patients with and without obesity; therefore, patients with obesity seem similarly eligible for the treatment with biologics targeting these disease endotypes.



**Keywords:** Asthma Control; BMI; Biomarker; Comorbidities; Exacerbations; Lung Function; Obesity; Registry; Severe Asthma.

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. 2023 Jul 3;9(4):00021-2023.

doi: 10.1183/23120541.00021-2023. eCollection 2023 Jul.

# [Pulmonary exacerbations in insured patients with bronchiectasis over 2 years](#)

[Patrick A Flume](#)<sup>1</sup>, [Joseph Feliciano](#)<sup>2</sup>, [Matthew Lucci](#)<sup>3</sup>, [Jasmanda Wu](#)<sup>2</sup>, [Sebastian Fucile](#)<sup>2</sup>, [Mariam Hassan](#)<sup>2</sup>, [Anjan Chatterjee](#)<sup>2</sup>

Affiliations [expand](#)

- PMID: 37404848
- PMCID: [PMC10316032](#)
- DOI: [10.1183/23120541.00021-2023](#)

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## Abstract

**Background:** Patients with bronchiectasis experience persistent symptoms and frequent pulmonary exacerbations; this study investigated the frequency of exacerbations and all-cause hospitalisation.

**Methods:** This longitudinal, retrospective, claims database study (IBM® MarketScan®) identified patients aged  $\geq 18$  years from 1 July 2015 through 30 September 2018. Exacerbations were identified by bronchiectasis inpatient claim or a healthcare interaction, followed by antibiotic prescription within 7 days. Patients with  $\geq 36$  months of continuous health plan enrolment (12 months preceding the first bronchiectasis claim, *i.e.*, baseline period and  $\geq 24$  months of follow-up) were included. Patients with cystic fibrosis at baseline were excluded. A multivariable logistic regression model identified baseline factors associated with having  $\geq 2$  exacerbations over the 2-year follow-up period.

**Results:** In total, 14 798 patients with bronchiectasis were identified; 64.5% were female, 82.7% were aged  $\geq 55$  years and 42.7% had  $\geq 2$  exacerbations at baseline. Having  $\geq 2$  exacerbations after 2 years was positively associated with chronic macrolide use, long-acting  $\beta_2$  agonist use, gastro-oesophageal reflux disease, heart failure and *Pseudomonas aeruginosa*. Frequent exacerbations ( $\geq 2$ ) at baseline were significantly associated with greater likelihood of experiencing  $\geq 2$  exacerbations during the first and second year's follow-up (unadjusted odds ratios 3.35 (95% CI 3.1-3.6) and 2.96 (95% CI 2.8-3.2), respectively). The proportion of patients experiencing  $\geq 1$  all-cause hospitalisation cumulatively increased from 41.0% in the first year of follow-up to 51.1% over 2 years' follow-up.

**Conclusion:** Frequent exacerbations in patients with bronchiectasis may increase the likelihood of future exacerbations over 2 years of follow-up, with increased hospitalisation rates over time.

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## Conflict of interest statement

Conflicts of interest: J. Wu reports support for the present manuscript from Insmed; the author is a current employee of Insmed and has stock and stock option, outside the submitted work. Conflicts of interest: M. Hassan reports support for the present manuscript from Insmed; the author is a current employee of Insmed and has stock, outside the submitted work; receipt of medical writing support from Insmed, outside the submitted work. Conflicts of interest: P.A. Flume reports support for the present manuscript from Insmed; grants or contracts from Insmed, outside the submitted work; and consulting fees from Insmed, outside the submitted work. Conflicts of interest: S. Fucile reports support for the present manuscript from Insmed; the author is a current employee of Insmed and has stock and stock option, outside the submitted work. Conflicts of interest: J. Feliciano reports support for the present manuscript from Insmed; the author is a current employee of Insmed and has stock, outside the submitted work; receipt of medical writing support from Insmed, outside the submitted work. Conflicts of interest: A. Chatterjee reports

support for the present manuscript from Insmed; the author is a current employee of Insmed and has stock and stock option, outside the submitted work. Conflicts of interest: M. Lucci has nothing to disclose.

- [25 references](#)
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BMC Pulm Med

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. 2023 Jul 4;23(1):243.

doi: 10.1186/s12890-023-02502-8.

# [Assessing the genetic relationship between gastroesophageal reflux disease and chronic respiratory diseases: a mendelian randomization study](#)

[Xiaoxue Cheng](#) <sup>#1</sup>, [Jiang Shi](#) <sup>#2 3 4</sup>, [Ding Zhang](#) <sup>#5</sup>, [Caichen Li](#) <sup>#2 3 4</sup>, [Haoxiang Xu](#) <sup>#6</sup>, [Jianxing He](#) <sup>2 3 4</sup>, [Wenhua Liang](#) <sup>7 8 9</sup>

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- PMID: 37403021
- PMCID: [PMC10318641](#)

- DOI: [10.1186/s12890-023-02502-8](https://doi.org/10.1186/s12890-023-02502-8)

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## Abstract

**Background:** Previous observational studies have found an association between gastroesophageal reflux disease (GERD) and chronic respiratory diseases, but it remains uncertain whether GERD causally influences these diseases. In this study, we aimed to estimate the causal associations between GERD and 5 chronic respiratory diseases.

**Methods:** 88 GERD-associated single nucleotide polymorphisms (SNPs) identified by the latest genome-wide association study were included as instrumental variables. Individual-level genetic summary data of participants were obtained from corresponding studies and the FinnGen consortium. We applied the inverse-variance weighted method to estimate the causality between genetically predicted GERD and 5 chronic respiratory diseases. Furthermore, the associations between GERD and common risk factors were investigated, and mediation analyses were conducted using multivariable MR. Various sensitivity analyses were also performed to verify the robustness of the findings.

**Results:** Our study demonstrated that genetically predicted GERD was causally associated with an increased risk of asthma (OR 1.39, 95%CI 1.25-1.56,  $P < 0.001$ ), idiopathic pulmonary fibrosis (IPF) (OR 1.43, 95%CI 1.05-1.95,  $P = 0.022$ ), chronic obstructive disease (COPD) (OR 1.64, 95%CI 1.41-1.93,  $P < 0.001$ ), chronic bronchitis (OR 1.77, 95%CI 1.15-2.74,  $P = 0.009$ ), while no correlation was observed for bronchiectasis (OR 0.93, 95%CI 0.68-1.27,  $P = 0.645$ ). Additionally, GERD was associated with 12 common risk factors for chronic respiratory diseases. Nevertheless, no significant mediators were discovered.

**Conclusions:** Our study suggested that GERD was a causal factor in the development of asthma, IPF, COPD and chronic bronchitis, indicating that GERD-associated micro-aspiration of gastric contents process might play a role in the development of pulmonary fibrosis in these diseases.

**Keywords:** Causality; Chronic respiratory diseases; Gastroesophageal reflux disease; Genetic; Mendelian randomization.

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## Conflict of interest statement

The authors declare no competing interests.

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

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